

## 最終報告書

表 題：4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験

試験番号：SR15146

株式会社化合物安全性研究所

## 陳述書

表 題：4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験

試験番号：SR15146

1. 本試験は、「新規化学物質等に係る試験を実施する試験施設に関する基準について」(平成 23 年 3 月 31 日 薬食発 0331 第 8 号・平成 23・03・29 製局第 6 号・環保企発第 110331010 号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知) に従い、試験方法は「新規化学物質等に係る試験の方法について」(平成 23 年 3 月 31 日薬食発 0331 第 7 号・平成 23・03・29 製局第 5 号・環保企発第 110331009 号) ならびに「新規化学物質等に係る試験の方法について」の一部改正について (平成 24 年 4 月 2 日薬食発 0402 第 1 号・平成 24・03・28 製局第 2 号・環保企発第 120402001 号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知) に基づいて実施したものです。
2. 本試験は、試験計画書に従って実施し、試験成績の信頼性に影響を及ぼしたと思われる環境要因は認められませんでした。

株式会社化合物安全性研究所

試験責任者

2016 年 3 月 22 日

## 信頼性保証書

表題 : 4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験

試験番号 : SR15146

本試験は、株式会社化合物安全性研究所 QAU によって、下記のとおり査察された。

| 査察段階           | 査察日                                   | 試験責任者<br>への報告日 | 運営管理者<br>への報告日 |
|----------------|---------------------------------------|----------------|----------------|
| 試験計画書          | 2015年11月16日                           | 2015年11月16日    | 2015年11月16日    |
| 被験物質の受入・表示・保存  | 2015年11月16日                           | 2015年11月16日    | 2015年11月16日    |
| 試験計画書          | 2015年11月25日                           | 2015年11月30日    | 2015年11月30日    |
| 動物受入・検疫・馴化     | 2015年11月25日                           | 2015年11月30日    | 2015年11月30日    |
| 投与液の調製         | 2015年12月8日                            | 2015年12月8日     | 2015年12月8日     |
| 投与液の化学分析       | 2015年12月8日                            | 2015年12月8日     | 2015年12月8日     |
| 群分け            | 2015年12月8日                            | 2015年12月8日     | 2015年12月8日     |
| 投与             | 2015年12月9日                            | 2015年12月9日     | 2015年12月9日     |
| 一般状態観察         | 2015年12月9日                            | 2015年12月9日     | 2015年12月9日     |
| 体重測定           | 2015年12月9日                            | 2015年12月9日     | 2015年12月9日     |
| 摂餌量測定          | 2015年12月9日                            | 2015年12月9日     | 2015年12月9日     |
| 性周期検査          | 2015年12月9日                            | 2015年12月9日     | 2015年12月9日     |
| 詳細な状態観察        | 2015年12月15日                           | 2015年12月15日    | 2015年12月15日    |
| 生殖能検査(交配)      | 2015年12月22日<br>2015年12月24日            | 015年12月24日     | 015年12月24日     |
| 試験計画書変更書(No.1) | 2015年12月29日                           | 2015年12月29日    | 2015年12月29日    |
| 尿検査            | 2015年12月30日<br>2015年12月31日            | 2016年1月4日      | 2016年1月4日      |
| 機能検査           | 2016年1月4日                             | 2016年1月4日      | 2016年1月4日      |
| 採血             | 2016年1月6日                             | 2016年1月6日      | 2016年1月6日      |
| 血液学的検査         | 2016年1月6日                             | 2016年1月6日      | 2016年1月6日      |
| 剖検・器官重量測定      | 2016年1月6日                             | 2016年1月6日      | 2016年1月6日      |
| 血液化学的検査        | 2016年1月7日                             | 2016年1月7日      | 2016年1月7日      |
| 病理組織学的検査(標本作製) | 2016年1月7日<br>2016年1月13日<br>2016年1月14日 | 2016年1月14日     | 2016年1月14日     |
| 分娩および哺育状態観察    | 2016年1月14日                            | 2016年1月14日     | 2016年1月14日     |
| 新生児の剖検         | 2016年1月18日                            | 2016年1月18日     | 2016年1月18日     |
| 病理組織学的検査(鏡検)   | 2016年1月28日                            | 2016年1月28日     | 2016年1月28日     |

| 査察段階            | 査察日  | 試験責任者<br>への報告日 | 運営管理者<br>への報告日 |
|-----------------|--|----------------|----------------|
| 試験計画書変更書 (No.2) | 2016年 2月 17 日  | 2016年 2月 17 日  | 2016年 2月 17 日  |
| 生データ            | 2016年 2月 26 日<br>2016年 2月 29 日<br>2016年 3月 1 日<br>2016年 3月 2 日 | 2016年 3月 2 日   | 2016年 3月 2 日   |
| 最終報告書 (草案) : 図表 | 2016年 2月 26 日<br>2016年 2月 29 日<br>2016年 3月 1 日<br>2016年 3月 2 日 | 2016年 3月 2 日   | 2016年 3月 2 日   |
| 最終報告書 (草案) : 本文 | 2016年 2月 26 日<br>2016年 2月 29 日<br>2016年 3月 1 日<br>2016年 3月 2 日 | 2016年 3月 2 日   | 2016年 3月 2 日   |
| 最終報告書           | 2016年 3月 22 日  | 2016年 3月 22 日  | 2016年 3月 22 日  |

本試験は、「新規化学物質等に係る試験を実施する試験施設に関する基準について」(平成23年3月31日 薬食発0331第8号・平成23・03・29製局第6号・環保企発第110331010号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知)に従い実施された。

本試験は、試験計画書に従って実施され、また、本報告書には当該試験に使用した方法および手順が正確に記載されており、試験成績には当該試験の実施過程において得られた生データが正確に反映していることを確認した。

株式会社化合物安全性研究所

QAU 責任者

2016年 3月 22 日

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**表題**

4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験

**試験番号**

SR15146

**試験目的**

4-メチルベンゼン-1-スルホン酸一水和物を雌雄ラットに反復経口投与してその毒性ならびに性腺機能、交尾行動、受胎および分娩等の生殖に及ぼす毒性を検討した。

**試験実施基準および試験法ガイドライン**

**試験実施基準 (GLP)** : 「新規化学物質等に係る試験を実施する試験施設に関する基準について」(平成 23 年 3 月 31 日 薬食発 0331 第 8 号・平成 23・03・29 製局第 6 号・環保企発第 110331010 号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知)

**試験法ガイドライン** : 「新規化学物質等に係る試験の方法について」(平成 23 年 3 月 31 日 薬食発 0331 第 7 号・平成 23・03・29 製局第 5 号・環保企発第 110331009 号) ならびに「新規化学物質等に係る試験の方法について」の一部改正について(平成 24 年 4 月 2 日 薬食発 0402 第 1 号・平成 24・03・28 製局第 2 号・環保企発第 120402001 号 厚生労働省医薬食品局長・経済産業省製造産業局長・環境省総合環境政策局長連名通知)

**動物愛護**

**法規および基準等** : 「動物の愛護及び管理に関する法律」(昭和 48 年 10 月 1 日 法律第 105 号, 最終改正 平成 26 年 5 月 30 日 法律第 46 号)  
 「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」(平成 18 年 4 月 28 日 環境省告示第 88 号, 最終改正 平成 25 年 8 月 30 日 環境省告示第 84 号)  
 「動物実験に関する指針」(昭和 62 年 5 月 22 日 承認 社団法人日本実験動物学会)  
 「厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針について」(平成 27 年 2 月 20 日 科発 0220 第 1 号)

## 動物実験倫理

: 本試験は、株式会社化合物安全性研究所の動物実験倫理規定に従い、  
動物実験の必要性および苦痛の軽減等について試験施設の動物実験  
倫理委員会で審議され、試験施設の運営管理者の承認を得て実施した。

## 試験委託者

名称 : 厚生労働省 医薬・生活衛生局  
所在地 : 東京都千代田区霞が関 1-2-2 (〒100-8916)  
連絡先 : 審査管理課 化学物質安全対策室

## 試験施設

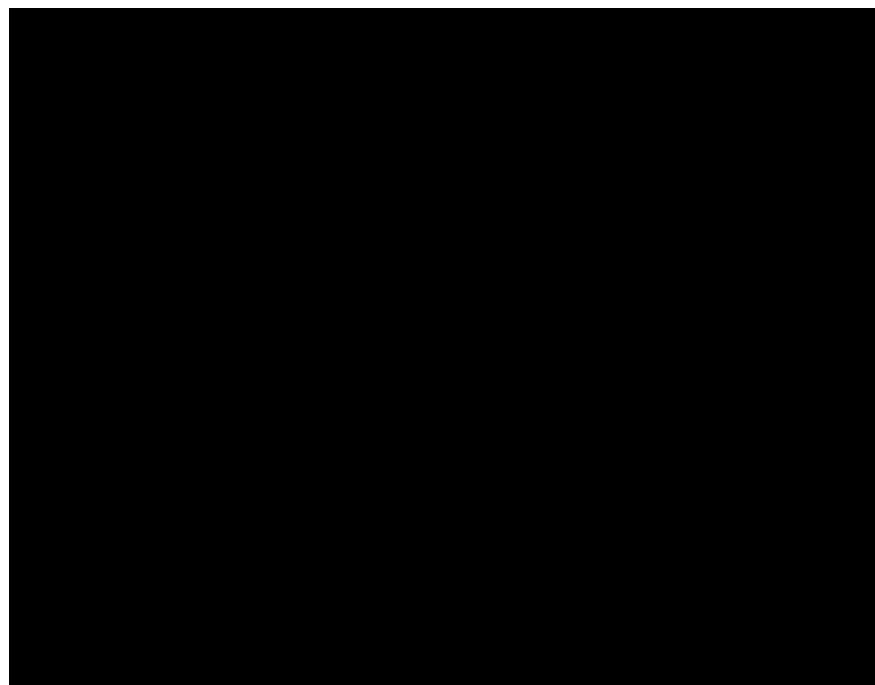
名称 : 株式会社化合物安全性研究所  
所在地 : 札幌市清田区真栄 363 番 24 (〒004-0839)  
運営管理者 : [REDACTED]

## 試験責任者

氏名 : [REDACTED]  
所属 : 株式会社化合物安全性研究所 安全性研究部

## 試験従事者およびその業務分担

被験物質管理



動物管理

検疫・馴化

投与・観察・測定

化学分析

臨床検査

病理検査

## 試験日程

試験開始日 : 2015年 11月 16日  
動物受入 : 2015年 11月 25日  
群分け : 2015年 12月 8日  
実験開始日 : 2015年 12月 9日  
投与開始 : 2015年 12月 9日  
交配開始 : 2015年 12月 22日  
雄動物およびサテライト群雌動物投与終了  
: 2016年 1月 5日  
雄動物およびサテライト群雌動物(投与終了時剖検例)投与終了時剖検  
: 2016年 1月 6日  
新生児剖検開始 : 2016年 1月 18日  
母動物剖検開始 : 2016年 1月 19日  
サテライト群雄および雌動物(回復終了時剖検例)剖検  
: 2016年 1月 20日  
実験終了日 : 2016年 2月 25日  
試験終了日 : 2016年 3月 22日

## 1 要約

4-メチルベンゼン-1-スルホン酸一水和物の0(溶媒対照, 精製水), 50, 200 および 800 mg/kg を1群雌雄各12匹のCrl:CD(SD)ラットに、雄に対しては交配前、交配期間および交配後を含む計28日間、雌に対しては交配前、交配および妊娠期間、ならびに分娩後4日までの期間経口投与し、雌雄動物への反復投与による影響、雌雄動物の生殖および新生児の発生に及ぼす影響について検討した。また、0(対照)および800 mg/kgについて、雄動物は各5匹を選抜して28日間の投与終了後14日間の回復性を検討し、雌動物は各10匹を別に設け、5匹は28日間の投与終了時に剖検し、5匹はさらに14日間の回復性についても検討した。

### 1.1 反復投与毒性

50および200 mg/kg群では、一般状態、詳細な状態観察、機能検査、体重、摂餌量、尿検査、血液学的検査、血液化学的検査、器官重量、剖検および病理組織学的検査の各検査項目に、雌雄とも被験物質投与の影響は認められなかった。

800 mg/kg群では、被験物質投与の影響として、非交配群の雌で、投与1日～3日の投与直後～約1時間の間に臨床症状（よろめき歩行、自発運動の低下）が観察され、投与3日に1例の死亡が認められた。投与4日の体重に有意な低値、投与4日および7日の摂餌量に低値傾向が認められた。投与4週の機能検査で、雄の握力に低値傾向または有意な低値が、非交配群雌の自発運動量に有意な増加が認められた。投与期間終了時の剖検では、雌雄の胃に境界縁の肥厚が認められ、病理組織学的検査では胃境界縁の扁平上皮過形成および過角化等が認められた。さらに、雌では腎臓の病理組織学的検査で尿細管の好塩基性化の発生頻度の有意な増加および憎悪化が認められた。以上の変化は回復期間中および回復終了時の検査では認められないか軽減しており、回復性を示した。

したがって、本試験条件下における4-メチルベンゼン-1-スルホン酸一水和物の反復投与毒性に関する無影響量(NOEL)および無毒性量(NOAEL)はいずれも雌雄とも200 mg/kg/dayであると考えられた。

### 1.2 生殖発生毒性

主試験群の生殖能検査および新生児の検査では、800 mg/kg群まで、いずれの項目にも被験物質投与に関連する変化はみられなかった。

したがって、本試験条件下における4-メチルベンゼン-1-スルホン酸一水和物の親動物の生殖に対する無影響量(NOEL)および無毒性量(NOAEL)ならびに新生児の発生に対する無影響量(NOEL)および無毒性量(NOAEL)はいずれも800 mg/kg/dayと考えられた。

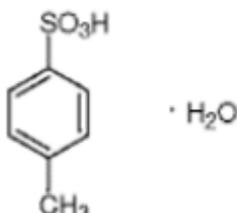
## 2 緒言

4-メチルベンゼン-1-スルホン酸一水和物の 0 (溶媒対照, 精製水), 50, 200 および 800 mg/kg を 1 群雌雄各 12 匹の Crl:CD(SD) ラットに, 雄に対しては交配前, 交配期間および交配後を含む計 28 日間, 雌に対しては交配前, 交配および妊娠期間, ならびに分娩後 4 日までの期間経口投与し, 雌雄動物への反復投与による影響, 雌雄動物の生殖および新生児の発生に及ぼす影響について検討した. また, 0(対照) および 800 mg/kg について, 雄動物は各 5 匹を選抜して 28 日間の投与終了後 14 日間の回復性を検討し, 雌動物は各 10 匹を別に設け, 5 匹は 28 日間の投与終了時に剖検し, 5 匹はさらに 14 日間の回復性についても検討した.

## 3 材料および方法

### 3.1 被験物質

|                          |                                      |
|--------------------------|--------------------------------------|
| 名称                       | : 4-メチルベンゼン-1-スルホン酸一水和物              |
| 別名 <sup>1)</sup>         | : p-トルエンスルホン酸一水和物 (PTSA Monohydrate) |
| CAS 番号                   | : 6192-52-5                          |
| 官報公示整理番号(化審法) : (3)-1901 |                                      |
| 構造式 <sup>2)</sup> :      |                                      |



|                       |   |
|-----------------------|---|
| 化学式 <sup>1)</sup>     | : C <sub>7</sub> H <sub>8</sub> O <sub>3</sub> S · H <sub>2</sub> O   |
| 分子量 <sup>2)</sup>     | : 172.20  |
| 物理化学的性質 <sup>1)</sup> | : 外観 ; 結晶 ~ 粉末, 白色 ~ ほとんど白色<br>融点 ; 106°C<br>沸点/沸騰範囲 ; 140°C/2.7kPa<br>溶解度 ; 水に可溶(67g/100mL),<br>その他の溶剤に可溶(エーテル, アルコール)<br>オクタノール/水分配係数 ; -0.62 |
| ロット番号                 | : JESNN   |
| 純度 (HPLC)             | : 100.0 area% (Annex 1-1)   |
| 製造業者                  | [REDACTED]  |
| 入手日                   | : 2015 年 8 月 24 日   |

入手量 : 500 g ×2 本 (関連試験と共に)

安定性 (非 GLP) : 関連試験を含めた試験操作終了後、残余被験物質を [REDACTED]  
 [REDACTED] に送付し純度分析を依頼した。分析の結果 (分析日 : 2016 年 2 月 13 および 16 日), 得られた純度は 100.0 area% (HPLC) および 100.3% (中和滴定) であり (Annex 1-2), 試験開始前 (分析日 : 2015 年 6 月 3 日) の純度の 100.0 area% (HPLC) および 100.2% (中和滴定) (Annex 1-1) と比べ変化はみられず、被験物質は試験期間中、安定であったことが確認された。

保存場所および保存期間 : 被験物質保存室の冷蔵室 ; 2015 年 8 月 24 日 (入手) ~ 2016 年 2 月 5 日 (特性分析用サンプル送付)

保存条件 : 冷蔵 (実測範囲 5.1 ~ 8.7°C), 気密、遮光、湿気を避ける、窒素ガスを充填。

取扱上の注意 : ゴム手袋、マスクおよび保護メガネを着用した。

サンプリング : 約 5 g を採取し、試験施設の資料保存室に保存した。

残余被験物質の処置 : 試験操作終了後、焼却処分するために、産業廃棄物として回収した。

### 3.2 媒体

名称 : 精製水「NikP」(日本薬局方精製水)

製造者 : 日医工株式会社

ロット番号 : LP160

保存条件 : 室温

取扱上の注意 : 特になし。

### 3.3 投与液の調製および化学分析

調製方法 : 投与量毎に被験物質を正確に秤量し、メートルグラスに移し入れた。所定の濃度となるように媒体を加えてメスアップし、スターラーを用いて溶解させた。

調製頻度 : 投与用の調製液は 3 ~ 7 日の間隔で調製し、7 日以内に使用した。

保存場所および保存期間 : 被験物質保存室の冷蔵庫 ; 2015 年 11 月 30 日 (安定性分析用調製) ~ 2016 年 1 月 31 日 (最終投与)

保存条件 : 冷蔵 (実測範囲 2.4 ~ 5.4°C), 遮光、気密

調製上の注意 : 被験物質はクリーンベンチ内で取扱い、調製の際にはマスク、手袋等を着用し、吸入、眼、皮膚および衣類等との接触を避けた。

- 残余投与液の処置 : 残余の投与液は、焼却処分するために産業廃棄物として回収した。
- 投与液の安定性の確認 : 5 および 80 mg/mL の濃度の調製液について、冷蔵保存 7 日（調製日を 0 日として起算）+ 室温 4 時間の安定性を確認した。安定性分析の結果では、5 および 80 mg/mL 調製液は、残存率がそれぞれ 99.8% および 99.6% であり、判定基準の 100±10.0% 以内であることが確認された（Annex 2-1）。
- 投与液の濃度確認 : 被験物質の全濃度に関する投与液中の濃度を、初回および全群の投与に使用する最終回調製時の調製液について確認した。分析結果では、5, 20 および 80 mg/mL 投与液の含有率はそれぞれ初回で 100.2%, 100.5% および 97.6%, 最終回で 99.2%, 98.5% および 97.4% であり、相対標準偏差はそれぞれ初回で 0.8%, 0.5% および 0.6%, 最終回で 1.3%, 0.5% および 0.8% であり、判定基準の 100±5.0% 以内および 5.0% 以下であることが確認された（Annex 2-2 および 2-3）。
- 濃度分析方法 : Annex 2-4 に示す。

### 3.4 試験系

- 種・系統 : ラット, Crl:CD(SD)
- 微生物統御 : SPF
- 生産業者 : 日本チャールス・リバー株式会社
- 微生物モニタリング : 動物生産業者よりデータを入手した。
- 動物選定理由 : ラットはこの種の試験で通常用いられている動物種であり、繁殖成績が安定していることと当研究所における背景対照データが利用できることからこの系統を選定した。
- 受入動物数 : 雄 50 匹, 雌 70 匹
- 受入動物週齢 : 雌雄とも 8 週齢
- 出荷体重基準 : 雄 240 ~ 330 g, 雌 160 ~ 230 g
- 受入時体重範囲 : 雄 273 ~ 308 g, 雌 180 ~ 223 g
- 投与開始時週齢 : 雌雄とも 10 週齢
- 群数 : 雄 6 群, 雌 8 群（主試験群 雌雄各 4 群, サテライト群 雄 2 群, 雌 非交配群 4 群）
- 各群動物数 : 主試験群 雌雄各 12 匹, サテライト群 雌雄各 5 匹

### 3.5 検疫および馴化

|       |   |
|-------|---|
| 期間    | : 検疫期間は受入日（検疫 1 日）から検疫 6 日までの期間。<br>馴化期間は検疫期間を含めた群分け日までの期間。                         |
| 方法    | : 一般状態を 1 日 1 回観察し、体重を受入時、検疫 6 日および群分け日に測定した。馴化期間中の一般状態および体重には、いずれの動物にも異常は認められなかった。 |
| 性周期検査 | : 雌動物について、性周期検査を膣垢スメア塗抹法により群分け日までの 9 日間に行った。検査の結果、性周期の異常が 2 例に認められた。                |

### 3.6 群分け

馴化期間中に実施した一般状態観察および体重測定、さらに雌については性周期検査の結果、性周期の異常を示す 2 例を除いたすべての動物を群分けに用いた。コンピュータシステム (MiTOX, 三井造船システム技研株式会社) を使用し、群分け日（投与開始前日）の体重に基づいて層化無作為抽出法により各群の平均体重が均一になるように群分けを行った。選抜した動物の体重範囲は、雄で 357 ~ 429 g、雌で 226 ~ 282 g であり、平均体重（雄 393.1 g、雌 248.3 g）の ± 20% 以内であった。群分けから外れた動物は、投与開始日に試験から除外し、標準操作手順書に従って取り扱った。

### 3.7 動物およびケージの識別

|       |   |
|-------|---|
| 動物    | : 群分け前は受入時に油性フェルトペンで尾部に印を付け、個体識別を行った。<br>群分け後は耳介に動物番号を入墨し、個体識別を行った。   |
| 飼育ケージ | : 群分け前は試験 No., 識別 No., 性別, ケージ No. および種 / 系統を印字したラベルを各ケージの前面に標示した。<br>群分け後は試験 No., 動物 No., 性別, 被験物質, 用量（経路）および種 / 系統を印字したラベルを各ケージの前面に標示した。交尾成立雌動物は上記と同様の項目を記載した新たなラベルに交換し、交尾成立日ならびに交尾成立日毎のグループ名を明記して表示した。分娩終了した雌は群分け後のラベルに交換して哺育 0 日ならびに哺育 0 日毎のグループ名を明記した。 |

### 3.8 動物飼育

#### 3.8.1 飼育環境

|       |   |
|-------|---|
| 飼育室番号 | : 308 号室  |
| 温度・湿度 | : $22 \pm 3^{\circ}\text{C}$ (実測範囲 $20 \sim 24^{\circ}\text{C}$ ), $50 \pm 20\%$ (実測範囲 $37 \sim 53\%$ ) |
| 換気回数  | : 10 ~ 15 回/時間  |
| 照明時間  | : 人工照明 12 時間 (8:00 ~ 20:00)   |

#### 3.8.2 飼育器材および飼育方法

|   |   |
|---|---|
| ケージの種類  | : ブラケット式金属製金網床ケージ (260W×380D×180H, mm)<br>ただし、交尾成立雌動物については妊娠 17 日から哺育 4 日まで同ケージの金網床を小型受皿に代えて実験動物用床敷 (ホワイトフレク, 日本チャールス・リバー株式会社) を使用した. |
| 1 ケージあたりの収容動物数：検疫および馴化期間中は 2 匹ずつ、群分け後は 1 匹、交配期間中は雌雄各 1 匹、分娩後は 1 腹とした. |   |
| ケージ交換   | : 群分け時および投与 14 日に実施した. ただし、交尾成立雌動物については妊娠 0 日および 14 日に実施した. 回復終了時剖検例は回復 1 日に実施した.   |
| 受皿交換  | : 週 2 回実施した.  |
| 小型受皿の交換   | : 妊娠 20 日に実施した.   |
| 給餌器交換   | : 群分け時および投与 14 日に実施した. ただし、交尾成立雌動物については妊娠 0 日および 14 日に実施した. 回復終了時剖検例は回復 1 日に実施した.   |
| 自動給水装置の水抜き  | : 週 1 回実施した.  |
| 給水器   | : 尿検査時にのみ使用した.  |
| 室内の清掃   | : 1 日 1 回実施した.  |
| 室内の消毒   | : 塩素系消毒薬およびヨウ素系消毒薬を 1 週間単位で交互に使用する清拭消毒を 1 日 1 回実施した.  |

#### 3.8.3 飼料

|          |  |
|----------|--|
| 種類・名称    | : 固型飼料, CRF-1                                    |
| ロット番号    | : 151008, 151112                                 |
| 製造業者     | : オリエンタル酵母工業株式会社                                 |
| 給餌方法     | : 金属製給餌器を用いて自由に摂取させた.<br>ただし、剖検前日の夕刻からは全例を絶食させた. |
| 汚染物質等の確認 | : 試験に悪影響を及ぼす恐れのある汚染物質等の有無を使用した各ロット               |

トの飼料について分析した。分析はユーロフィン・フードアンドプロダクト・テスティング株式会社（分析報告書：No. AR-15-JP-010462-01, AR-15-JP-014663-01）および飼料製造業者（分析試験報告書：No. 15G03-156, 15G03-173）が行い、分析データを飼料製造業者からロット毎に入手した。分析項目と許容値は株式会社化合物安全性研究所の標準操作手順書に準拠した。分析の結果、いずれの項目にも許容値を超える値は認められなかった。

### 3.8.4 飲料水

|          |  |
|----------|--|
| 種類       | : 札幌市水道水   |
| 給水方法     | : 自動給水装置あるいは給水器を用いて自由に摂取させた。   |
| 汚染物質等の確認 | : 試験に悪影響を及ぼす恐れのある汚染物質等について、2015年7月1日および2016年1月27日に当該飼育室と同系統配管の最末端（306号室）から試料を採取して確認した。分析は日本衛生株式会社（水質検査結果表：No. A271290, A275601）が行い、分析データを入手した。分析項目と許容値は株式会社化合物安全性研究所の標準操作手順書に準拠した。分析の結果、いずれの項目にも許容値を超える値は認められなかった。 |

## 3.9 被験物質の投与

### 3.9.1 投与量の設定

|      |  |
|------|--|
| 投与量  | : 0(対照), 50, 200 および 800 mg/kg/day   |
| 設定理由 | : 先に実施した予備試験（SR15146P <sup>3)</sup> （投与量 0, 30, 100, 300 および 1000 mg/kg/day, 雌雄各 3 匹/群, 14 日間反復経口投与）の結果、1000 mg/kg 群の雌で、投与 1～5 日の投与後によろめき歩行、横臥位/腹臥位/自発運動の低下、体温低下、被毛汚染等が観察され、投与 4 日の体重および摂餌量に低値が認められた。血液学的検査では、雌で赤血球数、HGB および HCT に低値が認められた。さらに雌の 1 例で剖検時に腎臓の褪色、血液化学的検査で尿素窒素およびクレアチニンの著しい高値が認められた。剖検では雌で胃に境界縁肥厚が認められ、器官重量では雄で腎臓、雌で肝臓重量の高値が認められた。300 mg/kg 以下の投与群では、被験物質投与に関連する変化は認められなかった。以上より、1000 mg/kg/day は投与期間の延長を考慮すると雌への毒性が強すぎると考えられることから、本試験では、800 mg/kg/day を高 |

用量とし、以下公比4として200および50 mg/kg/dayをそれぞれ中用量および低用量に設定した。そのほかに媒体のみを同様の方法で投与する対照群を設けた。

### 3.9.2 試験群の構成

試験群の構成と各群の動物番号は以下の通りとした。

| 試験群            | 投与量     | 濃度      | 投与容量    | 動物数(動物番号)  |                              |    |
|----------------|---------|---------|---------|--|------------------------------|----|
|                | (mg/kg) | (mg/mL) | (mL/kg) | 雄  | 雌                            | 識別 |
| <主試験群>         |         |         |         |  |                              |    |
| 対照             | 0       | 0       | 10.0    | 12 (10101~10112)   | 12 (50151~50162)             | 白  |
| 低用量            | 50      | 5       | 10.0    | 12 (10201~10212)   | 12 (50251~50262)             | 緑  |
| 中用量            | 200     | 20      | 10.0    | 12 (10301~10312)   | 12 (50351~50362)             | 青  |
| 高用量            | 800     | 80      | 10.0    | 12 (10401~10412)   | 12 (50451~50462)             | 赤  |
| <サテライト群>       |         |         |         |  |                              |    |
| 対照 (投与終了時剖検例)  | 0       | 0       | 10.0    |  | 5 (50551~50555) <sup>b</sup> | 白  |
| (回復終了時剖検例)     | 0       | 0       | 10.0    | 5 (10103, 10104,<br>10105, 10106<br>10111) <sup>a</sup>  | 5 (50556~50560) <sup>b</sup> | 白  |
| 高用量 (投与終了時剖検例) | 800     | 80      | 10.0    |  | 5 (50651~50655) <sup>b</sup> | 赤  |
| (回復終了時剖検例)     | 800     | 80      | 10.0    | 5 (10402, 10403,<br>10407, 10409,<br>10411) <sup>a</sup> | 5 (50656~50660) <sup>b</sup> | 赤  |

対照群には、他の群と同様の方法で媒体のみを投与した。

a : 主試験群から投与 21 日の体重に基づいて、各群の体重の平均値に近似するように、各群から 5 匹ずつ選抜した。ただし、交配中の雄動物は選抜から除いた。

b：非交配群

### 3.9.3 投与

投与方法および投与経路：ディスポーザブル胃ゾンデおよびディスポーザブルシリンジを用いて強制的に胃内に経口投与した。

投与回数 : 1 日 1 回, 連日投与した.

投与時刻 : 9:02 ~ 11:52

投与期間 : 雄 ; 交配 14 日前より 28 日間

雌；交配前 14 日間および交尾成立までの交配期間、さらに交尾成立例は妊娠期間および分娩後 4 日（哺育 0 日を分娩後 0 日として起算）までの期間

サテライト群については28日間

回復期間 : 投与期間終了後 14 日間

投与液量 : 各個体の投与液量は、投与日に最も近い測定日の体重に基づいて算出した。

投与方法、投与経路、投与回数および投与期間の選定理由 :

試験法ガイドラインに準拠して選定した。

### 3.10 観察、測定および検査項目

投与開始日を投与 1 日 (Day 1)、投与 28 日の翌日を回復 1 日 (Recovery Day 1) と起算し、雄動物およびサテライト群の剖検日は投与 28 日の翌日 (Day 29) および回復 14 日の翌日 (Recovery Day 15) とした。主試験群の雌動物は、交尾成立日を妊娠 0 日、分娩終了日を哺育 0 日と規定した。

#### 3.10.1 反復投与毒性

##### 3.10.1.1 一般状態観察

例数 : 全例  
 期間 : 投与 1 日から剖検日まで  
 頻度 : 投与期間中は投与前および投与後の 1 日 2 回、回復期間中は午前および午後の 1 日 2 回、剖検日は午前中に 1 回観察した。  
 観察方法 : 個々の動物の生死、外観、行動等について観察した。異常が認められる場合は、その症状ならびに症状の発現および消失について記録した。死亡した動物は発見後速やかに剖検した。

##### 3.10.1.2 詳細な状態観察

例数 : 全例  
 時期 : 投与開始前ならびに投与 7, 14, 21 および 28 日  
         主試験群の雌については、上記に加えて投与 35 および 42 日  
         回復期間中は、回復 7 および 14 日  
 観察方法 : あらかじめ定めたスコアリング基準を用いてスコア化した観察結果を記録した。

観察項目およびその方法 :

- [1] 体位・姿勢、呼吸状態、振戦・痙攣、常同行動 (回転・旋回)、異常行動 (自咬) をケージ外から観察した。
- [2] 取り出し易さ、取扱い易さ、筋収縮性、立毛、被毛の状態、皮膚、眼・眼球および粘膜の外観、瞳孔径、流涙、流涎、その他分泌物の有無について、ケージから取り出す時に観察した。
- [3] 歩行、運動協調性、環境刺激に対する反応、探索行動 (匂嗅ぎ・

立上り), 排泄状態(排尿・排糞), 常同行動(身づくろい・くびぶり), 異常行動(後ずさり・異常発声), 攻撃性について, オープンフィールド内で観察した.

### 3.10.1.3 機能検査

- 例数 : 各群の投与 21 日の体重の平均値に近似するように選抜した雄の各群 5 例およびサテライト群(回復終了時剖検例)の雌ならびに主試験群の雌の分娩日の早いものから順に選抜した各群 5 例.
- 時期 : 主試験群の雄およびサテライト群の雌は, 投与 4 週(投与 27 日)に実施した. 投与 4 週の検査の結果, 高用量群で雄の握力および雌の自発運動量に対照群と比較して有意な差が認められたため, 回復 2 週(回復 8 日)にも検査を実施した.  
主試験群の雌は哺育 4 日に実施した.
- 観察 / 測定方法 : あらかじめ定めたスコアリング基準を用いてスコア化した観察結果あるいは測定機器による測定値を記録した.
- 観察項目およびその方法 :
- [1] 刺激に対する感覚運動反応 : 検査台上で以下を観察した.  
視覚刺激, 触覚刺激, 聴覚刺激, 痛覚刺激, 固有受容器刺激, 空中正向反射
  - [2] 握力 : CPU ゲージ(アイコーエンジニアリング株式会社)を用いて前肢および後肢について各 3 回測定し, 1 g 単位で記録した.
  - [3] 自発運動量 : 自発運動量測定装置(スーパー・メックスおよび CompAct, 室町機械株式会社)を用いて, 上記に引き続き, 10 分間隔で 1 時間測定した.

### 3.10.1.4 体重測定

- 例数 : 全例
- 測定日 : 雄およびサテライト群の雌は, 投与 1, 4, 7, 14, 21 および 28 日の投与前, 回復 1, 7 および 14 日ならびに剖検日.  
主試験群の雌は, 投与 1, 4, 7, 14 日の投与前, 妊娠 0, 7, 14 および 20 日の投与前, 哺育 0 および 4 日の投与前ならびに分娩後 5 日の剖検日. ただし, 分娩遅延例は妊娠 26 日(剖検日)に, 交配期間が 2 週間に亘った動物については, 投与 21 日にも測定した.  
死亡例については, 死亡発見時の体重を記録した.
- 測定方法 : 電子式上皿天秤(GX-2000, 株式会社 エー・アンド・デイ)を用いて

測定した。

体重増加量 : 以下の式により算出した。

<雄およびサテライト群の雌>

投与期間 :

体重増加量 (g) = 投与 28 日体重 (g) - 投与 1 日体重 (g)

回復期間 :

体重増加量 (g) = 回復 14 日体重 (g) - 回復 1 日体重 (g)

<主試験群の雌>

妊娠前投与期間 :

体重増加量 (g) = 投与 14 日体重 (g) - 投与 1 日体重 (g)

妊娠期間 :

体重増加量 (g) = 妊娠 20 日体重 (g) - 妊娠 0 日体重 (g)

哺育期間 :

体重増加量 (g) = 哺育 4 日体重 (g) - 哺育 0 日体重 (g)

### 3.10.1.5 摂餌量測定

例数 : 全例

測定日 : 雌雄とも交配中の週および剖検日を除き、体重測定と同じ日に実施した。

測定方法 : 電子式上皿天秤 (GX-2000, 株式会社 エー・アンド・デイ) を用いて測定した。

投与 1 日または回復 1 日に適当量を測定後ケージ毎に給餌し、その後は測定日に残餌量および給餌量を測定した。ただし、最終回の測定は残餌量のみとした。主試験群の雌については、妊娠 20 日および哺育 4 日は残餌量のみ、妊娠 0 日および哺育 0 日は給餌量のみ測定した。次に示す式により、摂餌量 (g/rat/day) を算出した。

$$\text{摂餌量 (g/rat/day)} = \frac{\text{給餌量 (g/rat)} - \text{残餌量 (g/rat)}}{\text{測定日間の日数 (day)}}$$

### 3.10.1.6 尿検査

例数 : 雄は機能検査と同一の各群 5 例について、雌はサテライト群の回復終了時剖検例

時期 : 投与 4 週 (投与 22~23 日) および回復 2 週 (回復 8~9 日)。

採尿方法 : 非絶食下でラット用代謝ケージ (KN-646, B-1 型、夏目製作所) を用

いて採尿し、投与直後から約3時間の蓄尿で[1]～[9]を、また約21時間の蓄尿で[10]、[11]を実施した。[9]沈渣については、1500回転/分で5分間遠心分離後に検査を行った。採取した尿は検査終了後廃棄した。

#### 検査項目および検査方法：

|      |                         |                 |
|------|-------------------------|-----------------|
| [1]  | pH                      | 試験紙法            |
| [2]  | 蛋白 (Protein)            | 試験紙法            |
| [3]  | 糖 (Glucose)             | 試験紙法            |
| [4]  | ケトン体 (Ketone body)      | 試験紙法            |
| [5]  | ウロビリノーゲン (Urobilinogen) | 試験紙法            |
| [6]  | ビリルビン (Bilirubin)       | 試験紙法            |
| [7]  | 潜血反応 (Occult blood)     | 試験紙法            |
| [8]  | 色調 (Color)              | 肉眼観察            |
| [9]  | 尿沈渣 (Urinary sediments) | Sternheimer 染色法 |
| [10] | 尿量 (Urine Volume)       | 容量測定            |
| [11] | 比重 (Specific gravity)   | 屈折計法            |

[1]～[7] マルティスティックス、シーメンスヘルスケア・ダイアグノスティクス株式会社

[9] 顕微鏡 BH-2, BH2-MDO、オリンパス光学工業株式会社

[11] 尿比重屈折計ユリコン-S、株式会社アタゴ

#### 3.10.1.7 血液学的検査

例数 : 各群5例（主試験群の雄は機能検査に用いた動物以外から動物番号の若い順に選抜した。主試験群の雌は機能検査と同一例、サテライト群は全例）

時期 : 剖検時 [主試験群の雄およびサテライト群の雌（投与終了時剖検例）は投与28日の翌日、主試験群の雌は分娩後5日、サテライト群の雄および雌（回復終了時剖検例）は回復14日の翌日] に採血した。

検査方法 : 夕刻からの一晩の絶食下（16～22時間）でラットをペントバルビタールナトリウム麻酔（腹腔内）し、腹部大動脈より採血した。検査項目のうち[1]～[10]についてはEDTA・2K（ベノジェクトII真空採血管、テルモ株式会社）で処理した血液約1mLを用い、[11]、[12]については3.8%クエン酸ナトリウムで処理した血液約2mLを3500回転/分で10分間遠心分離して得られた血漿を用いた。得られた血液および血漿は検査終了後廃棄した。全例の白血球分画が得られたため、白血球塗抹標本は作製しなかった。

#### 検査項目および検査方法：

|     |                |         |
|-----|----------------|---------|
| [1] | 赤血球数 (RBC)     | 電気抵抗検出法 |
| [2] | ヘマトクリット値 (HCT) | 電気抵抗検出法 |

|      |  |               |
|------|--|---------------|
| [3]  | ヘモグロビン濃度 (HGB)                         | SLSヘモグロビン法    |
| [4]  | 平均赤血球容積 (MCV)                          | RBC, HCT値より算出 |
| [5]  | 平均赤血球ヘモグロビン量 (MCH)                     | RBC, HGB値より算出 |
| [6]  | 平均赤血球ヘモグロビン濃度 (MCHC)                   | HCT, HGB値より算出 |
| [7]  | 血小板数 (Platelet)                        | 電気抵抗検出法       |
| [8]  | 網赤血球数 (Reticulocyte)                   | フローサイトメトリー法   |
| [9]  | 白血球数 (WBC)                             | フローサイトメトリー法   |
| [10] | 白血球分画 (Differential count of WBC)      | フローサイトメトリー法   |
| 1    | 好中球 (Neutrophil, $10^2/\mu\text{L}$ )  |               |
| 2    | 好酸球 (Eosinophil, $10^2/\mu\text{L}$ )  |               |
| 3    | 好塩基球 (Basophil, $10^2/\mu\text{L}$ )   |               |
| 4    | 単球 (Monocyte, $10^2/\mu\text{L}$ )     |               |
| 5    | リンパ球 (Lymphocyte, $10^2/\mu\text{L}$ ) |               |
| [11] | プロトロンビン時間 (PT)                         | トロンボプラスチン法    |
| [12] | 活性化部分トロンボプラスチン時間 (APTT)                | エラジン酸法        |

[1] ~ [10] 自動血球分析装置 XT-2000 iV, シスメックス株式会社

[11], [12] 全自動血液凝固測定装置 CA-620, シスメックス株式会社

### 3.10.1.8 血液化学的検査

例数 : 血液学的検査と同一の各群 5 例

時期 : 割検時に採血した。

検査方法 : 夕刻からの一晩の絶食下 (16 ~ 22 時間) でラットをペントバルビタールナトリウム麻酔 (腹腔内) し、腹部大動脈より採血した。検査項目のうち [1], [5] については血液 1 mLあたりヘパリンナトリウム (ヘパリンナトリウム注 N「AY」, 1000 単位/mL, エイワイファーマ株式会社) 約 20 単位で処理後、3500 回転/分で 10 分間の遠心分離で得られた血漿を用いて検査した。他の項目については分離剤入り試験管 (セパクリーン A, 栄研器材株式会社) に血液を採取し、3500 回転/分で 10 分間の遠心分離で得られた血清を用いて検査した。また、血清の一部を甲状腺機能に関連するホルモン (TSH, T3 および T4) 測定用としてポリプロピレン製チューブ 4 本に約 150  $\mu\text{L}$  ずつ分注して凍結保存 (-80°C 設定) した。しかし、病理検査において下垂体-甲状腺系への影響が認められなかったため、測定は実施せず、標本は廃棄した。検査終了後の血漿および血清は、-20°C 以下で凍結保存し、試験終了日までに廃棄した。

検査項目および検査方法 :

|     |     |        |
|-----|-----|--------|
| [1] | AST | JSCC 法 |
| [2] | ALT | JSCC 法 |

|      |   |   |
|------|---|---|
| [3]  | アルカリホスファターゼ (ALP)                       | JSCC 法                                  |
| [4]  | $\gamma$ -GTP                           | L- $\gamma$ -グルタミル-3-カルボキシ-4-ニトロアニリド基質法 |
| [5]  | グルコース (Glucose)                         | ヘキソキナーゼ法                                |
| [6]  | 総コレステロール (T-Chol)                       | 酵素法                                     |
| [7]  | トリグリセリド (TG)                            | 遊離グリセロール消去法                             |
| [8]  | 総ビリルビン (T-Bil)                          | 酵素法                                     |
| [9]  | 総胆汁酸 (TBA)                              | 酵素サイクリング法                               |
| [10] | 尿素窒素 (UN)                               | ウレアーゼ・LED 法                             |
| [11] | クレアチニン (Crea)                           | 酵素法                                     |
| [12] | ナトリウム (Na)                              | イオン選択電極 (ISE) 法                         |
| [13] | カリウム (K)                                | イオン選択電極 (ISE) 法                         |
| [14] | クロール (Cl)                               | イオン選択電極 (ISE) 法                         |
| [15] | カルシウム (Ca)                              | OCPC 法                                  |
| [16] | 無機リン (IP)                               | Fiske-Subba Row 法                       |
| [17] | 総蛋白 (TP)                                | ビウレット法                                  |
| [18] | A/G 比 (A/G ratio)                       | 蛋白分画より算出                                |
| [19] | アルブミン (Albumin)                         | 総蛋白と蛋白分画より算出                            |
| [20] | 蛋白分画 (Protein fraction)                 | セルロースアセテート膜電気泳動法                        |
|      | 1 アルブミン (Albumin, %)                    |   |
|      | 2 $\alpha_1$ -グロブリン ( $\alpha_1$ -G, %) |   |
|      | 3 $\alpha_2$ -グロブリン ( $\alpha_2$ -G, %) |   |
|      | 4 $\beta$ -グロブリン ( $\beta$ -G, %)       |   |
|      | 5 $\gamma$ -グロブリン ( $\gamma$ -G, %)     |   |

[1] ~ [17] 自動分析装置 7080 形, 株式会社日立ハイテクノロジーズ

[18] ~ [20] 自動電気泳動装置 AES320, 三島オリンパス株式会社

### 3.10.1.9 病理検査

#### 3.10.1.9.1 剖検

|      |  |
|------|--|
| 例数   | : 全例   |
| 時期   | : 主試験群の雄およびサテライト群の雌 (投与終了時剖検例) は投与 28 日の翌日, 主試験群の雌は分娩後 5 日 (哺育 4 日の翌日), サテライト群の雄および雌 (回復終了時剖検例) は回復 14 日の翌日に剖検した. ただし, 分娩遅延例は妊娠 26 日に, 哺育 3 日に哺育児が全て死亡した例は分娩後 5 日に実施した. 死亡例は発見後速やかに実施した. |
| 検査方法 | : 体外表を観察し, ペントバルビタールナトリウムの腹腔内投与による麻酔下で, 血液検査実施例については腹部大動脈より採血後, 放血により安樂死させ, 全身の器官・組織を肉眼的に観察した. また, 以下の器官・組織を 10% 中性緩衝ホルマリン液に固定・保存した. なお, 眼球およびハーダー腺はデビッドソン液で固定・保存し, 精巣および                |

精巢上体はブアン液で固定、70%エタノールに保存した。肺については固定液を注入後浸漬固定した。左右のある器官については、左右とも固定・保存した。主試験群雌では、妊娠黄体数および着床数を数えた。

- 性周期の確認 : サテライト群の雌の死亡例を除く全例について剖検日の剖検前に膣垢を採取し、ギムザ染色を施して、光学顕微鏡下で観察して性周期段階を確認した。このデータは器官重量または病理組織学的評価の補助とした。
- 器官・組織名 : 脳（大脳、小脳および脳橋）、脊髄、下垂体、胸腺、甲状腺、上皮小体、副腎、脾臓、心臓、食道、胃、肝臓、胰臓、頸下腺、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、気管、肺、腎臓、膀胱、精巢、精巢上体、前立腺、精嚢（凝固腺含む）、卵巣、子宮（角部および頸部）、膣、眼球およびハーダー腺、乳腺（雌のみ、右腹部）、大腿骨（骨髓を含む、右）、腸間膜リンパ節、下頸リンパ節、骨格筋（腓腹筋、右）および坐骨神経。

### 3.10.1.9.2 器官重量測定

- 例数 : 途中死亡例を除く全例
- 時期 : 剖検時
- 測定方法 : 電子式上皿天秤（GR-200、株式会社 エー・アンド・デイ）を用いて、以下の器官の重量を測定した。なお、左右のある器官は左右合せて測定した。
- 器官・組織名 : 脳、心臓、肝臓、腎臓、精巢、精巢上体、精嚢（凝固腺含む）；以上 (g) 下垂体、甲状腺（上皮小体含む）、脾臓、胸腺、副腎、前立腺、卵巣、子宮；以上 (mg)
- 相対重量の算出 : 絶対重量と剖検日に測定した体重から相対重量を算出した。

$$\text{相対重量 (g/100 g または mg/100 g)} = \frac{\text{絶対重量 (g または mg)}}{\text{剖検日体重 (g)}} \times 100$$

### 3.10.1.9.3 病理組織学的検査

- 例数 : 主試験群の雌雄およびサテライト群の雌（投与終了時剖検例）は、剖検時に固定・保存した対照群および高用量群の全器官・組織について標本作製を実施し、全例について鏡検した。また、死亡例についても鏡検した。鏡検の結果、高用量群の雌雄で胃に、雌で腎臓に被験物質投与の影響と考えられる変化が認められたため、主試験群の低用量群

および中用量群、回復終了時剖検例について雌雄の胃および雌の腎臓の病理組織学的検査を実施した。

検査方法 : パラフィン包埋後薄切し、ヘマトキシリン・エオジン染色標本を作製して鏡検した。

### 3.10.2 生殖発生毒性

#### 3.10.2.1 性周期検査

例数 : 主試験群の雌の全例

期間 : 投与開始日から交尾成立まで。

方法 : ギムザ染色による膣垢塗抹標本を作製し、光学顕微鏡下で性周期段階を観察した。

判定 : 性周期の各段階（発情前期、発情期、発情後期および発情間期）を4日から6日の間隔で繰り返すものを正常とした。  
投与1日から投与14日までの14日間について発情期間隔、発情回数および性周期異常の動物数を算出した。

#### 3.10.2.2 生殖能検査

例数 : 主試験群の雌雄の全例

時期・方法 : 投与14日を交配開始日、交配開始日の翌日を交配1日とし、交配開始日の夕刻から、同試験群内の雌雄1対を交尾が確認されるまで14日間を限度として連続同居させた。

交配組み合せ : 同一群の動物番号末尾が同一の動物を一対とした。

交尾成立の確認方法 : 膣内または受皿上に落下した膣栓、あるいは膣垢スメア標本中の精子確認により判定した。いずれかが認められた日を妊娠0日とした。同居開始から交尾成立までの所要日数を計数した。  
次式から群毎に交尾率を算出した。

$$\text{交尾率 (Copulation index, \%)} = \frac{\text{交尾成立動物数}}{\text{同居動物数}} \times 100$$

受胎能 : 妊娠の確認を分娩の有無および剖検時に子宮内の着床痕の有無により行った。No. 50160およびNo. 50456については、剖検時に子宮内の着床痕が確認されなかつたため不妊と判断した。  
次式から群毎に受胎率を算出した。

$$\text{受胎率 (Fertility index, \%)} = \frac{\text{受胎動物数}}{\text{交尾成立動物数}} \times 100$$

### 3.10.2.3 分娩および哺育状態観察

- 例数 : 交尾成立した雌の全例
- 分娩観察 : 交尾が確認された雌動物は全例自然分娩させた。  
分娩状態を妊娠 21 日から 25 日まで、毎日少なくとも 3 回 (9 : 00, 13 : 00 および 17 : 00) 観察した。
- 分娩終了の確認 : 9 : 00 に母動物が児を巣の中に集めて腹の下に抱え込んでいるのが観察された場合に分娩終了とし、その日を哺育 0 日（生後 0 日）とした。  
1 匹以上の生存児を出産したものを正常出産とした。  
次式から群毎に出産率を算出した。
- $$\text{出産率 (Gestation index, \%)} = \frac{\text{正常出産雌数}}{\text{妊娠雌数}} \times 100$$
- 妊娠期間の算出 : 妊娠 0 日から哺育 0 日までの期間の日数を計数した。
- 着床率の算出 : 剖検時に各雌の子宮内の着床痕および卵巣の妊娠黄体数を計数した。  
次式から腹毎に着床率を算出した。
- $$\text{着床率 (Implantation index, \%)} = \frac{\text{着床数}}{\text{黄体数}} \times 100$$
- 出産児の観察 : 生後 0 日のすべての出産児について生死を確認し、外表を観察した。  
腹毎に生存児数と死亡児数とを計数し、それらの合計を出産児数とした。次式から腹毎に出生率および生存児の外表異常児出現率を算出した。
- $$\text{出生率 (Birth index, \%)} = \frac{\text{生後 0 日の生存児数}}{\text{着床数}} \times 100$$
- $$\text{外表異常児出現率} (\%) = (\text{外表異常児数} / \text{出産生児数}) \times 100$$
- $$\text{外表異常児を持つ腹の頻度} = \text{外表異常児を持つ腹数} / \text{出産動物数}$$
- 出産児の性比の算出 : 生後 0 および 4 日に個々の児動物の性を肛門と生殖突起の間の長さで判定した。死亡児を含めない生後 0 日の生存児を対象として群毎に以下を算出した。
- $$\text{生後 0 日の生存児の性比 (Sex ratio, \%)} = \frac{\text{雄生存児数}}{\text{雄生存児数} + \text{雌生存児数}} \times 100$$

哺育 4 日の哺育率の算出：次式から群毎に算出した。

$$\text{哺育率 (Nursing index, \%)} = \frac{\text{哺育 4 日に生存児を持つ雌数}}{\text{生児出産雌数}} \times 100$$

### 3.10.2.4 新生児の一般状態観察

- 例数 : 全例
- 頻度 : 1回／日
- 期間 : 生後0日から生後4日(剖検日)までとした。
- 観察方法 : 生存または死亡の確認、一般状態を観察した。  
死亡例および途中安楽死例は発見後速やかに剖検し、Whole bodyを  
10%中性緩衝ホルマリン液で固定・保存した。
- 新生児生存率の算出 : 生後0日および4日の新生児生存率を次式から腹毎に算出した。

$$\text{生後0日の生存率 (Viability index, %)} = \frac{\text{生後0日の生存児数}}{\text{出産児数}} \times 100$$

$$\text{生後4日の生存率 (Viability index, %)} = \frac{\text{生後4日の生存児数}}{\text{生後0日の生存児数}} \times 100$$

### 3.10.2.5 新生児の体重測定

- 例数・時期 : 生存児全例について、生後0および4日に実施した。
- 測定方法 : 電子式上皿天秤(GX-2000、株式会社エー・アンド・ディ)を用いて  
個体別に測定し、0.1gまで記録した。  
雌雄毎に腹当たりの平均体重を求めた。

### 3.10.2.6 新生児の剖検

- 時期・例数 : 生後4日に全例について実施した。ただし、生後0日に母動物が死亡  
した腹は、その日に安楽死させて剖検した。
- 検査方法 : 体外表(口腔内を含む)を観察し、ペントバルビタールナトリウム過  
剰投与(腹腔内)により安楽死させ、全身の器官・組織を肉眼的に観察  
した。

## 3.11 統計学的方法

コンピュータシステム(MiTOX)を用いて実施した。  
主試験群における握力(3回の平均)、自発運動量、体重、体重増加量、摂餌量、尿量、血液  
学的検査、血液化学的検査、器官の絶対重量および相対重量、発情期間隔、発情回数、交尾所  
要日数および着床数、出産児数、出産時の生存児数および死亡児数、出生率、妊娠期間および  
外表異常児出現率の成績について群平均および標準偏差を算出し、Bartlettの検定法を行い、  
等分散性を解析した。等分散( $p \geq 0.05$ )の場合は一元配置分散分析法で解析し、不等分散  
( $p < 0.05$ )の場合はKruskal-Wallisの検定法で解析した。一元配置分散分析の結果、有意差がみ

られた場合 ( $p<0.1$ ) は Dunnett の検定法を用いて対照群との比較を行った。 Kruskal-Wallis 法の解析の結果、有意差がみられた場合 ( $p<0.1$ ) は Steel の検定法を用い対照群との比較を行った。なお、妊娠黄体数、着床率ならびに生後 0 日および 4 日の生存率は別途統計解析システム（三研システム株式会社）および SAS システムを用いて上記と同様の検定を実施した。

主試験群における詳細な状態観察、刺激に対する感覚運動反応、尿量を除く尿検査の成績について、Kruskal-Wallis の検定法で解析し、有意差がみられた場合 ( $p<0.1$ ) は Steel の検定法を用いて対照群との比較を行った。

性周期の異常の発現率、交尾率、受胎率、出産率、生後 0 日の生存児の性比および外表異常児を持つ腹の頻度ならびに病理組織学的検査については、Fisher の正確確率検定法を用いた。なお、哺育率は別途 SAS システムを用いて上記と同様の検定を実施した。

サテライト群における握力 (3 回の平均)、自発運動量、体重、体重増加量、摂餌量、尿量、血液学的検査、血液化学的検査、器官の絶対重量および相対重量の成績について、群平均および標準偏差を算出し、F 検定による等分散の解析を行った。等分散 ( $p\geq 0.05$ ) の場合は Student の t 検定、不等分散 ( $p<0.05$ ) の場合は Welch の検定を用いて対照群との比較を行った。

サテライト群における詳細な状態観察、刺激に対する感覚運動反応、尿量を除く尿検査の成績について、Wilcoxon の順位和検定を用いて対照群との比較を行った。

不妊が確認された雌動物については、妊娠期間の体重、体重増加量および摂餌量、器官重量ならびに病理組織学的検査のデータを統計検定から除外した。また、自動給水装置のノズルの水漏れ事故のため哺育 3 日に哺育児が全て死亡した雌動物については、哺育 4 日の体重、体重増加量および摂餌量ならびに器官重量のデータを統計検定から除外した。試験中に死亡した動物については、病理組織学的検査のデータを統計検定から除外した。

なお、800 mg/kg 群で哺育 0 日に投与過誤で死亡した動物のデータについては、投与過誤は前日に発生したと推定されるが、9:00 の分娩終了時（哺育 0 日）の測定時に動物の状態に異常はみられなかったため、哺育 0 日の母動物の体重および新生児のデータを統計検定に含めた。

対照群との比較検定については、5%未満を有意とした。

### 3.12 コンピュータシステムの利用

以下に示すデータの収集には MiTOX を使用した。

オンラインデータ ; 親動物の一般状態、詳細な状態観察、機能検査（刺激に対する感覚運動反応、握力）、体重、摂餌量、血液学的検査（PT, APTT を除く）、血液化学的検査、器官重量、病理組織学的検査、新生児の体重

オフラインデータ ; 機能検査（自発運動量）、尿検査、血液学的検査（PT, APTT）、性周期検査、生殖能検査、着床数、生存児数、死亡児数、親動物の剖検、

### 新生児の一般状態、外表異常および性別

コンピュータプロトコールには、データ収集の項目、日程等を登録した。なお、親動物の一般状態において、一部の動物についてはオフラインデータとした(6 参照)。

## 4 成績

### 4.1 反復投与毒性

#### 4.1.1 一般状態

一般状態の成績を Table 1-1 ~ 1-8, Appendix 1-1 ~ 1-32 に示す。

##### [投与期間]

###### (1) 雄：主試験群

対照群を含むいずれの試験群の動物にも異常は認められなかった。

###### (2) 雌：主試験群

対照群、50 および 200 mg/kg 群では、いずれの試験群の動物にも異常は認められなかった。800 mg/kg 群では、哺育 0 日の分娩終了後に 1 例 (No. 50458) に呼吸困難が発現し、その後投与前に死亡した。なお、出産児は哺乳がされており正常であったが、母動物が死亡したためその日に安楽死させて剖検した。

###### (3) 雌：サテライト群（非交配群）

対照群の動物には異常は認められなかった。800 mg/kg 群では、投与 1~3 日の投与直後からよろめき歩行が 2 例および自発運動の低下が 1 例に観察され、いずれも投与後約 1 時間で回復した。また、投与 2~5 日の間に鼻周囲または外尿道口周囲被毛汚染が 1 または 2 例に観察された。投与 21 日にも外尿道口周囲被毛汚染が 1 例に観察された。さらに、投与 3 日の投与前に 1 例 (No. 50660) が死亡しているのが発見された。この例では、投与 1 および 2 日に異常は認められなかった。

##### [回復期間]

###### (1) 雄：サテライト群

対照群および 800 mg/kg 群の動物には異常は認められなかった。

###### (2) 雌：サテライト群（非交配群）

対照群および 800 mg/kg 群の動物には異常は認められなかった。

#### 4.1.2 詳細な状態観察

詳細な状態観察の成績を Table 2-1 ~ 4-5, Appendix 2-1 ~ 4-66 に示す。

##### [投与期間]

###### (1) 雄：主試験群

いずれの項目にも被験物質投与群と対照群の間に有意な差は認められなかった.

(2) 雌：主試験群

投与 7 日の検査で, 50 mg/kg 群の排尿回数に有意な高値が認められたが, 用量依存性がみられないことから, 偶発的な変化と考えられた. その他には, いずれの項目にも被験物質投与群と対照群の間に有意な差は認められなかった.

(3) 雌：サテライト群 (非交配群)

800 mg/kg 群では, いずれの項目にも対照群と比較して有意な差は認められなかった.

[回復期間]

(1) 雄：サテライト群

800 mg/kg 群では, いずれの項目にも対照群と比較して有意な差は認められなかった.

(2) 雌：サテライト群 (非交配群)

800 mg/kg 群では, いずれの項目にも対照群と比較して有意な差は認められなかった.

#### 4.1.3 機能検査

刺激に対する感覚運動反応の成績を Table 5-1 ~ 5-5, Appendix 5-1 ~ 5-14, 握力の成績を Table 6-1 ~ 6-5, Appendix 6-1 ~ 6-14, 自発運動量の成績を Table 7-1 ~ 7-5, Appendix 7-1 ~ 7-14 に示す.

[投与 4 週]

(1) 雄：主試験群

50 および 200 mg/kg 群では, いずれの項目にも対照群と比較して有意な差は認められなかつた. 800 mg/kg 群では, 握力検査において, 前肢に低値傾向, 後肢に有意な低値が認められた. その他の項目には対照群と比較して有意な差は認められなかった.

(2) 雌：サテライト群 (非交配群)

800 mg/kg 群では, 自発運動量の測定において, 20 ~ 30 分, 30 ~ 40 分, 40 ~ 50 分に有意な高値が認められ, 0 ~ 60 分の合計も有意な高値であった. その他の項目には対照群と比較して有意な差は認められなかった.

[回復 2 週]

(1) 雄：サテライト群

800 mg/kg 群では, いずれの項目にも対照群と比較して有意な差は認められなかった.

(2) 雌：サテライト群 (非交配群)

800 mg/kg 群では, 前肢の握力に対照群と比較して有意な高値が認められたが, 投与期間終了時には認められない変化であり, 被験物質投与と関連しないと考えられた. その他の項目には対照群と比較して有意な差は認められなかった.

## [哺育 4 日]

## (1) 雌：主試験群

いずれの項目にも被験物質投与群と対照群の間に有意な差は認められなかった.

## 4.1.4 体重

体重の成績を Figure 1-1 ~ 1-3, Table 8-1 ~ 8-7, Appendix 8-1 ~ 8-22 に示す.

## [投与期間]

## (1) 雄：主試験群

いずれの投与群においても、体重および体重増加量に対照群と比較して有意な差は認められなかった.

## (2) 雌：主試験群

いずれの投与群においても、体重および体重増加量に対照群と比較して有意な差は認められなかった.

## (3) 雌：サテライト群 (非交配群)

800 mg/kg 群では、投与 4 日の体重に対照群と比較して有意な低値が認められた. その他の期間には、有意な差は認められなかった.

## [回復期間]

## (1) 雄：サテライト群

800 mg/kg 群では、体重に対照群と比較して有意な差は認められなかった. 一方、体重増加量には有意な高値が認められたが、投与を休止したことによる反動と考えられた.

## (2) 雌：サテライト群 (非交配群)

800 mg/kg 群では、体重および体重増加量に対照群と比較して有意な差は認められなかった.

## 4.1.5 摂餌量

摂餌量の成績を Figure 2-1 ~ 2-3, Table 9-1 ~ 9-7, Appendix 9-1 ~ 9-22 に示す.

## [投与期間]

## (1) 雄：主試験群

いずれの投与群においても対照群と比較して有意な差は認められなかった.

## (2) 雌：主試験群

いずれの投与群においても対照群と比較して有意な差は認められなかった.

## (3) 雌：サテライト群 (非交配群)

800 mg/kg 群では、投与 4 および 7 日の摂餌量に、対照群と比較して統計学的に有意な差ではなかったが、低値傾向が認められた.

[回復期間]

(1) 雄：サテライト群

800 mg/kg 群では、対照群と比較して有意な差は認められなかった。

(2) 雌：サテライト群 (非交配群)

800 mg/kg 群では、対照群と比較して有意な差は認められなかった。

#### 4.1.6 尿検査

尿検査の成績を Table 10-1 ~ 10-22, Appendix 10-1 ~ 10-40 に示す。

[投与 4 週]

(1) 雄：主試験群

いずれの項目にも被験物質投与群と対照群の間に有意な差は認められなかった。

(2) 雌：サテライト群 (非交配群)

いずれの項目にも 800 mg/kg 群と対照群の間に有意な差は認められなかった。

[回復 2 週]

(1) 雄：サテライト群

800 mg/kg 群では、いずれの項目にも対照群と比較して有意な差は認められなかった。

(2) 雌：サテライト群 (非交配群)

800 mg/kg 群では、いずれの項目にも対照群と比較して有意な差は認められなかった。

#### 4.1.7 血液学的検査

血液学的検査の成績を Table 11-1 ~ 11-5, Appendix 11-1 ~ 11-14 に示す。

[投与期間終了時]

(1) 雄：主試験群

50 mg/kg 群では、PT に対照群と比較して有意な高値が認められた。200 mg/kg 群では、ヘモグロビン濃度 (HGB) および APTT に有意な高値が認められた。これらの項目は 800 mg/kg 群では有意な差は認められなかったことから、偶発的な変化と考えられた。800 mg/kg 群では、血小板数に有意な高値が認められた。

(2) 雌：主試験群

50 mg/kg 群では、網赤血球数に有意な高値が認められたが、用量依存性がみられないことから、偶発的な変化と考えられた。200 および 800 mg/kg 群では、いずれの項目にも対照群と比較して有意な差は認められなかった。

(3) 雌：サテライト群 (非交配群)

800 mg/kg 群では、平均赤血球ヘモグロビン濃度 (MCHC) および PT に対照群と比較して有

意な低値が認められた。

[回復期間終了時]

(1) 雄：サテライト群

800 mg/kg 群では、いずれの検査項目にも対照群と比較して有意な差は認められなかった。

(2) 雌：サテライト群（非交配群）

800 mg/kg 群では、いずれの検査項目にも対照群と比較して有意な差は認められなかった。

#### 4.1.8 血液化学的検査

血液化学的検査の成績を Table 12-1 ~ 12-7, Appendix 12-1 ~ 12-14 に示す。

[投与期間終了時]

(1) 雄：主試験群

50 および 200 mg/kg 群では、いずれの検査項目にも対照群と比較して有意な差は認められなかつた。800 mg/kg 群では、クレアチニンに対照群と比較して有意な低値が認められた。

(2) 雌：主試験群

200 mg/kg 群では、いずれの検査項目にも対照群と比較して有意な差は認められなかつた。

50 および 800 mg/kg 群では、無機リンに対照群と比較して有意な低値が認められた。しかし、50 mg/kg 群の変化については、200 mg/kg 群では有意な差はないことから、被験物質投与と関連のない変化と考えられた。

(3) 雌：サテライト群（非交配群）

800 mg/kg 群では、総ビリルビンに対照群と比較して有意な低値が認められた。その他の検査項目には対照群と比較して有意な差は認められなかつた。

[回復期間終了時]

(1) 雄：サテライト群

800 mg/kg 群では、いずれの検査項目にも対照群と比較して有意な差は認められなかつた。

(2) 雌：サテライト群（非交配群）

800 mg/kg 群では、いずれの検査項目にも対照群と比較して有意な差は認められなかつた。

#### 4.1.9 病理検査

##### 4.1.9.1 剖検

剖検所見を Table 13-1 ~ 13-8, Appendix 13-1 ~ 13-15 に示す。

[投与期間終了時]

(1) 雄：主試験群

対照群、50 および 200 mg/kg 群では、異常所見は認められなかつた。800 mg/kg 群では、胃

境界縁の肥厚が 3 例に、精巣上体尾部に黄白色巣が 1 例に認められた。

(2) 雌：主試験群

対照群、50 および 200 mg/kg 群では、異常所見は認められなかった。800 mg/kg 群では、胃境界縁の肥厚が分娩例の 6 例および不妊の 1 例に認められた。

800 mg/kg 群で哺育 0 日に死亡した 1 例では、胃境界縁の肥厚が認められた。

(3) 雌：サテライト群（非交配群）

対照群では、異常所見は認められなかった。800 mg/kg 群では、胃境界縁の肥厚が 2 例に認められた。投与 3 日に死亡した 1 例では、胃幽門部粘膜赤色化および腺胃粘膜多巣性赤色巣が観察された。

[回復期間終了時]

(1) 雄：サテライト群

対照群および 800 mg/kg 群ともに異常所見は認められなかった。

(2) 雌：サテライト群（非交配群）

対照群および 800 mg/kg 群ともに異常所見は認められなかった。

#### 4.1.9.2 器官重量

器官重量の成績を Table 14-1 ~ 14-7, Appendix 14-1 ~ 14-20 に示す。

[投与期間終了時]

(1) 雄：主試験群

測定したいずれの器官重量にも、被験物質投与群と対照群の間に有意な差は認められなかった。

(2) 雌：主試験群

200 mg/kg 群で胸腺の相対重量に有意な高値が認められたが、800 mg/kg 群で有意な変化がみられないことから、被験物質投与に関連しない変化と考えられた。その他の器官重量には、被験物質投与群と対照群の間に有意な差は認められなかった。

(3) 雌：サテライト群（非交配群）

800 mg/kg 群では、脳の絶対重量に対照群と比較して有意な高値が認められた。しかし、相対重量では有意な差は認められなかったことから、偶発的な変化と考えられた。

[回復期間終了時]

(1) 雄：サテライト群

800 mg/kg 群では、測定したいずれの器官重量にも、対照群と比較して有意な差は認められなかった。

(2) 雌：サテライト群（非交配群）

800 mg/kg 群では、測定したいずれの器官重量にも、対照群と比較して有意な差は認められなかった。

#### 4.1.9.3 病理組織学的検査

病理組織学的所見を Table 15-1 ~ 15-26, Appendix 15-1 ~ 15-28 に示す。

##### [投与期間終了時]

###### (1) 雄：主試験群

50 および 200 mg/kg 群では、異常は認められなかった。

800 mg/kg 群では、胃境界縁の扁平上皮過形成（軽微）が 6 例に認められ、その発生頻度は対照群と比較して有意な増加であった。その他に、肺に肺胞内マクロファージ集簇（軽微）、脾臓に限局性腺房細胞委縮（軽微）、肝臓に小肉芽腫（軽微）、心臓に限局性心筋症（軽微）、腎臓に尿細管の好塩基性化（軽微）、精巢上体に精子肉芽腫（軽微）、前立腺に間質の炎症（軽微）が散見されたが、対照群あるいは試験施設の背景データ<sup>4)</sup>に認められる所見であり、発生頻度の増加はみられないことから、被験物質投与と関連のない変化と考えられた。なお、甲状腺に鰓後体（軽微）が対照群のみに 1 例に認められた。

###### (2) 雌：主試験群

50 mg/kg 群では、異常は認められなかった。

200 mg/kg 群では、胃に異常は認められなかった。一方、腎臓では、尿細管の好塩基性化（軽微）が 3 例に認められたが、対照群と比較して発生頻度に有意な差は認められなかった。

800 mg/kg 群では、胃境界縁の扁平上皮過形成（軽微）が 7 例に認められ、その発生頻度は対照群と比較して有意な増加であった。さらに、胃境界縁の過角化（軽微）が 3 例に認められた。また、腎臓では尿細管の好塩基性化が 8 例（軽微 7 例、軽度 1 例）に認められ、その発生頻度は対照群と比較して有意な増加であった。不妊動物においても胃境界縁の扁平上皮過形成（軽微）および尿細管の好塩基性（軽度）が認められた。その他に、肝臓に小葉周辺性肝細胞空胞化（軽微）、甲状腺に鰓後体（軽微）、不妊動物で腎臓に硝子円柱（軽微）が散見されたが、対照群あるいは試験施設の背景データ<sup>4)</sup>に認められる所見であり、対照群と比較して発生頻度の増加はみられないことから、被験物質投与と関連のない変化と考えられた。なお、肺に肺胞内マクロファージ集簇（軽微）、肝臓に小肉芽腫（軽微）、下垂体に前葉囊胞（軽微）が対照群のみに 1 または 2 例に認められた。

800 mg/kg 群の哺育 0 日に死亡した 1 例では、肺に気管支上皮の壊死（中等度）、肺胞水腫（中等度）、血管周囲水腫（軽度）および好中球浸潤（軽度）が認められた。その他に胃境界縁の扁平上皮過形成（軽微）が認められた。

###### (3) 雌：サテライト群（非交配群）

800 mg/kg 群では、胃境界縁の扁平上皮過形成（軽微）が 5 例に認められ、その発生頻度は対照群と比較して有意な増加であった。さらに、胃境界縁の過角化（軽微）が 3 例に、腺胃粘膜固有層の線維化（軽微）が 1 例に認められた。また、腎臓では尿細管の好塩基性化が 3 例（軽微 2 例、中等度 1 例）に、皮質の鉱質沈着（軽度）が 1 例に認められた。その他に、肝臓に小肉芽腫（軽微）、甲状腺に鰓後体（軽微）が散見されたが、対照群あるいは試験施設の背景データ<sup>4)</sup>に認められる所見であり、発生頻度の増加はみられないことから、被験物質投与と関連のない変化と考えられた。なお、下垂体に異所性頭蓋咽頭組織（軽微）が対照群のみに 1 例に認められた。

投与 3 日に死亡した 1 例では、腺胃のびらん（軽微）、胃幽門部粘膜の壊死（中等度）、腎臓に皮質尿細管壊死（重度）、脾臓に白脾髄の委縮（軽度）、下垂体に前葉囊胞（軽微）が認められた。

#### [回復期間終了時]

##### (1) 雄：サテライト群

800 mg/kg 群では、胃境界縁の扁平上皮過形成（軽微）が 2 例に認められたが、発生頻度に有意な差はみられなかった。

##### (2) 雌：サテライト群（非交配群）

800 mg/kg 群では、胃に異常は認められなかった。腎臓では、尿細管の好塩基性化（軽微）が 2 例、尿細管上皮の過形成（軽微）が 1 例、囊胞（軽微）が 1 例に観察されたが、発生頻度に有意な差はみられなかった。

## 4.2 生殖発生毒性

### 4.2.1 性周期検査

性周期検査の成績を Table 16, Appendix 16-1 ~ 16-8 に示す。

交配前 14 日間の性周期観察において、性周期の異常の発現率、発情期間隔および発情回数には被験物質投与群と対照群の間に有意な差は認められなかった。

### 4.2.2 生殖能検査

生殖能検査の成績を Table 17-1 および 17-2, Appendix 17-1 ~ 17-8 に示す。

交尾率、受胎率および交尾所要日数には、被験物質投与群と対照群の間に有意な差は認められなかった。

### 4.2.3 分娩および哺育状態観察

分娩および哺育状態観察の成績を Table 18-1 ~ 18-3, Appendix 18-1 ~ 18-12 に示す。

妊娠黄体数、着床数、着床率、出生率、妊娠期間、出産率、出産児数、出産児の生存児数および死亡児数、性比ならびに哺育 4 日の哺育率には、いずれの被験物質投与群においても対照群と比較して有意な差は認められなかつた。また、いずれの出産生児にも外表異常は認められなかつた。

800 mg/kg 群の 1 例 (No. 50458) で哺育 0 日の分娩終了後に死亡が認められたが、哺育児は授乳されており、分娩には異常はないと考えられた。この動物の病理組織学的検査の結果、投与過誤によると考えられる肺の異常が認められ、被験物質投与と関係のない変化と判断した。

なお、800 mg/kg 群の 1 腹 (No. 50455) のケージで哺育 3 日に自動給水装置のノズルの水漏れ事故が発生し、全哺育児の死亡がみられたが、被験物質投与と関係のない変化と判断した。

#### 4.2.4 新生児の一般状態および生存率

新生児の一般状態および生存率の成績を Table 19 および 20, Appendix 19-1 ~ 19-8 および 20-1 ~ 20-4 に示す。

被験物質投与に起因する一般状態の変化はいずれの投与群においても認められなかつた。

なお、800 mg/kg 群で母動物 1 例 (No. 50458) が投与過誤により哺育 0 日に死亡したが、哺育児の一般状態に異常は認められなかつた。生存哺育児は全例その日（生後 0 日）に安楽死させて剖検した。

生後 0 日および 4 日の生存率には、被験物質投与群と対照群の間に有意な差は認められなかつた。

#### 4.2.5 新生児の体重

新生児の体重の成績を Figure 3, Table 21, Appendix 21-1 ~ 21-4 に示す。

生後 0 日および 4 日の体重には、雌雄とも被験物質投与群と対照群の間に有意な差は認められなかつた。

#### 4.2.6 新生児の剖検

新生児の剖検の成績を Table 22, Appendix 22-1 ~ 22-4 に示す。

生後 4 日の生存児の剖検では、800 mg/kg 群で腎孟拡張が雄の 1 例にみられたのみで、他の動物に異常は認められなかつた。

生後 0-4 日の間に発見された死亡児では、いずれの動物にも異常は認められなかつた。

なお、800 mg/kg 群で母動物が死亡したため生後 0 日に剖検した哺育児には、異常は認められなかつた。

## 5 考察

### 5.1 反復投与毒性

200 および 50 mg/kg 群では、投与期間中の一般状態、体重および摂餌量、詳細な状態観察、機能検査、尿検査、血液学的検査、血液化学的検査、剖検および器官重量には、雌雄とも被験物質投与に関連する変化は認められなかった。また、病理組織学的検査では、雌雄とも被験物質投与に関連する変化は認められなかった。

800 mg/kg 群では、主試験群雄の投与 4 週の握力検査において、前肢に低値傾向、後肢に有意な低値が認められた。一方、非交配群雌の投与 4 週の自発運動量測定において、有意な増加が認められた。回復 2 週の検査では、同様の変化は認められず、回復性を示した。

非交配群雌で、投与 1 日～3 日の投与直後～約 1 時間に臨床症状（よろめき歩行、自発運動の低下）が観察され、投与 2～5 日および 21 日には被毛汚染が 1 または 2 例に認められた。投与 3 日の投与前には 1 例の死亡が認められ、剖検で胃幽門部粘膜赤色化および腺胃粘膜多巣性赤色巣、病理組織学的検査で腺胃のびらんおよび胃幽門部粘膜の壊死が観察された。投与 4 日の体重に有意な低値、投与 4 日および 7 日の摂餌量に低値傾向が認められ、いずれも被験物質投与に起因する変化と考えられた。

投与期間終了時の血液学的検査では、雄で血小板数に有意な高値が認められたが、5 例中 4 例の値が試験施設の背景データ（平均値  $\pm$  2SD :  $112.09 \pm 20.58 \text{ } 10^4/\mu\text{L}$ 、例数 : 41、試験期間 : 2012～2015 年)<sup>5)</sup> の範囲内であることに加えて、その他の血液学的検査項目に変化はみられないことから、毒性学的に意味のない変化と考えられた。非交配群雌では、MCHC および PT に有意な低値が認められた。しかし、MCHC については、全例の値が試験施設の背景データ（平均値  $\pm$  2SD :  $35.72 \pm 1.04 \text{ g/dL}$ 、例数 : 51、試験期間 : 2012～2015 年)<sup>5)</sup> の範囲内であり、他の血液学的検査項目に変化はみられないことから、また PT の低値については、臨床的意義が乏しいことから、いずれも毒性学的に意味のない変化と考えられた。また、血液化学的検査では、雄でクレアチニンに有意な低値が認められたが、全例の値が試験施設の背景データ（平均値  $\pm$  2SD :  $0.288 \pm 0.074 \text{ mg/dL}$ 、例数 : 41、試験期間 : 2012～2015 年)<sup>6)</sup> の範囲内であることに加えて、その他の血液化学的検査項目に変化はみられないことから、毒性学的に意味のない変化と考えられた。主試験群雌では、無機リンに有意な低値が認められたが、全例の値が試験施設の背景データ（平均値  $\pm$  2SD :  $8.89 \pm 1.46 \text{ mg/dL}$ 、例数 : 40、試験期間 : 2011～2015 年)<sup>7)</sup> の範囲内であり、カルシウムに変化がみられないことから、毒性学的に意味のない変化と考えられた。非交配群雌では、総ビリルビンの有意な低値が認められたが、貧血がみられないことと全例の値が試験施設の背景データ（平均値  $\pm$  2SD :  $0.078 \pm 0.040 \text{ mg/dL}$ 、例数 : 51、試験期間 : 2012～2015 年)<sup>6)</sup> の範囲内であることから、毒性学的に意味のない変化と考えられた。以上の変化は回復期間終了時の検査では認められず、回復性を示した。

投与期間終了時の剖検では、雌雄の胃に境界縁の肥厚が認められた。病理組織学的検査でもこれに対応して、雌雄で胃境界縁の扁平上皮過形成が観察され、雌では境界縁の過角化あるいは腺胃粘膜固有層の線維化を伴っている例もみられた。これらは、被験物質の胃粘膜に対する刺激性を示唆する変化と考えられた。さらに、主試験群および非交配群の雌の腎臓の病理組織学的検査で、尿細管の好塩基性化の発生頻度の有意な増加および憎悪化が認められた。しかし、明らかな尿細管の変性、壊死等の変化はみられず、尿検査または血液化学的検査でも腎機能の異常を示唆する変化は認められなかったことから、被験物質の腎臓に対する軽度の影響と考えられた。また、投与3日の死亡例で腎臓に重度の皮質尿細管壊死が認められ、1例のみの変化であるが被験物質の腎臓に対する影響が示唆された。これらの変化は回復期間終了時の剖検または病理組織学的検査では認められないか軽減しており、回復傾向を示した。なお、200 mg/kg群の雌の腎臓でも軽微な尿細管の好塩基性化が認められたが、対照群と比較して発生頻度の増加はみられないことから、被験物質投与と関連のない変化と考えられた。

なお、800 mg/kg群で哺育0日の分娩終了後に呼吸困難を示してから死亡した1例では、病理組織学的検査の結果、肺に気管支上皮の壊死、肺胞水腫、血管周囲水腫および好中球浸潤が認められた。この動物の死因は、被験物質投与液が気管内に入った投与過誤に起因する呼吸障害によるものであり、被験物質投与に関連はないと考えられた。

その他の項目（詳細な状態観察、尿検査および器官重量）には、投与期間中（終了時）および回復期間中（終了時）の雌雄とも被験物質投与に関連した変化は認められなかった。

以上のように、50および200 mg/kg群では、雌雄とも被験物質投与の影響は認められなかつた。800 mg/kg群では、雌で一般状態の変化および死亡、体重および摂餌量の低値が認められ、剖検および病理組織学的検査で雌雄の胃および雌の腎臓に異常が認められた。したがって、本試験条件下における4-メチルベンゼン-1-スルホン酸一水和物の反復投与毒性に関する無影響量（NOEL）および無毒性量（NOAEL）はいずれも雌雄とも200 mg/kg/dayであると考えられた。

## 5.2 生殖発生毒性

生殖能検査では、800 mg/kg群まで、性周期の異常の発現率、発情期間隔および発情回数、交尾率、受胎率、交尾所要日数、妊娠黄体数、着床数、着床率、出生率、妊娠期間、出産率、出産児数、出産児の生存児数および死亡児数ならびに哺育4日の哺育率には、被験物質投与に関連する変化はみられなかった。

新生児の体重、一般状態、生存率、性比および剖検では、800 mg/kg群まで、被験物質投与に関連する変化はみられなかった。

以上のように、800 mg/kg 群まで、親動物の生殖能および新生児の発生に被験物質投与に関連した変化は認められなかつたため、本試験条件下における 4-メチルベンゼン-1-スルホン酸一水和物の親動物の生殖に対する無影響量 (NOEL) および無毒性量 (NOAEL) ならびに新生児の発生に対する無影響量 (NOEL) および無毒性量 (NOAEL) はいずれも 800 mg/kg/day と考えられた。

## 6 試験成績の信頼性に影響を及ぼしたと思われる環境要因

試験計画書からの逸脱：親動物の一般状態をオンラインデータとして収集すると規定されていたが、一部の動物 [2015 年 12 月 9 日 (No. 50652), 12 月 10 日 (No. 50651), 12 月 11 日 (No. 50651)] の投与後の症状およびその発現時刻と消失時刻を記録用紙に記録した。出現した症状の持続時間を記録するための対応措置であることから、この逸脱による試験の信頼性に対する影響は無いと判断した。

新生児の一般状態をオフラインデータとして収集すると規定されていたが、No.50458 の哺育 0 日のデータがオフラインで処理されていなかった。しかし、新生児の一般状態については記録用紙が生データであり、データは正しく記録されていることから、試験の信頼性に対する影響は無いと判断した。

No. 50455 のケージで自動給水装置のノズルの水漏れ事故により哺育 3 日に全哺育児の死亡が発生し、その後のデータを統計検定から除外した。また、No. 50458 が哺育 0 日に投与過誤により死亡し、その後のデータが得られなかつた。これらのデータの損失によって例数が減つたものの、試験法ガイドラインに規定される「妊娠末期において 1 群 8 匹以上の妊娠動物を確保する」ことができていることから、試験は成立すると判断した。

標準操作手順書からの逸脱：主試験群雌の剖検日の体重測定を生殖毒性の MiTOX プロトコール (MiTOX 試験 No. SR15146A) を使用してオンライン収集すると規定されていたが、2016 年 1 月 19 日に誤って一般毒性の MiTOX プロトコール (MiTOX 試験 No. SR15146) を使用してオンライン収集した。当該日の体重については、オンラインで収集した値を生データとして処理し、このデータに基づいて以後の作業を実施し問題は生じなかつた。従って、この逸脱による試験の信頼性に対する影響は無いと判断した。

予見することができなかつた事態：No. 50458 の哺育 0 日の死亡後の生存哺育児の処置についての規定がなかつたが、その日に安楽死させて剖検し、途中安楽死例として Whole body を 10% 中性緩衝ホルマリン液で固定・保存した。この処置は適切と考えられ、試験の信頼性に対する影響はないと判断した。

投与期間終了時の低用量群の雄の PT に顕著な高値を示す個体が数例認められた。しかし、測定手技に異常は発見されず、最高用量群では対照群と比較して変化がないことから、安全性

評価には影響ないと考えられた。

その他に試験成績の信頼性に影響を及ぼしたと思われる環境要因はなかった。

## 7 資料の保存

### 7.1 資料の種類

以下を株式会社化合物安全性研究所の資料保存室に保存する。

1. 試験計画書および試験計画書変更書
2. 生データその他の記録文書
3. 最終報告書
4. 標本
5. 被験物質サンプル

### 7.2 保存期間

試験終了後 10 年間保存し、その後の保存については試験委託者との協議により決定する。

## 8 参考資料

- 1) 安全データシート. [REDACTED]
- 2) [REDACTED] ホームページ. オンラインカタログ
- 3) 最終報告書 : 4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験のための予備試験 (SR15146P), 株式会社化合物安全性研究所 2015 年
- 4) Histrical data of Crl:CD(SD) female rats: Histopathological findings (2006-2011) 株式会社化合物安全性研究所 社内資料
- 5) 血液学的検査 背景データ Crl:CD(SD) ラット(雌雄 : 12 ~ 16 週齢) (2012-2015) 株式会社化合物安全性研究所 社内資料
- 6) 血液化学的検査 背景データ Crl:CD(SD) ラット(雌雄 : 12 ~ 16 週齢) (2012-2015) 株式会社化合物安全性研究所 社内資料
- 7) 血液化学的検査 背景データ Crl:CD(SD) ラット(雌 : 分娩後 5/6 日) (2011-2015) 株式会社化合物安全性研究所 社内資料

Figure 1 - 1

Study No. : SR15146

Body weight, Male

Period : Administration day 1-28, Recovery day 1-14

Species : Rat

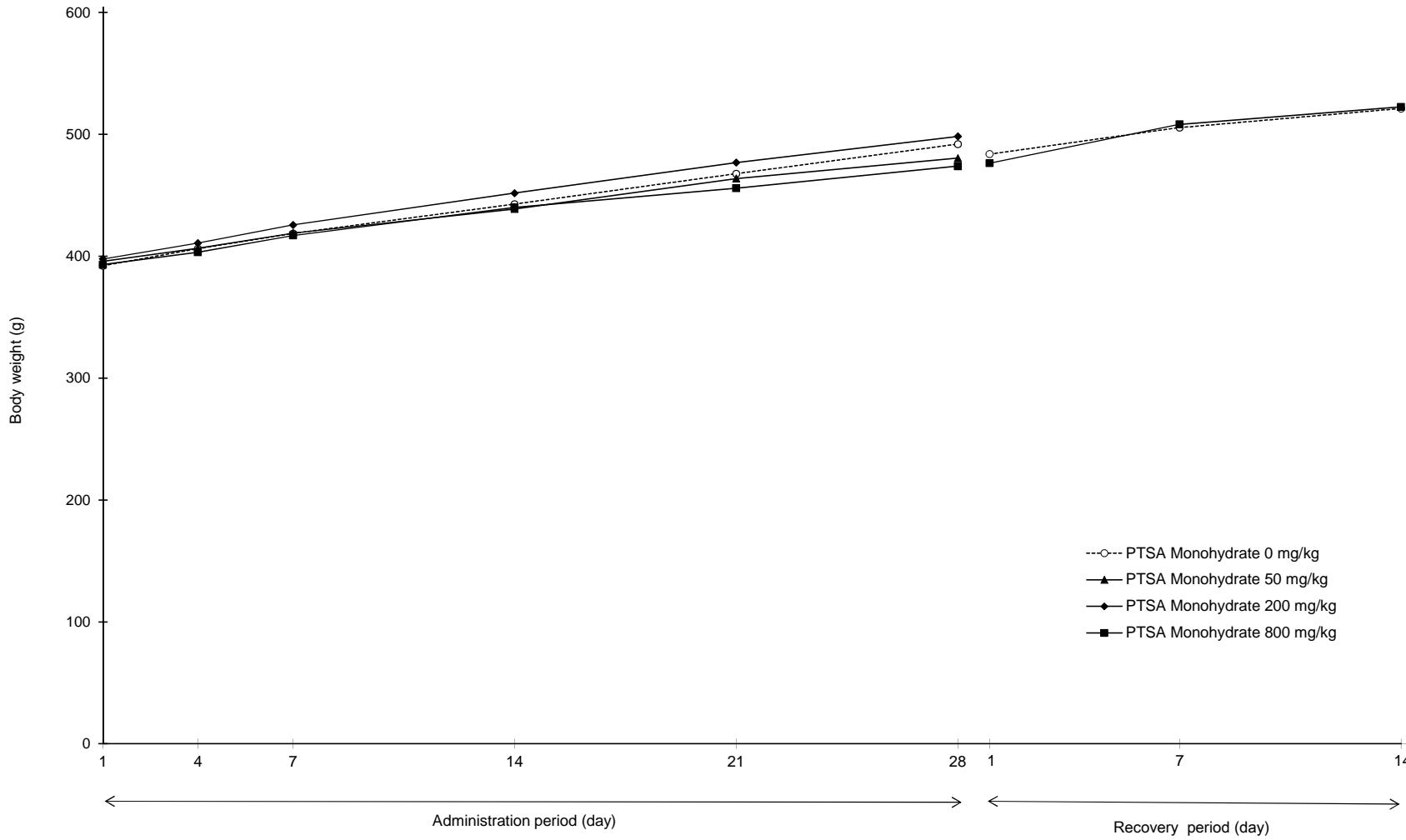


Figure 1 - 2

Study No. : SR15146

Body weight, Female

Period : F0 before mating Day 1-14, F0 gestation Day 0-20, F0 lactation Day 0-4

Species : Rat

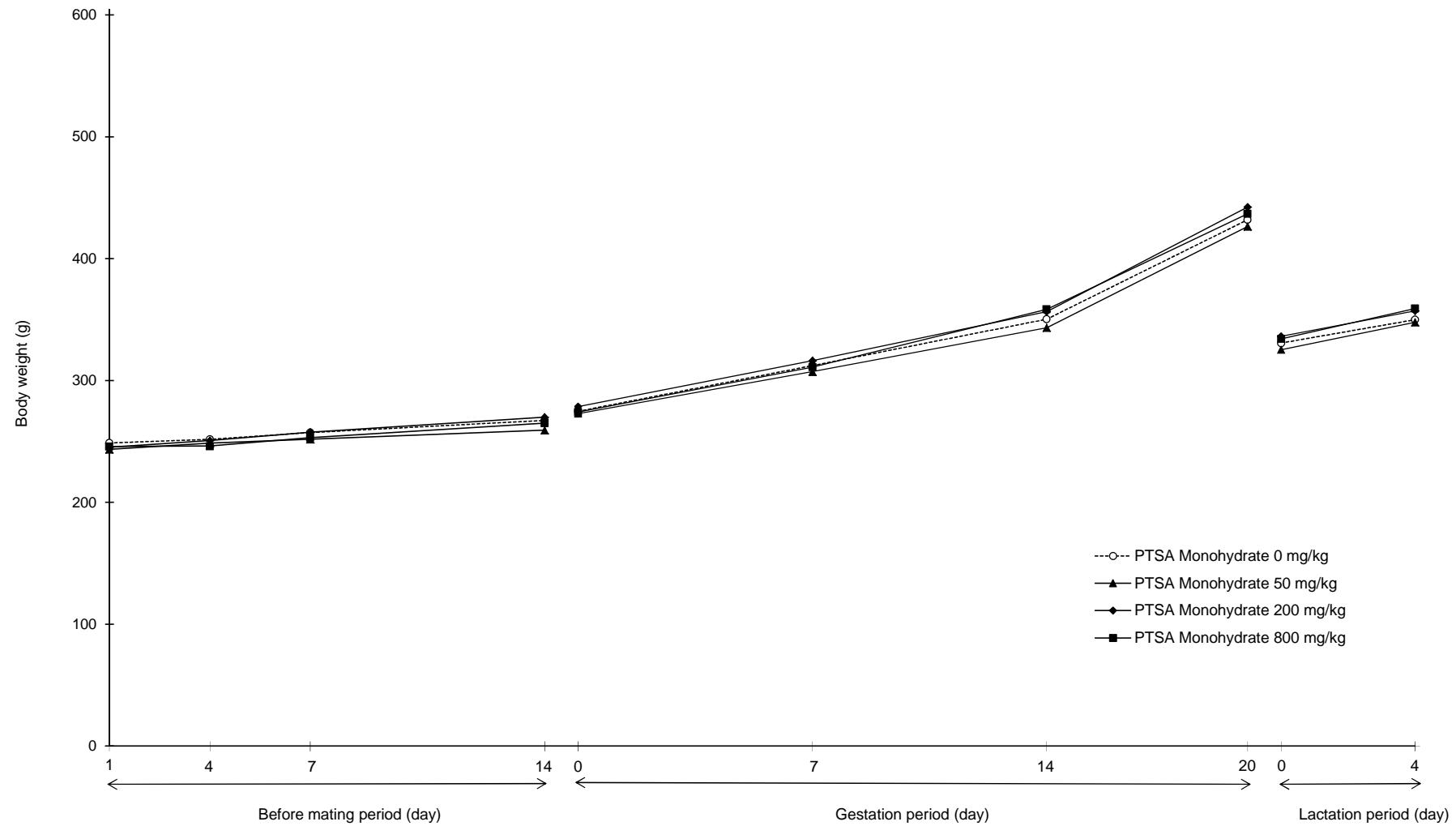


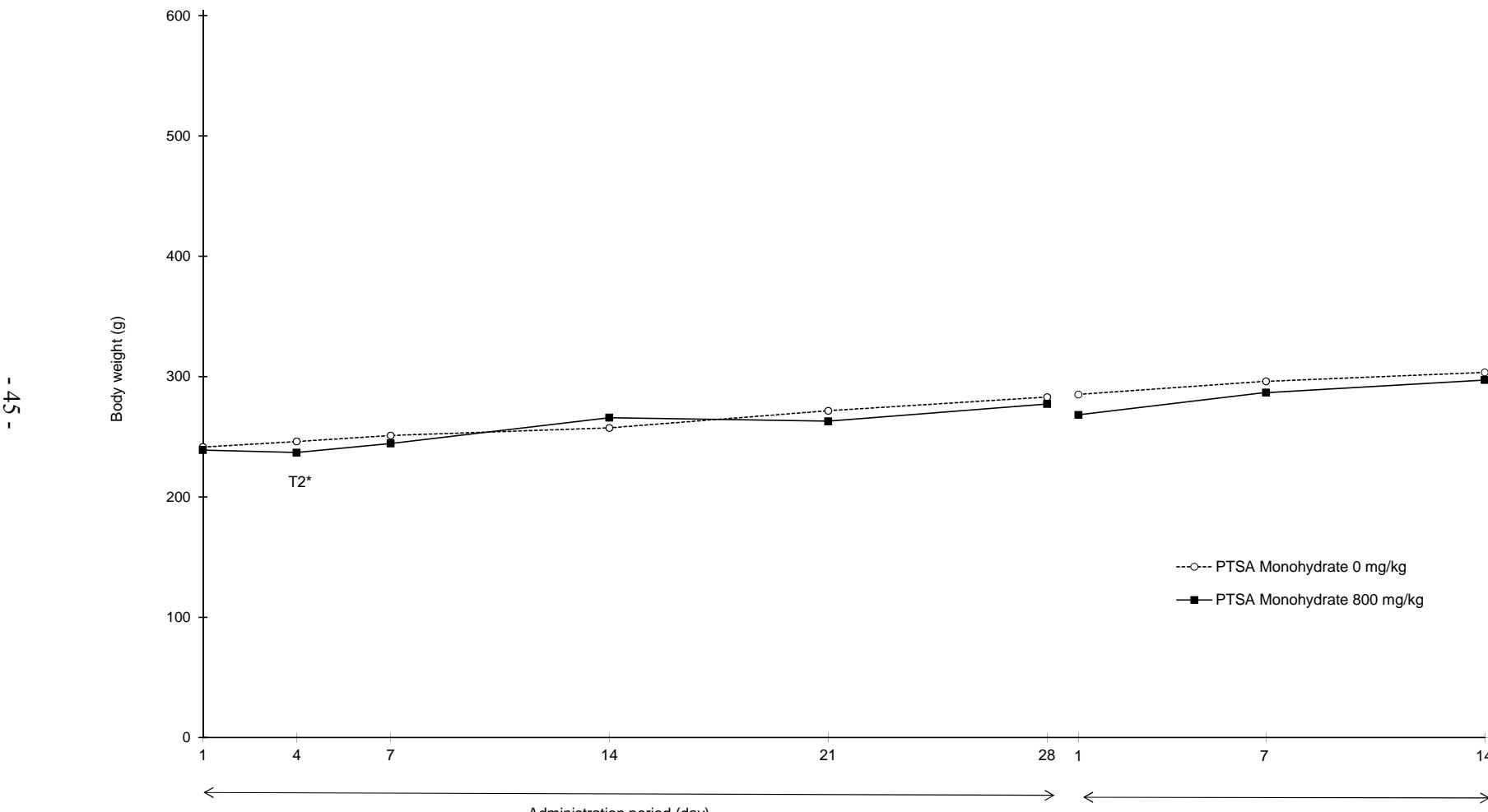
Figure 1 - 3

Study No. : SR15146

Body weight, Female (satellite)

Period : Administration day 1-28, Recovery day 1-14

Species : Rat



Significantly different from PTSA Monohydrate 0 mg/kg: \*  $P < 0.05$

T2 : Student t-test (two-side)

Figure 2 - 1

Study No. : SR15146

Food consumption, Male

Period : Administration day 1-28, Recovery day 1-14

Species : Rat

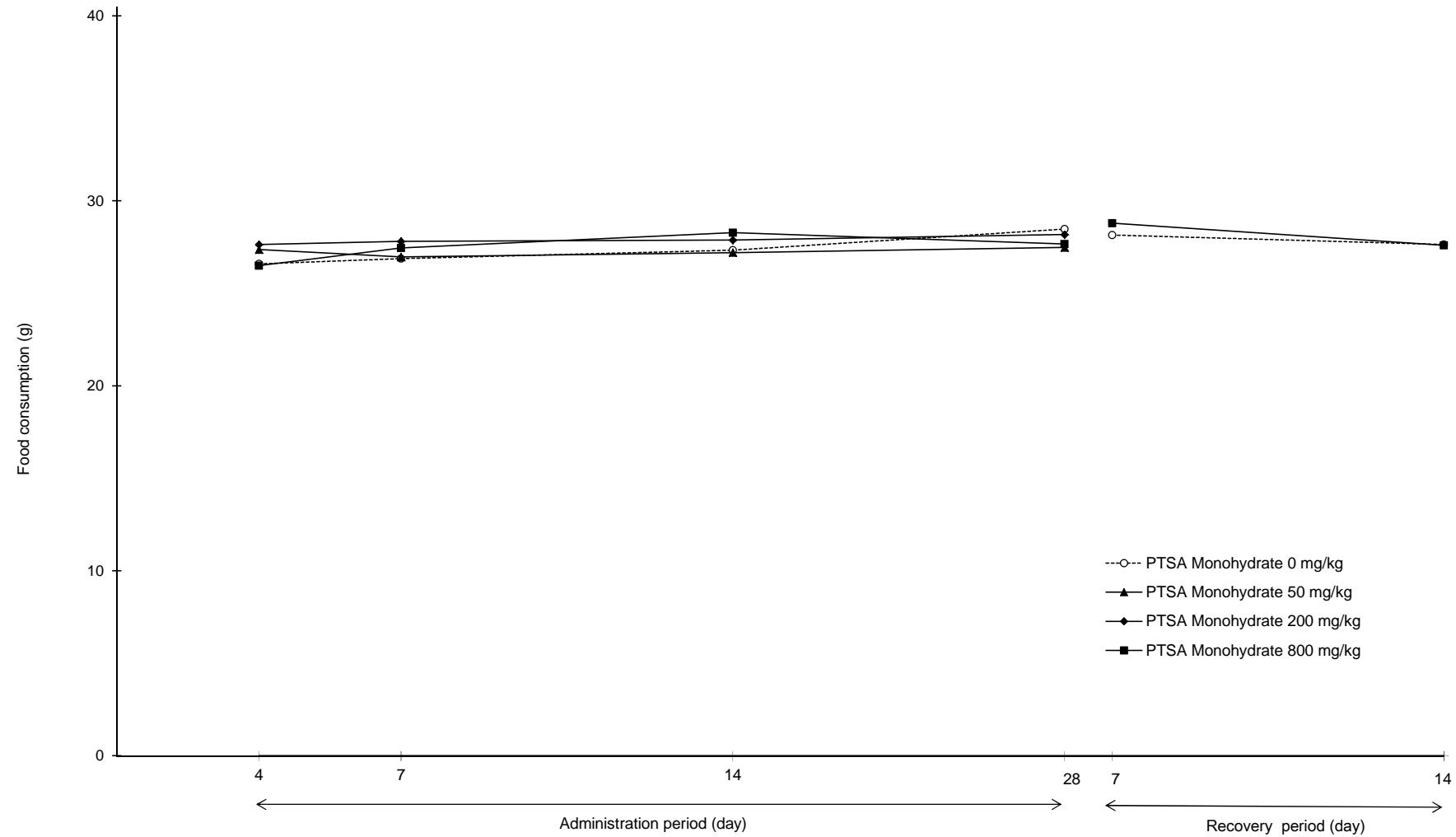


Figure 2 - 2

Study No. : SR15146

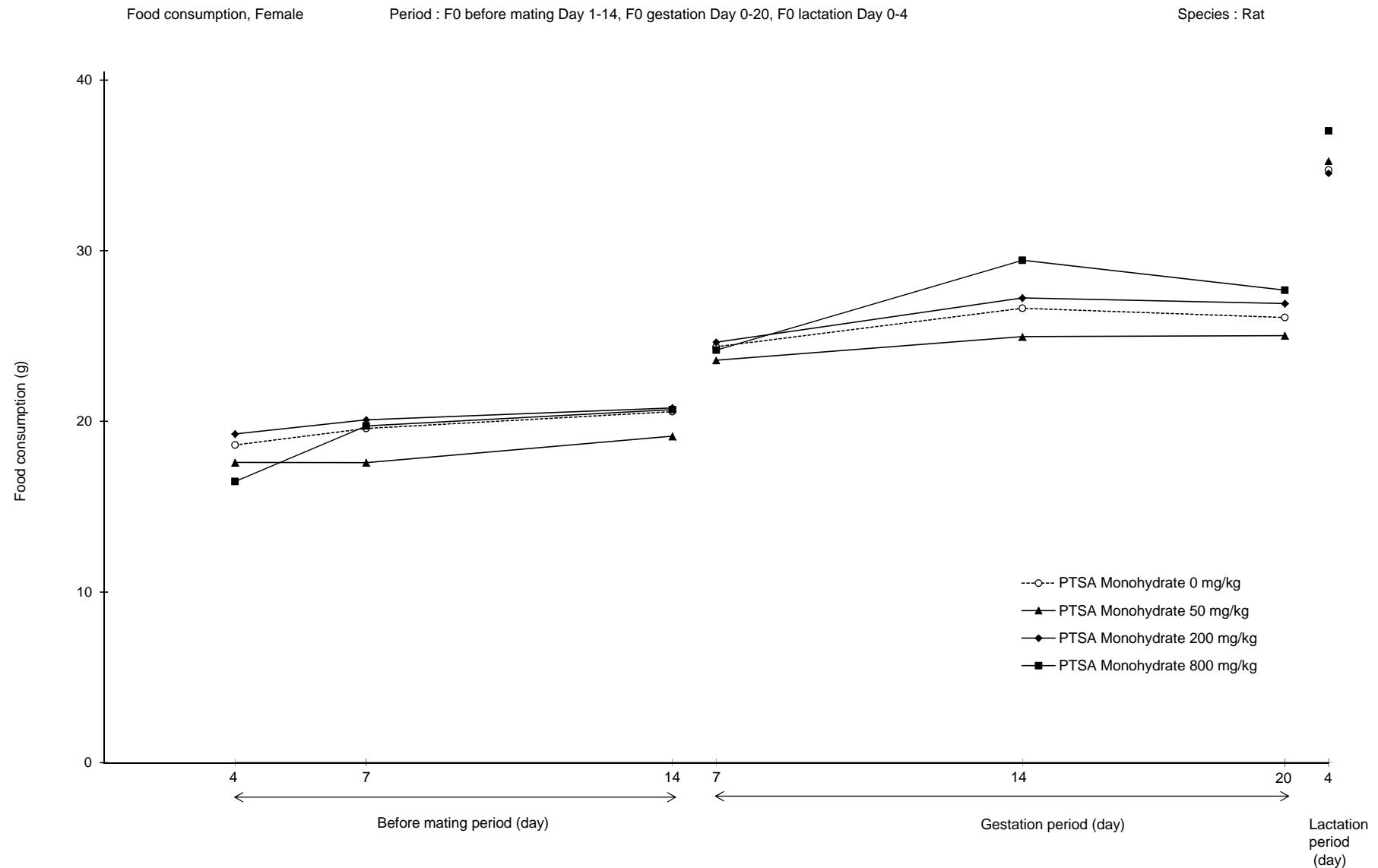


Figure 2 - 3

Study No. : SR15146

Food consumption, Female (satellite) Period : Administration day 1-28, Recovery day 1-14

Species : Rat

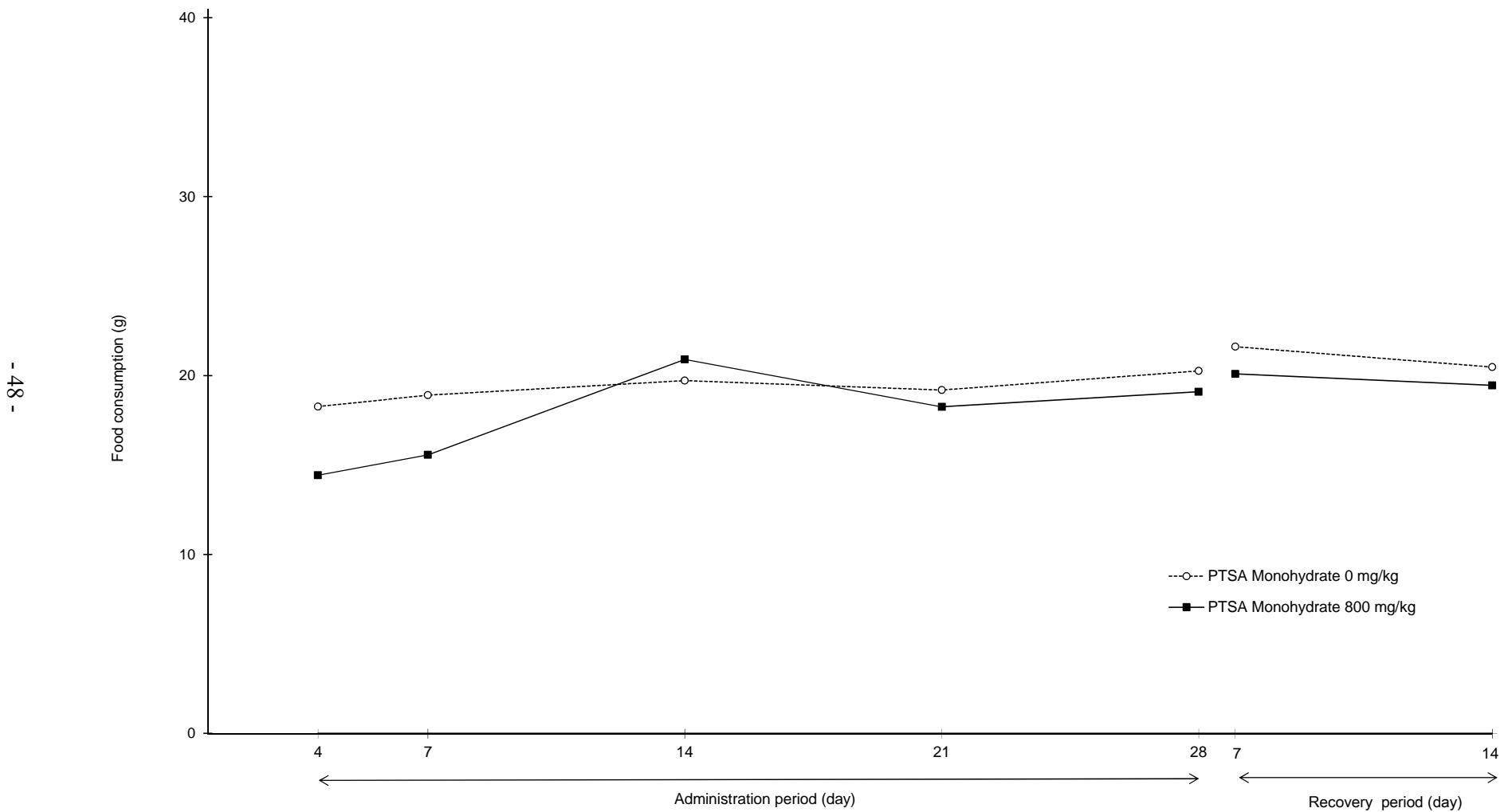


Figure 3

Study No. : SR15146

Body weight of offspring

Period : Postnatal Day 0-4

Species : Rat

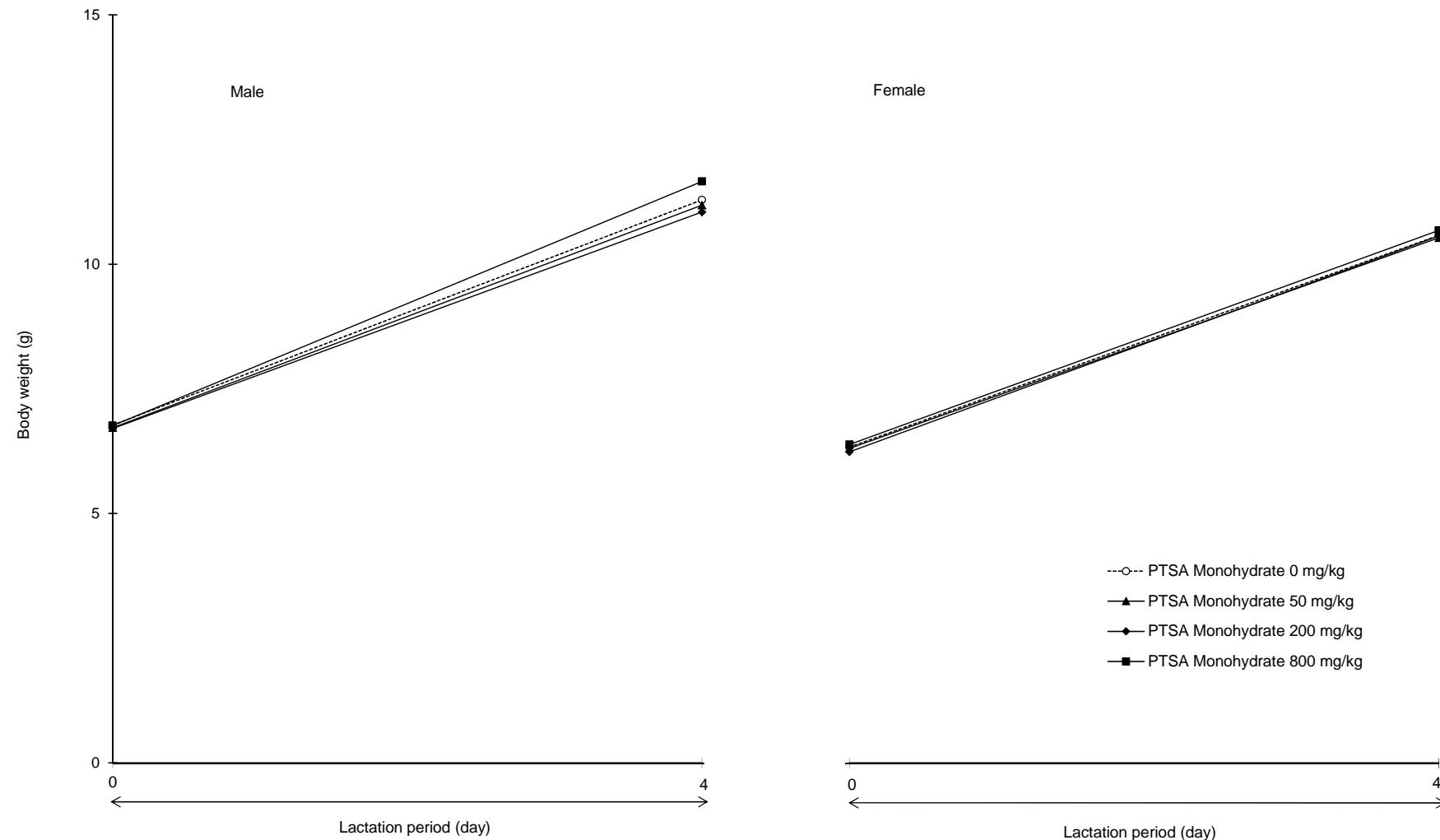


Table 1 - 1

Study No. : SR15146

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29 |      |    |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |
|-----------------------------|----------------|----------------------------------|------|----|----|----|----|----|----|----|----|----|----|----|----|---------------|----|
| Test article                | Dose           | Clinical signs                   | Day  |    | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  |    |    |    |               |    |
|                             |                |                                  | Time |    | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             |    |
| PTSA Monohydrate            | n              |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 0 mg/kg                     | No abnormality |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 50 mg/kg                    | No abnormality |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 200 mg/kg                   | No abnormality |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 800 mg/kg                   | No abnormality |                                  |      |    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| Test article                |                | Day                              |      | 9  | 10 | 11 | 12 | 13 | 14 | 15 | 16 |    |    |    |    |               |    |
| Dose                        | Clinical signs | Time                             |      | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1             | 2  |
|                             |                | Time                             |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 0 mg/kg                     | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 50 mg/kg                    | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 200 mg/kg                   | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 800 mg/kg                   | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| Test article                |                | Day                              |      | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |    |    |    |    |               |    |
| Dose                        | Clinical signs | Time                             |      | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1             | 2  |
|                             |                | Time                             |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 0 mg/kg                     | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 50 mg/kg                    | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 200 mg/kg                   | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 800 mg/kg                   | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| Test article                |                | Day                              |      | 25 | 26 | 27 | 28 | 29 |    |    |    |    |    |    |    |               |    |
| Dose                        | Clinical signs | Time                             |      | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 3  |    |    |    |               |    |
|                             |                | Time                             |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 7  |    |    |    |               |    |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 7  |    |    |    |               |    |
| 0 mg/kg                     | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 7  |    |    |    |               |    |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |    |    |    |               |    |
| 50 mg/kg                    | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |    |    |    |               |    |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |    |    |    |               |    |
| 200 mg/kg                   | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |    |    |    |               |    |
| PTSA Monohydrate            | n              |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 7  |    |    |    |               |    |
| 800 mg/kg                   | No abnormality |                                  |      | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 7  |    |    |    |               |    |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

Table 1 - 2

Study No. : SR15146

| Clinical sign<br>Sex : Female |                | Period : F0 before mating Day 1-14 |    |    |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |
|-------------------------------|----------------|------------------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|---------------|----|
|                               |                | Day 1                              |    | 2  |    | 3  |    | 4  |    | 5  |    | 6  |    | 7  |    |               |    |
| Test article                  | Dose           | Time                               | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             |    |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 0 mg/kg                       | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 50 mg/kg                      | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 200 mg/kg                     | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 800 mg/kg                     | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| Test article                  |                | Day 9                              |    | 10 |    | 11 |    | 12 |    | 13 |    | 14 |    |    |    |               |    |
|                               |                | Time                               | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |               |    |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 0 mg/kg                       | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 50 mg/kg                      | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 200 mg/kg                     | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate              | n              |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| 800 mg/kg                     | No abnormality |                                    | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |

F0 before mating)1 : Pre-dosing, 2 : Post-dosing

Table 1 - 3

Study No. : SR15146

| Test article<br>Dose          | Clinical sign<br>Sex : Female | Period : F0 mating Day 15-27 |    |    |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |   |
|-------------------------------|-------------------------------|------------------------------|----|----|---|----|---|----|---|----|---|----|---|----|---|---------------|---|---|
|                               |                               | Day 15                       |    | 16 |   | 17 |   | 18 |   | 19 |   | 20 |   | 21 |   |               |   |   |
|                               |                               | Time                         | 1  | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             |   |   |
| PTSA Monohydrate<br>0 mg/kg   | n<br>No abnormality           |                              | 8  | 8  | 7 | 7  | 7 | 7  | 1 | 1  | 1 | 1  | 1 | 1  | 1 | 1             | 0 | 0 |
| PTSA Monohydrate<br>50 mg/kg  | n<br>No abnormality           |                              | 10 | 10 | 9 | 9  | 8 | 8  | 0 | 0  | 0 | 0  | 0 | 0  | 0 | 0             | 0 | 0 |
| PTSA Monohydrate<br>200 mg/kg | n<br>No abnormality           |                              | 8  | 8  | 4 | 4  | 2 | 2  | 1 | 1  | 1 | 1  | 1 | 1  | 1 | 1             | 1 | 1 |
| PTSA Monohydrate<br>800 mg/kg | n<br>No abnormality           |                              | 8  | 8  | 6 | 6  | 5 | 5  | 0 | 0  | 0 | 0  | 0 | 0  | 0 | 0             | 0 | 0 |
| Test article<br>Dose          |                               | Day 23                       |    | 24 |   | 25 |   | 26 |   | 27 |   |    |   |    |   |               |   |   |
|                               |                               | Time                         | 1  | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  |   |    |   |               |   |   |
| PTSA Monohydrate<br>0 mg/kg   | n<br>No abnormality           |                              | 0  | 0  | 0 | 0  | 0 | 0  | 0 | 0  | 0 | 0  |   |    |   |               |   |   |
| PTSA Monohydrate<br>50 mg/kg  | n<br>No abnormality           |                              | 0  | 0  | 0 | 0  | 0 | 0  | 0 | 0  | 0 | 0  |   |    |   |               |   |   |
| PTSA Monohydrate<br>200 mg/kg | n<br>No abnormality           |                              | 1  | 1  | 1 | 1  | 1 | 1  | 1 | 1  | 1 | 1  |   |    |   |               |   |   |
| PTSA Monohydrate<br>800 mg/kg | n<br>No abnormality           |                              | 0  | 0  | 0 | 0  | 0 | 0  | 0 | 0  | 0 | 0  |   |    |   |               |   |   |

F0 mating 1 : Pre-dosing, 2 : Post-dosing

Table 1 - 4

Study No. : SR15146

| Clinical sign<br>Sex : Female |                | Period : F0 gestation Day 0-22 |      |    |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |
|-------------------------------|----------------|--------------------------------|------|----|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|
|                               |                | Day 0                          |      | 1  |    | 2  |    | 3  |    | 4  |    | 5  |    | 6  |    |               |    |    |
| Test article                  | Dose           | Time                           | 1    | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             |    |    |
| PTSA Monohydrate              | n              |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| 0 mg/kg                       | No abnormality |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| PTSA Monohydrate              | n              |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| 50 mg/kg                      | No abnormality |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| PTSA Monohydrate              | n              |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| 200 mg/kg                     | No abnormality |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| PTSA Monohydrate              | n              |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| 800 mg/kg                     | No abnormality |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| Test article                  |                | Day 8                          |      | 9  |    | 10 |    | 11 |    | 12 |    | 13 |    | 14 |    | 15            |    |    |
|                               |                | Clinical signs                 | Time | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1             | 2  |    |
| PTSA Monohydrate              | n              |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| 0 mg/kg                       | No abnormality |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| PTSA Monohydrate              | n              |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| 50 mg/kg                      | No abnormality |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| PTSA Monohydrate              | n              |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| 200 mg/kg                     | No abnormality |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 | 12 |
| PTSA Monohydrate              | n              |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| 800 mg/kg                     | No abnormality |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 | 11 |
| Test article                  |                | Day 16                         |      | 17 |    | 18 |    | 19 |    | 20 |    | 21 |    | 22 |    |               |    |    |
|                               |                | Clinical signs                 | Time | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |               |    |    |
| PTSA Monohydrate              | n              |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 1             | 1  |    |
| 0 mg/kg                       | No abnormality |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 1             | 1  |    |
| PTSA Monohydrate              | n              |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 3             | 3  |    |
| 50 mg/kg                      | No abnormality |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 3             | 3  |    |
| PTSA Monohydrate              | n              |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 1             | 1  |    |
| 200 mg/kg                     | No abnormality |                                | 12   | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 1             | 1  |    |
| PTSA Monohydrate              | n              |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 2             | 2  |    |
| 800 mg/kg                     | No abnormality |                                | 11   | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 2             | 2  |    |

F0 gestation)1 : Pre-dosing, 2 : Post-dosing

Table 1 - 5

Study No. : SR15146

| Test article<br>Dose          | Clinical sign<br>Sex : Female<br>Clinical signs | Period : F0 lactation Day 0-5 |    |    |    |    |    |    |    |    |    | Species : Rat |    |
|-------------------------------|---|-------------------------------|----|----|----|----|----|----|----|----|----|---------------|----|
|                               |   | Day                           |    | 0  |    | 1  |    | 2  |    | 3  |    |               |    |
|                               |   | Time                          | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             |    |
| PTSA Monohydrate<br>0 mg/kg   | n<br>No abnormality                             |                               | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 |
| PTSA Monohydrate<br>50 mg/kg  | n<br>No abnormality                             |                               | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11            | 11 |
| PTSA Monohydrate<br>200 mg/kg | n<br>No abnormality                             |                               | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
| PTSA Monohydrate<br>800 mg/kg | n<br>No abnormality<br>Dyspnea<br>Death         |                               | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12            | 12 |
|                               |   |                               | 11 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 |
|                               |   |                               | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 |
|                               |   |                               | 1  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |
|                               |   |                               | 1  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |

F0 lactation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

Table 1 - 6

Study No. : SR15146

| Clinical sign<br>Sex : Female (satellite) |                                | Period : Administration Day 1-29 |    |        |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |  |
|---|--------------------------------|----------------------------------|----|--------|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|--|
| Test article                              | Dose                           | Clinical signs                   |    | Day 1  |    | 2  |    | 3  |    | 4  |    | 5  |    | 6  |    | 7             |    |    |  |
|   |                                | Time                             | 1  | 2      | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  |  |
| PTSA Monohydrate                          | n                              |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 | 10 |  |
| 0 mg/kg                                   | No abnormality                 |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 | 10 |  |
| PTSA Monohydrate                          | n                              |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 9  | 9  |  |
| 800 mg/kg                                 | No abnormality                 |                                  | 10 | 9      | 9  | 9  | 8  | 7  | 7  | 7  | 8  | 8  | 8  | 9  | 9  | 9             | 9  | 9  |  |
|   | Death                          |                                  | 0  | 0      | 0  | 0  | 1  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Decrease in locomotor activity |                                  | 0  | 0      | 0  | 1  | 0  | 1  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Staggering gait                |                                  | 0  | 1      | 0  | 0  | 0  | 1  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Soil of perinasal fur          |                                  | 0  | 0      | 0  | 0  | 1  | 1  | 1  | 1  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Soil of perigenital fur        |                                  | 0  | 0      | 1  | 1  | 1  | 2  | 2  | 2  | 1  | 1  | 0  | 0  | 0  | 0             | 0  | 0  |  |
| Test article                              | Dose                           | Clinical signs                   |    | Day 9  |    | 10 |    | 11 |    | 12 |    | 13 |    | 14 |    | 15            |    | 16 |  |
| Time                                      | 1                              | 2                                | 1  | 2      | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  |  |
| PTSA Monohydrate                          | n                              |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 | 10 |  |
| 0 mg/kg                                   | No abnormality                 |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 | 10 |  |
| PTSA Monohydrate                          | n                              |                                  | 9  | 9      | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 9  | 9  |  |
| 800 mg/kg                                 | No abnormality                 |                                  | 9  | 9      | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 9  | 9  |  |
|   | Death                          |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Decrease in locomotor activity |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Staggering gait                |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Soil of perinasal fur          |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Soil of perigenital fur        |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
| Test article                              | Dose                           | Clinical signs                   |    | Day 17 |    | 18 |    | 19 |    | 20 |    | 21 |    | 22 |    | 23            |    | 24 |  |
| Time                                      | 1                              | 2                                | 1  | 2      | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  |  |
| PTSA Monohydrate                          | n                              |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 | 10 |  |
| 0 mg/kg                                   | No abnormality                 |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 10 | 10 |  |
| PTSA Monohydrate                          | n                              |                                  | 9  | 9      | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 9  | 9  |  |
| 800 mg/kg                                 | No abnormality                 |                                  | 9  | 9      | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 9  | 9  |  |
|   | Death                          |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Decrease in locomotor activity |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Staggering gait                |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Soil of perinasal fur          |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  | 0  |  |
|   | Soil of perigenital fur        |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 1  | 1  | 0  | 0             | 0  | 0  |  |
| Test article                              | Dose                           | Clinical signs                   |    | Day 25 |    | 26 |    | 27 |    | 28 |    | 29 |    |    |    |               |    |    |  |
| Time                                      | 1                              | 2                                | 1  | 2      | 1  | 2  | 1  | 2  | 1  | 2  |    |    |    |    |    |               |    |    |  |
| PTSA Monohydrate                          | n                              |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 5  |    |  |
| 0 mg/kg                                   | No abnormality                 |                                  | 10 | 10     | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10            | 5  |    |  |
| PTSA Monohydrate                          | n                              |                                  | 9  | 9      | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 5  |    |  |
| 800 mg/kg                                 | No abnormality                 |                                  | 9  | 9      | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9  | 9             | 5  |    |  |
|   | Death                          |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |    |  |
|   | Decrease in locomotor activity |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |    |  |
|   | Staggering gait                |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |    |  |
|   | Soil of perinasal fur          |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |    |  |
|   | Soil of perigenital fur        |                                  | 0  | 0      | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 0             | 0  |    |  |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

In the 800 mg/kg group, the findings except soil of fur appeared immediately after dosing and disappeared by approximately 1 hr after dosing.

Table 1 - 7

Study No. : SR15146

| Clinical sign<br>Sex : Male |                | Period : Recovery Day 1-15 |   |   |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |   |
|-----------------------------|----------------|----------------------------|---|---|---|----|---|----|---|----|---|----|---|----|---|---------------|---|---|
|                             |                | Day                        |   | 1 |   | 2  |   | 3  |   | 4  |   | 5  |   | 6  |   | 7             |   |   |
| Test article                | Dose           | Time                       | 1 | 2 | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2 |
| PTSA Monohydrate            | n              |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| 0 mg/kg                     | No abnormality |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| PTSA Monohydrate            | n              |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| 800 mg/kg                   | No abnormality |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| Test article                |                | Day                        |   | 9 |   | 10 |   | 11 |   | 12 |   | 13 |   | 14 |   | 15            |   |   |
|                             |                | Time                       | 1 | 2 | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 3 |   |
| PTSA Monohydrate            | n              |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 |   |
| 0 mg/kg                     | No abnormality |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 |   |
| PTSA Monohydrate            | n              |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 |   |
| 800 mg/kg                   | No abnormality |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 |   |

Recovery)1 : AM, 2 : PM, 3 : Necropsy day

Table 1 - 8

Study No. : SR15146

| Clinical sign<br>Sex : Female (satellite) |                | Period : Recovery Day 1-15 |   |   |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |   |
|---|----------------|----------------------------|---|---|---|----|---|----|---|----|---|----|---|----|---|---------------|---|---|
|   |                | Day                        |   | 1 |   | 2  |   | 3  |   | 4  |   | 5  |   | 6  |   | 7             |   |   |
| Test article                              | Dose           | Time                       | 1 | 2 | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2 |
| PTSA Monohydrate                          | n              |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| 0 mg/kg                                   | No abnormality |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| PTSA Monohydrate                          | n              |                            | 4 | 4 | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4             | 4 | 4 |
| 800 mg/kg                                 | No abnormality |                            | 4 | 4 | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4             | 4 | 4 |
| Test article                              |                | Day                        |   | 9 |   | 10 |   | 11 |   | 12 |   | 13 |   | 14 |   | 15            |   |   |
|   |                | Time                       | 1 | 2 | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 3 |   |
| PTSA Monohydrate                          | n              |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| 0 mg/kg                                   | No abnormality |                            | 5 | 5 | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5  | 5 | 5             | 5 | 5 |
| PTSA Monohydrate                          | n              |                            | 4 | 4 | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4             | 4 | 4 |
| 800 mg/kg                                 | No abnormality |                            | 4 | 4 | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4  | 4 | 4             | 4 | 4 |

Recovery)1 : AM, 2 : PM, 3 : Necropsy day

Table 2 - 1

Study No. : SR15146

Detailed clinical observation (in the cage)  
Sex : Male

Species : Rat

| Stage  | Group     | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Stereotype |    | Bizarre behavior |
|--------|-----------|---------------------------|------------------------|-----------------------|------------|----|------------------|
|        |           |                           |                        |                       | 1          | 1  | 1                |
| Pre    | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 7  | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 14 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 21 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 28 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal,rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic,systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 2 - 2

Study No. : SR15146

## Detailed clinical observation (in the cage)

Sex : Female

Species : Rat

| Stage  | Group     | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Stereotype |    | Bizarre behavior |
|--------|-----------|---------------------------|------------------------|-----------------------|------------|----|------------------|
|        |           |                           |                        |                       | 1          | 1  | 1                |
| Pre    | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 7  | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 14 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 21 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 28 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 35 | 0 mg/kg   | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 50 mg/kg  | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 200 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
|        | 800 mg/kg | n                         | 12                     | 12                    | 12         | 12 | 12               |
| Day 42 | 0 mg/kg   | n                         | 8                      | 8                     | 8          | 8  | 8                |
|        | 50 mg/kg  | n                         | 10                     | 10                    | 10         | 10 | 10               |
|        | 200 mg/kg | n                         | 8                      | 8                     | 8          | 8  | 8                |
|        | 800 mg/kg | n                         | 7                      | 7                     | 7          | 7  | 7                |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal,rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic,systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 2 - 3

Study No. : SR15146

Detailed clinical observation (in the cage)  
 Sex : Female (satellite)

Species : Rat

| Stage  | Group     | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Stereotype |                        | Bizarre behavior |
|--------|-----------|---------------------------|------------------------|-----------------------|------------|------------------------|------------------|
|        |           |                           |                        |                       | Rolling    | Repetitive<br>circling | Self biting      |
| Pre    | 0 mg/kg   | n                         | 10                     | 10                    | 10         | 10                     | 10               |
|        | 800 mg/kg | n                         | 10                     | 10                    | 10         | 10                     | 10               |
| Day 7  | 0 mg/kg   | n                         | 10                     | 10                    | 10         | 10                     | 10               |
|        | 800 mg/kg | n                         | 9                      | 9                     | 9          | 9                      | 9                |
| Day 14 | 0 mg/kg   | n                         | 10                     | 10                    | 10         | 10                     | 10               |
|        | 800 mg/kg | n                         | 9                      | 9                     | 9          | 9                      | 9                |
| Day 21 | 0 mg/kg   | n                         | 10                     | 10                    | 10         | 10                     | 10               |
|        | 800 mg/kg | n                         | 9                      | 9                     | 9          | 9                      | 9                |
| Day 28 | 0 mg/kg   | n                         | 10                     | 10                    | 10         | 10                     | 10               |
|        | 800 mg/kg | n                         | 9                      | 9                     | 9          | 9                      | 9                |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 2 - 4

Study No. : SR15146

Detailed clinical observation (in the cage)  
Sex : Male

Species : Rat

| Stage    | Group     | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Stereotype |   | Bizarre behavior |
|----------|-----------|---------------------------|------------------------|-----------------------|------------|---|------------------|
|          |           |                           |                        |                       | 1          | 1 | 1                |
| Recovery | 0 mg/kg   | n                         | 5                      | 5                     | 5          | 5 | 5                |
| Day 7    | 800 mg/kg | n                         | 5                      | 5                     | 5          | 5 | 5                |
| Recovery | 0 mg/kg   | n                         | 5                      | 5                     | 5          | 5 | 5                |
| Day 14   | 800 mg/kg | n                         | 5                      | 5                     | 5          | 5 | 5                |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal,rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic,systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 2 - 5

Study No. : SR15146

Detailed clinical observation (in the cage)  
Sex : Female (satellite)

Species : Rat

| Stage    | Group     | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Stereotype |   | Bizarre behavior |
|----------|-----------|---------------------------|------------------------|-----------------------|------------|---|------------------|
|          |           |                           |                        |                       | 1          | 1 | 1                |
| Recovery | 0 mg/kg   | n                         | 5                      | 5                     | 5          | 5 | 5                |
| Day 7    | 800 mg/kg | n                         | 4                      | 4                     | 4          | 4 | 4                |
| Recovery | 0 mg/kg   | n                         | 5                      | 5                     | 5          | 5 | 5                |
| Day 14   | 800 mg/kg | n                         | 4                      | 4                     | 4          | 4 | 4                |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 3 - 1

Study No. : SR15146

## Detailed clinical observation (on the hand)

Sex : Male

Species : Rat

| Stage  | Group     | Ease of |          | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes |    | Pupil size | Lacration | Salivation | Secretions/Excretions |    |
|--------|-----------|---------|----------|-------------|--------------|-----|------|------------------|----|------------|-----------|------------|-----------------------|----|
|        |           | Removal | Handling |             |              |     |      | 1                | 0  |            |           |            | 1                     | 0  |
| Pre    | 0 mg/kg   | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 50 mg/kg  | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 200 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 800 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
| Day 7  | 0 mg/kg   | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 50 mg/kg  | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 200 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 800 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
| Day 14 | 0 mg/kg   | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 50 mg/kg  | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 200 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 800 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
| Day 21 | 0 mg/kg   | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 50 mg/kg  | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 200 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 800 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
| Day 28 | 0 mg/kg   | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 50 mg/kg  | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 200 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |
|        | 800 mg/kg | n       | 12       | 12          | 12           | 12  | 12   | 12               | 12 | 12         | 12        | 12         | 12                    | 12 |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 3 - 2

Study No. : SR15146

Detailed clinical observation (on the hand)

Sex : Female

Species : Rat

| Stage  | Group     | Ease of |          | Muscle |              | Fur | Eyes | Mucous    |      | Pupil | Secretions/ |    |    |
|--------|-----------|---------|----------|--------|--------------|-----|------|-----------|------|-------|-------------|----|----|
|        |           | Removal | Handling | tone   | Piloerection |     |      | membranes | Skin |       | 1           | 1  | 0  |
|        |           | 1       | 1        | 2      | 1            | 1   | 1    | 0         | 1    | 1     | 1           | 1  | 0  |
| Pre    | 0 mg/kg   | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 50 mg/kg  | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 200 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 800 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
| Day 7  | 0 mg/kg   | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 50 mg/kg  | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 200 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 800 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
| Day 14 | 0 mg/kg   | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 50 mg/kg  | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 200 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 800 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
| Day 21 | 0 mg/kg   | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 50 mg/kg  | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 200 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 800 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
| Day 28 | 0 mg/kg   | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 50 mg/kg  | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 200 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 800 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
| Day 35 | 0 mg/kg   | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 50 mg/kg  | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 200 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
|        | 800 mg/kg | n       | 12       | 12     | 12           | 12  | 12   | 12        | 12   | 12    | 12          | 12 | 12 |
| Day 42 | 0 mg/kg   | n       | 8        | 8      | 8            | 8   | 8    | 8         | 8    | 8     | 8           | 8  | 8  |
|        | 50 mg/kg  | n       | 10       | 10     | 10           | 10  | 10   | 10        | 10   | 10    | 10          | 10 | 10 |
|        | 200 mg/kg | n       | 8        | 8      | 8            | 8   | 8    | 8         | 8    | 8     | 8           | 8  | 8  |
|        | 800 mg/kg | n       | 7        | 7      | 7            | 7   | 7    | 7         | 7    | 7     | 7           | 7  | 7  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 3 - 3

Study No. : SR15146

Detailed clinical observation (on the hand)  
Sex : Female (satellite)

Species : Rat

| Stage  | Group     | Ease of |          | Muscle tone | Piloerection | Fur |   | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation | Secretions/<br>Excretions |
|--------|-----------|---------|----------|-------------|--------------|-----|---|------|------------------|------|------------|-----------|------------|---------------------------|
|        |           | Removal | Handling |             |              | 1   | 2 |      |                  |      |            |           |            |                           |
| Pre    | 0 mg/kg   | n       | 10       | 10          | 10           | 10  | 0 | 10   | 10               | 10   | 10         | 10        | 10         | 10                        |
|        | 800 mg/kg | n       | 10       | 10          | 10           | 10  | 0 | 10   | 10               | 10   | 10         | 10        | 10         | 10                        |
| Day 7  | 0 mg/kg   | n       | 10       | 10          | 10           | 10  | 0 | 10   | 10               | 10   | 10         | 10        | 10         | 10                        |
|        | 800 mg/kg | n       | 9        | 9           | 9            | 9   | 0 | 9    | 9                | 9    | 9          | 9         | 9          | 9                         |
| Day 14 | 0 mg/kg   | n       | 10       | 10          | 10           | 10  | 0 | 10   | 10               | 10   | 10         | 10        | 10         | 10                        |
|        | 800 mg/kg | n       | 9        | 9           | 9            | 9   | 0 | 9    | 9                | 9    | 9          | 9         | 9          | 9                         |
| Day 21 | 0 mg/kg   | n       | 10       | 10          | 10           | 10  | 0 | 10   | 10               | 10   | 10         | 10        | 10         | 10                        |
|        | 800 mg/kg | n       | 9        | 9           | 9            | 9   | 1 | 9    | 9                | 9    | 9          | 9         | 9          | 9                         |
| Day 28 | 0 mg/kg   | n       | 10       | 10          | 10           | 10  | 0 | 10   | 10               | 10   | 10         | 10        | 10         | 10                        |
|        | 800 mg/kg | n       | 9        | 9           | 9            | 9   | 0 | 9    | 9                | 9    | 9          | 9         | 9          | 9                         |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 3 - 4

Study No. : SR15146

## Detailed clinical observation (on the hand)

Sex : Male

Species : Rat

| Stage           | Group     | Ease of |          | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes |   | Pupil size | Lacration | Salivation | Secretions/<br>Excretions |
|-----------------|-----------|---------|----------|-------------|--------------|-----|------|------------------|---|------------|-----------|------------|---------------------------|
|                 |           | Removal | Handling |             |              |     |      | 1                | 0 |            |           |            |                           |
| Recovery Day 7  | 0 mg/kg   | n       | 5        | 5           | 5            | 5   | 5    | 5                | 5 | 5          | 5         | 5          | 5                         |
|                 | 800 mg/kg | n       | 5        | 5           | 5            | 5   | 5    | 5                | 5 | 5          | 5         | 5          | 5                         |
| Recovery Day 14 | 0 mg/kg   | n       | 5        | 5           | 5            | 5   | 5    | 5                | 5 | 5          | 5         | 5          | 5                         |
|                 | 800 mg/kg | n       | 5        | 5           | 5            | 5   | 5    | 5                | 5 | 5          | 5         | 5          | 5                         |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 3 - 5

Study No. : SR15146

Detailed clinical observation (on the hand)

Sex : Female (satellite)

Species : Rat

| Stage           | Group     | Ease of |          | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes |   | Pupil size | Lacration | Salivation | Secretions/Excretions |   |
|-----------------|-----------|---------|----------|-------------|--------------|-----|------|------------------|---|------------|-----------|------------|-----------------------|---|
|                 |           | Removal | Handling |             |              |     |      | 1                | 0 |            |           |            | 1                     | 0 |
| Recovery Day 7  | 0 mg/kg   | n       | 5        | 5           | 5            | 5   | 5    | 5                | 5 | 5          | 5         | 5          | 5                     | 5 |
|                 | 800 mg/kg | n       | 4        | 4           | 4            | 4   | 4    | 4                | 4 | 4          | 4         | 4          | 4                     | 4 |
| Recovery Day 14 | 0 mg/kg   | n       | 5        | 5           | 5            | 5   | 5    | 5                | 5 | 5          | 5         | 5          | 5                     | 5 |
|                 | 800 mg/kg | n       | 4        | 4           | 4            | 4   | 4    | 4                | 4 | 4          | 4         | 4          | 4                     | 4 |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 4 - 1

Study No. : SR15146

## Detailed clinical observation (in the open-field)

Sex : Male

Species : Rat

| Stage  | Group     | Gait | Co-ordination<br>of movement | Reactivity to<br>stimuli | Searching | Urination | Defecation | Stereotype |   | Bizarre behavior      |                          |                     | Aggression |
|--------|-----------|------|------------------------------|--------------------------|-----------|-----------|------------|------------|---|-----------------------|--------------------------|---------------------|------------|
|        |           |      |                              |                          |           |           |            | 0          | 1 | Excessive<br>grooming | Unusual head<br>movement | Walking<br>backward |            |
| Pre    | 0 mg/kg   | n    | 12                           | 12                       | 12        | 7         | 5          | 7          | 5 | 11                    | 1                        | 12                  | 12         |
|        | 50 mg/kg  | n    | 12                           | 12                       | 12        | 10        | 2          | 10         | 2 | 12                    | 0                        | 12                  | 12         |
|        | 200 mg/kg | n    | 12                           | 12                       | 12        | 11        | 1          | 7          | 5 | 12                    | 0                        | 12                  | 12         |
|        | 800 mg/kg | n    | 12                           | 12                       | 12        | 10        | 2          | 9          | 3 | 12                    | 0                        | 12                  | 12         |
| Day 7  | 0 mg/kg   | n    | 12                           | 12                       | 12        | 11        | 1          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 50 mg/kg  | n    | 12                           | 12                       | 12        | 11        | 1          | 11         | 1 | 12                    | 0                        | 12                  | 12         |
|        | 200 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 800 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
| Day 14 | 0 mg/kg   | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 50 mg/kg  | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 200 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 800 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
| Day 21 | 0 mg/kg   | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 50 mg/kg  | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 200 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 800 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
| Day 28 | 0 mg/kg   | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 50 mg/kg  | n    | 12                           | 12                       | 12        | 11        | 1          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 200 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |
|        | 800 mg/kg | n    | 12                           | 12                       | 12        | 12        | 0          | 12         | 0 | 12                    | 0                        | 12                  | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 4 - 2

Study No. : SR15146

Detailed clinical observation (in the open-field)

Sex : Female

Species : Rat

| Stage  | Group     | Gait | Co-ordination |    | Reactivity to |    | Searching | Urination | Defecation | Stereotype |    | Bizarre behavior |    |                    |
|--------|-----------|------|---------------|----|---------------|----|-----------|-----------|------------|------------|----|------------------|----|--------------------|
|        |           |      | 1             | 1  | 1             | 1  |           |           |            | 0          | 1  | 0                | 0  | Excessive grooming |
| Pre    | 0 mg/kg   | n    | 12            | 12 | 12            | 12 | 8         | 4         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 50 mg/kg  | n    | 12            | 12 | 12            | 12 | 9         | 3         | 10         | 2          | 12 | 12               | 12 | 12                 |
|        | 200 mg/kg | n    | 12            | 12 | 12            | 12 | 10        | 2         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 800 mg/kg | n    | 12            | 12 | 12            | 12 | 8         | 4         | 10         | 2          | 12 | 12               | 12 | 12                 |
| Day 7  | 0 mg/kg   | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 50 mg/kg  | n    | 12            | 12 | 12            | 12 | 6         | 6         | ST \$      | 11         | 1  | 12               | 12 | 12                 |
|        | 200 mg/kg | n    | 12            | 12 | 12            | 12 | 10        | 2         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 800 mg/kg | n    | 12            | 12 | 12            | 12 | 11        | 1         | 11         | 1          | 12 | 12               | 12 | 12                 |
| Day 14 | 0 mg/kg   | n    | 12            | 12 | 12            | 12 | 11        | 1         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 50 mg/kg  | n    | 12            | 12 | 12            | 12 | 8         | 4         | 11         | 1          | 12 | 12               | 12 | 12                 |
|        | 200 mg/kg | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 800 mg/kg | n    | 12            | 12 | 12            | 12 | 9         | 3         | 11         | 1          | 12 | 12               | 12 | 12                 |
| Day 21 | 0 mg/kg   | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 50 mg/kg  | n    | 12            | 12 | 12            | 12 | 11        | 1         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 200 mg/kg | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 800 mg/kg | n    | 12            | 12 | 12            | 12 | 9         | 3         | 10         | 2          | 12 | 12               | 12 | 12                 |
| Day 28 | 0 mg/kg   | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 50 mg/kg  | n    | 12            | 12 | 12            | 12 | 11        | 1         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 200 mg/kg | n    | 12            | 12 | 12            | 12 | 11        | 1         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 800 mg/kg | n    | 12            | 12 | 12            | 12 | 11        | 1         | 12         | 0          | 12 | 12               | 12 | 12                 |
| Day 35 | 0 mg/kg   | n    | 12            | 12 | 12            | 12 | 11        | 1         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 50 mg/kg  | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 200 mg/kg | n    | 12            | 12 | 12            | 12 | 12        | 0         | 12         | 0          | 12 | 12               | 12 | 12                 |
|        | 800 mg/kg | n    | 12            | 12 | 12            | 12 | 10        | 2         | 11         | 1          | 12 | 12               | 12 | 12                 |
| Day 42 | 0 mg/kg   | n    | 8             | 8  | 8             | 8  | 8         | 0         | 8          | 0          | 8  | 8                | 8  | 8                  |
|        | 50 mg/kg  | n    | 10            | 10 | 10            | 10 | 8         | 2         | 10         | 0          | 10 | 10               | 10 | 10                 |
|        | 200 mg/kg | n    | 8             | 8  | 8             | 8  | 8         | 0         | 8          | 0          | 8  | 8                | 8  | 8                  |
|        | 800 mg/kg | n    | 7             | 7  | 7             | 7  | 7         | 0         | 7          | 0          | 7  | 7                | 7  | 7                  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

Significantly different from PTSA Monohydrate 0 mg/kg: \$ P&lt;0.05

ST : Steel test (two-side)

Table 4 - 3

Study No. : SR15146

Detailed clinical observation (in the open-field)

Sex : Female (satellite)

Species : Rat

| Stage  | Group     | Gait | Co-ordination |    | Reactivity to |    | Searching | Urination | Defecation | Stereotype         |                       | Bizarre behavior |              |            |
|--------|-----------|------|---------------|----|---------------|----|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|        |           |      | of movement   | 1  | stimuli       | 1  |           |           |            | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| Pre    | 0 mg/kg   | n    | 10            | 10 | 10            | 10 | 10        | 0         | 9          | 1                  | 10                    | 10               | 10           | 10         |
|        | 800 mg/kg | n    | 10            | 10 | 10            | 10 | 9         | 1         | 10         | 0                  | 10                    | 10               | 10           | 10         |
| Day 7  | 0 mg/kg   | n    | 10            | 10 | 10            | 10 | 10        | 0         | 10         | 0                  | 10                    | 10               | 10           | 10         |
|        | 800 mg/kg | n    | 9             | 9  | 9             | 9  | 9         | 0         | 9          | 0                  | 9                     | 9                | 9            | 9          |
| Day 14 | 0 mg/kg   | n    | 10            | 10 | 10            | 10 | 10        | 0         | 10         | 0                  | 10                    | 10               | 10           | 10         |
|        | 800 mg/kg | n    | 9             | 9  | 9             | 9  | 9         | 0         | 9          | 0                  | 9                     | 9                | 9            | 9          |
| Day 21 | 0 mg/kg   | n    | 10            | 10 | 10            | 10 | 10        | 0         | 10         | 0                  | 10                    | 10               | 10           | 10         |
|        | 800 mg/kg | n    | 9             | 9  | 9             | 9  | 9         | 0         | 9          | 0                  | 9                     | 9                | 9            | 9          |
| Day 28 | 0 mg/kg   | n    | 10            | 10 | 10            | 10 | 10        | 0         | 10         | 0                  | 10                    | 10               | 10           | 10         |
|        | 800 mg/kg | n    | 9             | 9  | 9             | 9  | 9         | 0         | 9          | 0                  | 9                     | 9                | 9            | 9          |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 4 - 4

Study No. : SR15146

Detailed clinical observation (in the open-field)

Sex : Male

Species : Rat

| Stage           | Group                | Gait   | Co-ordination |        | Reactivity to |        | Defecation | Stereotype         |                       | Bizarre behavior |              |            |
|-----------------|----------------------|--------|---------------|--------|---------------|--------|------------|--------------------|-----------------------|------------------|--------------|------------|
|                 |                      |        | of movement   | 1      | stimuli       | 1      |            | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| Recovery Day 7  | 0 mg/kg<br>800 mg/kg | n<br>n | 5<br>5        | 5<br>5 | 5<br>5        | 5<br>4 | 0<br>1     | 5<br>5             | 5<br>5                | 5<br>5           | 5<br>5       | 5<br>5     |
| Recovery Day 14 | 0 mg/kg<br>800 mg/kg | n<br>n | 5<br>5        | 5<br>5 | 5<br>5        | 5<br>5 | 0<br>0     | 5<br>5             | 5<br>5                | 5<br>5           | 5<br>5       | 5<br>5     |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 4 - 5

Study No. : SR15146

Detailed clinical observation (in the open-field)

Sex : Female (satellite)

Species : Rat

| Stage           | Group                | Gait   | Co-ordination |         | Reactivity to |           | Defecation | Stereotype         |                       | Bizarre behavior |              |            |
|-----------------|----------------------|--------|---------------|---------|---------------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|                 |                      |        | of movement   | stimuli | Searching     | Urination |            | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| Recovery Day 7  | 0 mg/kg<br>800 mg/kg | n<br>n | 5<br>4        | 5<br>4  | 5<br>4        | 5<br>4    | 5<br>4     | 5<br>4             | 5<br>4                | 5<br>4           | 5<br>4       | 5<br>4     |
| Recovery Day 14 | 0 mg/kg<br>800 mg/kg | n<br>n | 5<br>4        | 5<br>4  | 5<br>4        | 5<br>4    | 5<br>4     | 5<br>4             | 5<br>4                | 5<br>4           | 5<br>4       | 5<br>4     |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 5 - 1

Study No. : SR15146

Functional observations (on the desk)  
Sex : Male

Stage : Week 4

Species : Rat

| Group     | n | Reactivity  |            |               |           |                     | Righting<br>reflex |
|-----------|---|-------------|------------|---------------|-----------|---------------------|--------------------|
|           |   | Visual<br>4 | Touch<br>2 | Auditory<br>1 | Pain<br>2 | Proprioceptive<br>1 |                    |
| 0 mg/kg   | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 50 mg/kg  | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 200 mg/kg | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 800 mg/kg | n | 5           | 5          | 5             | 5         | 5                   | 5                  |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 5 - 2

Functional observations (on the desk)  
Sex : Female

Stage : Lactation day 4

Study No. : SR15146

Species : Rat

| Group     | n | Reactivity  |            |               |           |                     | Righting<br>reflex |
|-----------|---|-------------|------------|---------------|-----------|---------------------|--------------------|
|           |   | Visual<br>4 | Touch<br>2 | Auditory<br>1 | Pain<br>2 | Proprioceptive<br>1 |                    |
| 0 mg/kg   | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 50 mg/kg  | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 200 mg/kg | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 800 mg/kg | n | 5           | 5          | 5             | 5         | 5                   | 5                  |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1:Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 5 - 3

Study No. : SR15146

Functional observations (on the desk)  
Sex : Female (satellite)

Stage : Week 4

Species : Rat

| Group     | n | Reactivity  |            |               |           |                     | Righting<br>reflex |
|-----------|---|-------------|------------|---------------|-----------|---------------------|--------------------|
|           |   | Visual<br>4 | Touch<br>2 | Auditory<br>1 | Pain<br>2 | Proprioceptive<br>1 |                    |
| 0 mg/kg   | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 800 mg/kg | n | 4           | 4          | 4             | 4         | 4                   | 4                  |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 5 - 4

Study No. : SR15146

Functional observations (on the desk)  
Sex : Male

Stage : Recovery Week 2

Species : Rat

| Group     | n | Reactivity  |            |               |           |                     | Righting<br>reflex |
|-----------|---|-------------|------------|---------------|-----------|---------------------|--------------------|
|           |   | Visual<br>4 | Touch<br>2 | Auditory<br>1 | Pain<br>2 | Proprioceptive<br>1 |                    |
| 0 mg/kg   | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 800 mg/kg | n | 5           | 5          | 5             | 5         | 5                   | 5                  |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 5 - 5

Study No. : SR15146

Functional observations (on the desk)  
Sex : Female (satellite)

Stage : Recovery Week 2

Species : Rat

| Group     | n | Reactivity  |            |               |           |                     | Righting<br>reflex |
|-----------|---|-------------|------------|---------------|-----------|---------------------|--------------------|
|           |   | Visual<br>4 | Touch<br>2 | Auditory<br>1 | Pain<br>2 | Proprioceptive<br>1 |                    |
| 0 mg/kg   | n | 5           | 5          | 5             | 5         | 5                   | 5                  |
| 800 mg/kg | n | 4           | 4          | 4             | 4         | 4                   | 4                  |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 6 - 1

Study No. : SR15146

| Sex : Male       | Grip strength |          | Stage : Week 4 | Species : Rat |
|------------------|---------------|----------|----------------|---------------|
|                  | Forelimb      | Hindlimb |                |               |
| Test article     |               | g        |                |               |
| Dose             |               | g        |                |               |
| PTSA Monohydrate | n             | 5        | 5              |               |
| 0 mg/kg          | Mean          | 1592.80  | 734.40         |               |
|                  | S.D.          | 113.27   | 81.35          |               |
| PTSA Monohydrate | n             | 5        | 5              |               |
| 50 mg/kg         | Mean          | 1500.20  | 610.88         |               |
|                  | S.D.          | 255.42   | 107.58         |               |
| PTSA Monohydrate | n             | 5        | 5              |               |
| 200 mg/kg        | Mean          | 1502.72  | 595.08         |               |
|                  | S.D.          | 223.65   | 116.37         |               |
| PTSA Monohydrate | n             | 5        | 5              |               |
| 800 mg/kg        | Mean          | 1387.06  | 548.66         |               |
|                  | S.D.          | 110.97   | 95.47          |               |
|                  |               | DT *     |                |               |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

DT : Dunnett test (two-side)

Table 6 - 2

Study No. : SR15146

| Sex : Female     | Grip strength |          | Stage : Lactation Day 4 | Species : Rat |
|------------------|---------------|----------|-------------------------|---------------|
|                  | Forelimb      | Hindlimb |                         |               |
| Test article     | g             | g        |                         |               |
| Dose             |               |          |                         |               |
| PTSA Monohydrate | n             | 5        | 5                       |               |
| 0 mg/kg          | Mean          | 1144.46  | 476.66                  |               |
|                  | S.D.          | 102.68   | 77.63                   |               |
| PTSA Monohydrate | n             | 5        | 5                       |               |
| 50 mg/kg         | Mean          | 1330.20  | 527.68                  |               |
|                  | S.D.          | 122.11   | 79.12                   |               |
| PTSA Monohydrate | n             | 5        | 5                       |               |
| 200 mg/kg        | Mean          | 1100.26  | 390.12                  |               |
|                  | S.D.          | 159.58   | 56.01                   |               |
| PTSA Monohydrate | n             | 5        | 5                       |               |
| 800 mg/kg        | Mean          | 1247.56  | 471.78                  |               |
|                  | S.D.          | 120.51   | 47.72                   |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 6 - 3

Study No. : SR15146

|                  | Grip strength |          | Stage : Week 4 | Species : Rat |
|------------------|---------------|----------|----------------|---------------|
|                  | Forelimb      | Hindlimb |                |               |
| Test article     |               | g        | g              |               |
| Dose             |               |          |                |               |
| PTSA Monohydrate | n             | 5        | 5              |               |
| 0 mg/kg          | Mean          | 1063.60  | 437.08         |               |
|                  | S.D.          | 89.02    | 12.69          |               |
| PTSA Monohydrate | n             | 4        | 4              |               |
| 800 mg/kg        | Mean          | 1087.23  | 448.50         |               |
|                  | S.D.          | 83.39    | 70.94          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 6 - 4

Study No. : SR15146

| Grip strength<br>Sex : Male | Stage : Recovery Week 2 |          | Species : Rat |
|-----------------------------|-------------------------|----------|---------------|
|                             | Forelimb                | Hindlimb |               |
| Test article                | g                       | g        |               |
| Dose                        |                         |          |               |
| PTSA Monohydrate            | n                       | 5        |               |
| 0 mg/kg                     | Mean                    | 1700.92  | 677.94        |
|                             | S.D.                    | 169.36   | 74.07         |
| PTSA Monohydrate            | n                       | 5        |               |
| 800 mg/kg                   | Mean                    | 1639.98  | 551.08        |
|                             | S.D.                    | 200.82   | 175.36        |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 6 - 5

Study No. : SR15146

|                  | Grip strength            |          | Stage : Recovery Week 2 | Species : Rat |
|------------------|--------------------------|----------|-------------------------|---------------|
|                  | Sex : Female (satellite) | Forelimb |                         |               |
| Test article     |                          | g        | g                       |               |
| Dose             |                          |          |                         |               |
| PTSA Monohydrate | n                        | 5        | 5                       |               |
| 0 mg/kg          | Mean                     | 1156.66  | 464.00                  |               |
|                  | S.D.                     | 146.59   | 40.15                   |               |
| PTSA Monohydrate | n                        | 4        | 4                       |               |
| 800 mg/kg        | Mean                     | 1386.18  | 477.85                  |               |
|                  | S.D.                     | 109.36   | 77.58                   |               |
|                  | T2 *                     |          |                         |               |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

T2 : Student t-test (two-side)

Table 7 - 1

Study No. : SR15146

|                  | Motor activity measurements |       | Stage : Week 4 |           |           |           |           | Species : Rat |  |
|------------------|-----------------------------|-------|----------------|-----------|-----------|-----------|-----------|---------------|--|
|                  | Sex : Male                  |       | 0' - 10'       | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60'     |  |
| Test article     | No.                         | No.   | No.            | No.       | No.       | No.       | No.       | No.           |  |
| Dose             | n                           | 5     | 5              | 5         | 5         | 5         | 5         | 5             |  |
| PTSA Monohydrate | Mean                        | 503.0 | 414.8          | 230.8     | 215.8     | 195.8     | 129.8     | 1690.0        |  |
| 0 mg/kg          | S.D.                        | 194.2 | 88.0           | 105.4     | 156.0     | 94.7      | 54.5      | 583.5         |  |
| PTSA Monohydrate | n                           | 5     | 5              | 5         | 5         | 5         | 5         | 5             |  |
| 50 mg/kg         | Mean                        | 675.6 | 577.6          | 357.8     | 260.0     | 213.6     | 175.8     | 2260.4        |  |
|                  | S.D.                        | 303.7 | 349.1          | 191.2     | 114.8     | 181.3     | 118.0     | 769.4         |  |
| PTSA Monohydrate | n                           | 5     | 5              | 5         | 5         | 5         | 5         | 5             |  |
| 200 mg/kg        | Mean                        | 619.8 | 423.8          | 287.8     | 215.8     | 167.8     | 115.6     | 1830.6        |  |
|                  | S.D.                        | 178.9 | 167.0          | 137.9     | 143.5     | 164.0     | 120.9     | 760.7         |  |
| PTSA Monohydrate | n                           | 5     | 5              | 5         | 5         | 5         | 5         | 5             |  |
| 800 mg/kg        | Mean                        | 560.2 | 401.0          | 323.4     | 245.2     | 262.4     | 186.4     | 1978.6        |  |
|                  | S.D.                        | 360.4 | 248.4          | 222.3     | 181.6     | 228.2     | 111.9     | 1215.7        |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 7 - 2

Study No. : SR15146

| Test article<br>Dose          | Motor activity measurements<br>Sex : Female |                     |                     |                     |                     |                     |                     | Species : Rat         |
|-------------------------------|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|-----------------------|
|                               | 0' - 10'                                    | 10' - 20'           | 20' - 30'           | 30' - 40'           | 40' - 50'           | 50' - 60'           | 0' - 60'            |                       |
| PTSA Monohydrate<br>0 mg/kg   | n<br>Mean<br>S.D.                           | 5<br>539.6<br>306.0 | 5<br>250.6<br>289.6 | 5<br>155.0<br>154.0 | 5<br>192.8<br>288.0 | 5<br>142.4<br>279.9 | 5<br>168.0<br>370.6 | 5<br>1448.4<br>1488.0 |
| PTSA Monohydrate<br>50 mg/kg  | n<br>Mean<br>S.D.                           | 5<br>757.6<br>247.1 | 5<br>404.0<br>180.4 | 5<br>113.8<br>177.1 | 5<br>77.2<br>101.8  | 5<br>108.0<br>154.6 | 5<br>101.8<br>223.2 | 5<br>1562.4<br>550.5  |
| PTSA Monohydrate<br>200 mg/kg | n<br>Mean<br>S.D.                           | 5<br>562.6<br>212.1 | 5<br>291.2<br>227.9 | 5<br>147.6<br>93.5  | 5<br>70.6<br>123.5  | 5<br>57.6<br>128.8  | 5<br>79.8<br>163.2  | 5<br>1209.4<br>515.4  |
| PTSA Monohydrate<br>800 mg/kg | n<br>Mean<br>S.D.                           | 5<br>692.6<br>364.0 | 5<br>228.8<br>250.0 | 5<br>265.0<br>390.9 | 5<br>306.6<br>380.2 | 5<br>90.2<br>113.7  | 5<br>155.8<br>242.1 | 5<br>1739.0<br>1483.4 |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 7 - 3

Study No. : SR15146

| Test article<br>Dose     | Stage : Week 4 |           |           |           |           |           |          | Species : Rat |
|--------------------------|----------------|-----------|-----------|-----------|-----------|-----------|----------|---------------|
|                          | 0' - 10'       | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60' |               |
| Sex : Female (satellite) | No.            | No.       | No.       | No.       | No.       | No.       | No.      |               |
| PTSA Monohydrate         | n              | 5         | 5         | 5         | 5         | 5         | 5        |               |
| 0 mg/kg                  | Mean           | 1064.2    | 801.6     | 623.2     | 269.2     | 223.2     | 221.8    | 3203.2        |
|                          | S.D.           | 322.5     | 266.0     | 189.5     | 127.6     | 163.2     | 245.8    | 1043.4        |
| PTSA Monohydrate         | n              | 4         | 4         | 4         | 4         | 4         | 4        |               |
| 800 mg/kg                | Mean           | 1139.5    | 804.0     | 927.3     | 863.5     | 788.0     | 586.5    | 5108.8        |
|                          | S.D.           | 370.2     | 253.8     | 132.3     | 188.7     | 296.2     | 222.3    | 1157.7        |
|                          |                | T2 *      |           | T2 **     |           | T2 **     |          | T2 *          |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05, \*\* P&lt;0.01

T2 : Student t-test (two-side)

Table 7 - 4

Study No. : SR15146

|                  | Motor activity measurements |       | Stage : Recovery Week 2 |           |           |           |           | Species : Rat |  |
|------------------|-----------------------------|-------|-------------------------|-----------|-----------|-----------|-----------|---------------|--|
|                  | Sex : Male                  |       | 0' - 10'                | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60'     |  |
| Test article     | No.                         | No.   | No.                     | No.       | No.       | No.       | No.       | No.           |  |
| Dose             |                             |       |                         |           |           |           |           |               |  |
| PTSA Monohydrate | n                           | 5     | 5                       | 5         | 5         | 5         | 5         | 5             |  |
| 0 mg/kg          | Mean                        | 729.2 | 437.6                   | 395.4     | 229.2     | 260.2     | 185.4     | 2237.0        |  |
|                  | S.D.                        | 286.3 | 94.2                    | 160.7     | 156.7     | 106.5     | 37.4      | 654.2         |  |
| PTSA Monohydrate | n                           | 5     | 5                       | 5         | 5         | 5         | 5         | 5             |  |
| 800 mg/kg        | Mean                        | 877.8 | 562.0                   | 445.2     | 377.4     | 339.6     | 175.2     | 2777.2        |  |
|                  | S.D.                        | 321.5 | 268.7                   | 209.9     | 248.2     | 160.0     | 142.1     | 1146.3        |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 7 - 5

Study No. : SR15146

|                  | Motor activity measurements |       | Stage : Recovery Week 2 |           |           |           |           | Species : Rat |  |
|------------------|-----------------------------|-------|-------------------------|-----------|-----------|-----------|-----------|---------------|--|
|                  | Sex : Female (satellite)    |       | 0' - 10'                | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60'     |  |
| Test article     | No.                         | No.   | No.                     | No.       | No.       | No.       | No.       | No.           |  |
| Dose             |                             |       |                         |           |           |           |           |               |  |
| PTSA Monohydrate | n                           | 5     | 5                       | 5         | 5         | 5         | 5         | 5             |  |
| 0 mg/kg          | Mean                        | 824.0 | 691.4                   | 503.6     | 296.0     | 212.8     | 112.4     | 2640.2        |  |
|                  | S.D.                        | 369.1 | 306.7                   | 238.5     | 155.4     | 152.2     | 98.6      | 856.7         |  |
| PTSA Monohydrate | n                           | 4     | 4                       | 4         | 4         | 4         | 4         | 4             |  |
| 800 mg/kg        | Mean                        | 749.5 | 679.3                   | 375.8     | 295.8     | 193.0     | 161.0     | 2454.3        |  |
|                  | S.D.                        | 214.0 | 190.0                   | 133.6     | 76.2      | 133.1     | 142.5     | 578.7         |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 8 - 1

Study No. : SR15146

| Test article     | Dose | Body weight<br>Sex : Male |       | Period : Administration Day 1-28 |       |       |       |       | Unit : g | Species : Rat |       |
|------------------|------|---------------------------|-------|----------------------------------|-------|-------|-------|-------|----------|---------------|-------|
|                  |      | /Day                      |       | 1                                | 4     | 7     | 14    | 21    | 28       |               |       |
| PTSA Monohydrate | n    | 12                        | 12    | 12                               | 12    | 12    | 12    | 12    | 12       | 12            |       |
| 0 mg/kg          | Mean | 392.2                     | 406.3 | 418.7                            | 442.8 | 467.7 | 492.0 | 492.0 | 492.0    | 492.0         | 99.8  |
|                  | S.D. | 18.5                      | 22.1  | 26.0                             | 31.4  | 35.1  | 43.5  | 43.5  | 43.5     | 43.5          | 30.0  |
| PTSA Monohydrate | n    | 12                        | 12    | 12                               | 12    | 12    | 12    | 12    | 12       | 12            |       |
| 50 mg/kg         | Mean | 395.8                     | 406.6 | 419.0                            | 438.7 | 463.7 | 480.4 | 480.4 | 480.4    | 480.4         | 84.7  |
|                  | S.D. | 17.8                      | 20.9  | 22.4                             | 22.9  | 26.1  | 25.9  | 25.9  | 25.9     | 25.9          | 15.5  |
| PTSA Monohydrate | n    | 12                        | 12    | 12                               | 12    | 12    | 12    | 12    | 12       | 12            |       |
| 200 mg/kg        | Mean | 397.8                     | 410.8 | 425.7                            | 451.8 | 476.8 | 498.3 | 498.3 | 498.3    | 498.3         | 100.4 |
|                  | S.D. | 20.2                      | 22.8  | 24.0                             | 28.4  | 31.1  | 34.8  | 34.8  | 34.8     | 34.8          | 16.5  |
| PTSA Monohydrate | n    | 12                        | 12    | 12                               | 12    | 12    | 12    | 12    | 12       | 12            |       |
| 800 mg/kg        | Mean | 393.1                     | 403.3 | 417.1                            | 440.1 | 455.8 | 473.9 | 473.9 | 473.9    | 473.9         | 80.8  |
|                  | S.D. | 22.2                      | 27.1  | 24.6                             | 28.4  | 26.5  | 29.9  | 29.9  | 29.9     | 29.9          | 12.8  |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 8 - 2

Study No. : SR15146

| Test article<br>Dose          | Sex : Female<br>/Day | Period : F0 before mating Day 1-14 |       |       |       |                  | Unit : g | Species : Rat |
|-------------------------------|----------------------|------------------------------------|-------|-------|-------|------------------|----------|---------------|
|                               |                      | 1                                  | 4     | 7     | 14    | Body weight gain |          |               |
| PTSA Monohydrate<br>0 mg/kg   | n                    | 12                                 | 12    | 12    | 12    | 12               |          |               |
|                               | Mean                 | 248.8                              | 251.8 | 257.3 | 267.4 | 18.7             |          |               |
|                               | S.D.                 | 15.3                               | 17.3  | 20.9  | 26.6  | 13.0             |          |               |
| PTSA Monohydrate<br>50 mg/kg  | n                    | 12                                 | 12    | 12    | 12    | 12               |          |               |
|                               | Mean                 | 243.6                              | 248.6 | 251.8 | 259.3 | 15.7             |          |               |
|                               | S.D.                 | 15.6                               | 15.3  | 16.3  | 19.6  | 6.4              |          |               |
| PTSA Monohydrate<br>200 mg/kg | n                    | 12                                 | 12    | 12    | 12    | 12               |          |               |
|                               | Mean                 | 245.3                              | 250.8 | 257.6 | 270.0 | 24.7             |          |               |
|                               | S.D.                 | 16.9                               | 17.6  | 18.4  | 18.7  | 6.4              |          |               |
| PTSA Monohydrate<br>800 mg/kg | n                    | 12                                 | 12    | 12    | 12    | 12               |          |               |
|                               | Mean                 | 245.8                              | 246.2 | 253.1 | 265.0 | 19.3             |          |               |
|                               | S.D.                 | 16.8                               | 20.9  | 22.1  | 27.1  | 14.2             |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 8 - 3

Study No. : SR15146

| Test article     | Sex : Female | Period : F0 gestation Day 0-20 |       |       |       |       | Unit : g         | Species : Rat |
|------------------|--------------|--------------------------------|-------|-------|-------|-------|------------------|---------------|
|                  |              | /Day                           | 0     | 7     | 14    | 20    | Body weight gain |               |
| PTSA Monohydrate | n            | 11                             | 11    | 11    | 11    | 11    | 11               |               |
| 0 mg/kg          | Mean         | 274.9                          | 312.3 | 350.5 | 431.9 | 431.9 | 157.0            |               |
|                  | S.D.         | 26.5                           | 28.9  | 32.0  | 30.8  | 30.8  | 11.7             |               |
| PTSA Monohydrate | n            | 12                             | 12    | 12    | 12    | 12    | 12               |               |
| 50 mg/kg         | Mean         | 273.0                          | 307.3 | 343.4 | 426.5 | 426.5 | 153.5            |               |
|                  | S.D.         | 22.1                           | 25.3  | 26.5  | 28.8  | 28.8  | 13.2             |               |
| PTSA Monohydrate | n            | 12                             | 12    | 12    | 12    | 12    | 12               |               |
| 200 mg/kg        | Mean         | 278.7                          | 316.3 | 356.5 | 442.4 | 442.4 | 163.8            |               |
|                  | S.D.         | 26.0                           | 26.5  | 28.4  | 33.1  | 33.1  | 16.4             |               |
| PTSA Monohydrate | n            | 11                             | 11    | 11    | 11    | 11    | 11               |               |
| 800 mg/kg        | Mean         | 274.2                          | 311.0 | 358.5 | 436.9 | 436.9 | 162.7            |               |
|                  | S.D.         | 28.3                           | 34.1  | 38.7  | 45.7  | 45.7  | 27.7             |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 8 - 4

Study No. : SR15146

| Test article     | Sex : Female | Period : F0 lactation Day 0-4 |       |                  | Unit : g | Species : Rat |
|------------------|--------------|-------------------------------|-------|------------------|----------|---------------|
|                  |              | /Day                          | 0     | 4                |          |               |
| PTSA Monohydrate | n            | 11                            | 11    | Body weight gain |          |               |
|                  | Mean         | 330.8                         | 349.9 | 19.1             |          |               |
|                  | S.D.         | 36.4                          | 36.6  | 10.4             |          |               |
| PTSA Monohydrate | n            | 12                            | 12    | 12               |          |               |
|                  | Mean         | 325.3                         | 347.8 | 22.6             |          |               |
|                  | S.D.         | 26.2                          | 26.6  | 11.9             |          |               |
| PTSA Monohydrate | n            | 12                            | 12    | 12               |          |               |
|                  | Mean         | 336.3                         | 357.2 | 20.9             |          |               |
|                  | S.D.         | 28.0                          | 29.7  | 8.5              |          |               |
| PTSA Monohydrate | n            | 11                            | 9     | 9                |          |               |
|                  | Mean         | 334.3                         | 359.2 | 22.3             |          |               |
|                  | S.D.         | 40.4                          | 39.2  | 7.7              |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 8 - 5

Study No. : SR15146

| Test article<br>Dose          | Body weight<br>Sex : Female (satellite)<br>/Day | Period : Administration Day 1-28 |       |       |       |       |       | Unit : g | Species : Rat |
|-------------------------------|---|----------------------------------|-------|-------|-------|-------|-------|----------|---------------|
|                               |   | 1                                | 4     | 7     | 14    | 21    | 28    |          |               |
| PTSA Monohydrate<br>0 mg/kg   | n   | 10                               | 10    | 10    | 10    | 10    | 10    | 10       | 10            |
|                               | Mean  | 241.6                            | 246.2 | 251.1 | 257.4 | 271.7 | 283.0 | 41.4     |               |
|                               | S.D.  | 6.4                              | 7.8   | 11.0  | 11.4  | 12.1  | 12.2  | 12.7     |               |
| PTSA Monohydrate<br>800 mg/kg | n   | 10                               | 9     | 9     | 9     | 9     | 9     | 9        | 9             |
|                               | Mean  | 238.9                            | 236.9 | 244.4 | 265.9 | 262.9 | 277.2 | 37.0     |               |
|                               | S.D.  | 11.2                             | 10.6  | 13.3  | 17.2  | 17.0  | 19.4  | 14.3     |               |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

T2 : Student t-test (two-side)

Table 8 - 6

Study No. : SR15146

| Test article<br>Dose          | Body weight<br>Sex : Male<br>/Day | Period : Recovery Day 1-14 |                    |                    |                  |      | Unit : g | Species : Rat |
|-------------------------------|-----------------------------------|----------------------------|--------------------|--------------------|------------------|------|----------|---------------|
|                               |                                   | 1                          | 7                  | 14                 | Body weight gain |      |          |               |
| PTSA Monohydrate<br>0 mg/kg   | n<br>Mean<br>S.D.                 | 5<br>483.8<br>24.0         | 5<br>505.6<br>26.1 | 5<br>521.2<br>26.2 | 5<br>37.4<br>3.6 |      |          |               |
| PTSA Monohydrate<br>800 mg/kg | n<br>Mean<br>S.D.                 | 5<br>476.4<br>21.3         | 5<br>508.2<br>20.3 | 5<br>522.6<br>20.6 | 5<br>46.2<br>5.9 | T2 * |          |               |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

T2 : Student t-test (two-side)

Table 8 - 7

Study No. : SR15146

| Test article<br>Dose          | Body weight<br>Sex : Female (satellite) |       | Period : Recovery Day 1-14 |       |      | Unit : g            | Species : Rat |
|-------------------------------|---|-------|----------------------------|-------|------|---------------------|---------------|
|                               | /Day                                    |       | 1                          | 7     | 14   | Body weight<br>gain |               |
| PTSA Monohydrate<br>0 mg/kg   | n                                       | 5     | 5                          | 5     | 5    | 5                   |               |
|                               | Mean                                    | 285.2 | 296.2                      | 303.6 | 18.4 |                     |               |
|                               | S.D.                                    | 11.0  | 21.4                       | 14.9  | 8.6  |                     |               |
| PTSA Monohydrate<br>800 mg/kg | n                                       | 4     | 4                          | 4     | 4    |                     |               |
|                               | Mean                                    | 268.3 | 286.8                      | 297.3 | 29.0 |                     |               |
|                               | S.D.                                    | 29.3  | 32.5                       | 36.4  | 9.8  |                     |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 1

Study No. : SR15146

| Test article     | Sex : Male | Food consumption /Day |       |       |       | Period : Administration Day 1-28 | Unit : g | Species : Rat |
|------------------|------------|-----------------------|-------|-------|-------|----------------------------------|----------|---------------|
|                  |            | 4                     | 7     | 14    | 28    |                                  |          |               |
| PTSA Monohydrate | n          | 12                    | 12    | 12    | 11    |                                  |          |               |
| 0 mg/kg          | Mean       | 26.60                 | 26.88 | 27.34 | 28.47 |                                  |          |               |
|                  | S.D.       | 1.90                  | 2.58  | 2.41  | 2.78  |                                  |          |               |
| PTSA Monohydrate | n          | 12                    | 12    | 12    | 12    |                                  |          |               |
| 50 mg/kg         | Mean       | 27.37                 | 26.96 | 27.20 | 27.48 |                                  |          |               |
|                  | S.D.       | 2.45                  | 2.26  | 1.75  | 1.89  |                                  |          |               |
| PTSA Monohydrate | n          | 12                    | 12    | 12    | 11    |                                  |          |               |
| 200 mg/kg        | Mean       | 27.63                 | 27.81 | 27.88 | 28.17 |                                  |          |               |
|                  | S.D.       | 2.15                  | 2.27  | 2.31  | 2.89  |                                  |          |               |
| PTSA Monohydrate | n          | 12                    | 12    | 12    | 12    |                                  |          |               |
| 800 mg/kg        | Mean       | 26.50                 | 27.45 | 28.28 | 27.66 |                                  |          |               |
|                  | S.D.       | 3.61                  | 2.36  | 1.88  | 2.01  |                                  |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 2

Study No. : SR15146

| Test article     | Sex : Female | Food consumption /Day |       |       | Period : F0 before mating Day 1-14 | Unit : g | Species : Rat |
|------------------|--------------|-----------------------|-------|-------|------------------------------------|----------|---------------|
|                  |              | 4                     | 7     | 14    |                                    |          |               |
| PTSA Monohydrate | n            | 12                    | 12    | 12    |                                    |          |               |
| 0 mg/kg          | Mean         | 18.62                 | 19.59 | 20.58 |                                    |          |               |
|                  | S.D.         | 1.78                  | 2.15  | 1.86  |                                    |          |               |
| PTSA Monohydrate | n            | 12                    | 12    | 12    |                                    |          |               |
| 50 mg/kg         | Mean         | 17.59                 | 17.58 | 19.13 |                                    |          |               |
|                  | S.D.         | 1.60                  | 1.58  | 1.43  |                                    |          |               |
| PTSA Monohydrate | n            | 12                    | 12    | 12    |                                    |          |               |
| 200 mg/kg        | Mean         | 19.26                 | 20.09 | 20.79 |                                    |          |               |
|                  | S.D.         | 1.91                  | 2.30  | 2.06  |                                    |          |               |
| PTSA Monohydrate | n            | 12                    | 12    | 12    |                                    |          |               |
| 800 mg/kg        | Mean         | 16.48                 | 19.73 | 20.69 |                                    |          |               |
|                  | S.D.         | 4.09                  | 3.58  | 2.91  |                                    |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 3

Study No. : SR15146

| Test article     | Sex : Female | Food consumption /Day |       |       | Period : F0 gestation Day 0-20 | Unit : g | Species : Rat |
|------------------|--------------|-----------------------|-------|-------|--------------------------------|----------|---------------|
|                  |              | 7                     | 14    | 20    |                                |          |               |
| PTSA Monohydrate | n            | 11                    | 11    | 11    |                                |          |               |
| 0 mg/kg          | Mean         | 24.38                 | 26.64 | 26.09 |                                |          |               |
|                  | S.D.         | 2.65                  | 3.07  | 1.93  |                                |          |               |
| PTSA Monohydrate | n            | 12                    | 12    | 12    |                                |          |               |
| 50 mg/kg         | Mean         | 23.58                 | 24.96 | 25.03 |                                |          |               |
|                  | S.D.         | 1.54                  | 1.81  | 2.22  |                                |          |               |
| PTSA Monohydrate | n            | 12                    | 12    | 12    |                                |          |               |
| 200 mg/kg        | Mean         | 24.64                 | 27.24 | 26.90 |                                |          |               |
|                  | S.D.         | 1.99                  | 1.66  | 2.09  |                                |          |               |
| PTSA Monohydrate | n            | 11                    | 11    | 11    |                                |          |               |
| 800 mg/kg        | Mean         | 24.19                 | 29.44 | 27.69 |                                |          |               |
|                  | S.D.         | 4.49                  | 4.79  | 4.15  |                                |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 4

Study No. : SR15146

| Test article     | Food consumption |       | Period : F0 lactation Day 0-4 | Unit : g | Species : Rat |
|------------------|------------------|-------|-------------------------------|----------|---------------|
|                  | Sex : Female     | /Day  |                               |          |               |
| Dose             |                  | 4     |                               |          |               |
| PTSA Monohydrate | n                | 11    |                               |          |               |
| 0 mg/kg          | Mean             | 34.74 |                               |          |               |
|                  | S.D.             | 3.89  |                               |          |               |
| PTSA Monohydrate | n                | 12    |                               |          |               |
| 50 mg/kg         | Mean             | 35.25 |                               |          |               |
|                  | S.D.             | 3.63  |                               |          |               |
| PTSA Monohydrate | n                | 12    |                               |          |               |
| 200 mg/kg        | Mean             | 34.54 |                               |          |               |
|                  | S.D.             | 2.29  |                               |          |               |
| PTSA Monohydrate | n                | 9     |                               |          |               |
| 800 mg/kg        | Mean             | 37.03 |                               |          |               |
|                  | S.D.             | 4.90  |                               |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 5

Study No. : SR15146

| Test article     | Food consumption<br>Sex : Female (satellite) | Period : Administration Day 1-28 |       |       |       |       | Unit : g | Species : Rat |
|------------------|--|----------------------------------|-------|-------|-------|-------|----------|---------------|
|                  |  | /Day                             | 4     | 7     | 14    | 21    |          |               |
| Dose             |  |                                  | 4     | 7     | 14    | 21    | 28       |               |
| PTSA Monohydrate | n  |                                  | 10    | 10    | 10    | 10    | 10       |               |
| 0 mg/kg          | Mean   | 18.27                            | 18.91 | 19.72 | 19.19 | 20.26 |          |               |
|                  | S.D.   | 1.65                             | 2.13  | 1.75  | 1.68  | 1.93  |          |               |
| PTSA Monohydrate | n  |                                  | 9     | 9     | 9     | 9     | 9        |               |
| 800 mg/kg        | Mean   | 14.43                            | 15.58 | 20.91 | 18.26 | 19.09 |          |               |
|                  | S.D.   | 5.20                             | 5.68  | 3.27  | 1.78  | 3.20  |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 6

Study No. : SR15146

| Test article     | Food consumption<br>Sex : Male<br>/Day | Period : Recovery Day 1-14 |       | Unit : g | Species : Rat |
|------------------|--|----------------------------|-------|----------|---------------|
|                  |  | 7                          | 14    |          |               |
| PTSA Monohydrate | n                                      | 5                          | 5     |          |               |
| 0 mg/kg          | Mean                                   | 28.16                      | 27.64 |          |               |
|                  | S.D.                                   | 1.71                       | 1.10  |          |               |
| PTSA Monohydrate | n                                      | 5                          | 5     |          |               |
| 800 mg/kg        | Mean                                   | 28.80                      | 27.60 |          |               |
|                  | S.D.                                   | 1.24                       | 1.22  |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 9 - 7

Study No. : SR15146

| Test article     | Food consumption<br>Sex : Female (satellite) |       |       | Period : Recovery Day 1-14 | Unit : g | Species : Rat |
|------------------|--|-------|-------|----------------------------|----------|---------------|
|                  | /Day   | 7     | 14    |                            |          |               |
| Dose             |  |       |       |                            |          |               |
| PTSA Monohydrate | n  | 5     | 5     |                            |          |               |
| 0 mg/kg          | Mean   | 21.62 | 20.48 |                            |          |               |
|                  | S.D.   | 4.54  | 1.12  |                            |          |               |
| PTSA Monohydrate | n  | 4     | 4     |                            |          |               |
| 800 mg/kg        | Mean   | 20.10 | 19.45 |                            |          |               |
|                  | S.D.   | 3.80  | 3.38  |                            |          |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 1

Study No. : SR15146

| Urinary findings<br>Sex : Male |   | Stage : Week 4 |     |     |     |     |     |     |   | Species : Rat |   |
|--------------------------------|---|----------------|-----|-----|-----|-----|-----|-----|---|---------------|---|
|                                |   | pH             |     |     |     |     |     |     |   |               |   |
| <b>Test article</b>            |   |                |     |     |     |     |     |     |   |               |   |
| Dose                           |   | 5.0            | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |   |               |   |
| PTSA Monohydrate               | n | 0              | 0   | 0   | 0   | 0   | 0   | 5   |   |               |   |
| 0 mg/kg                        |   |                |     |     |     |     |     |     |   |               |   |
| PTSA Monohydrate               | n | 0              | 0   | 0   | 0   | 0   | 1   | 4   |   |               |   |
| 50 mg/kg                       |   |                |     |     |     |     |     |     |   |               |   |
| PTSA Monohydrate               | n | 0              | 0   | 0   | 0   | 0   | 1   | 4   |   |               |   |
| 200 mg/kg                      |   |                |     |     |     |     |     |     |   |               |   |
| PTSA Monohydrate               | n | 0              | 0   | 1   | 0   | 2   | 0   | 2   |   |               |   |
| 800 mg/kg                      |   |                |     |     |     |     |     |     |   |               |   |
| <br>                           |   |                |     |     |     |     |     |     |   |               |   |
| Protein                        |   |                |     |     |     |     |     |     |   |               |   |
| Dose                           |   | -              | ±   | +   | 2+  | 3+  |     |     |   |               |   |
| PTSA Monohydrate               | n | 0              | 3   | 2   | 0   | 0   |     |     |   |               |   |
| 0 mg/kg                        |   |                |     |     |     |     |     |     |   |               |   |
| PTSA Monohydrate               | n | 0              | 4   | 1   | 0   | 0   | 5   | 0   | 0 | 0             | 0 |
| 50 mg/kg                       |   |                |     |     |     |     |     |     |   |               |   |
| PTSA Monohydrate               | n | 1              | 4   | 0   | 0   | 0   | 5   | 0   | 0 | 0             | 0 |
| 200 mg/kg                      |   |                |     |     |     |     |     |     |   |               |   |
| PTSA Monohydrate               | n | 0              | 1   | 4   | 0   | 0   | 5   | 0   | 0 | 0             | 0 |
| 800 mg/kg                      |   |                |     |     |     |     |     |     |   |               |   |
| <br>                           |   |                |     |     |     |     |     |     |   |               |   |
| EF                             |   |                |     |     |     |     |     |     |   |               |   |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 2

Study No. : SR15146

| Urinary findings<br>Sex : Male |      | Stage : Week 4 |   |   |    |    |     |              | Species : Rat |   |    |       |  |
|--------------------------------|------|----------------|---|---|----|----|-----|--------------|---------------|---|----|-------|--|
|                                |      | Ketone body    |   |   |    |    |     | Urobilinogen |               |   |    |       |  |
| Test article                   | Dose | -              | ± | + | 2+ | 3+ | 0.1 | 1            | 2             | 4 | 8  | EU/dL |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 5            | 1             | 0 | 2  | 0     |  |
| 0 mg/kg                        |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 5            | 0             | 0 | 0  | 0     |  |
| 50 mg/kg                       |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 5            | 0             | 0 | 0  | 0     |  |
| 200 mg/kg                      |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 5            | 0             | 0 | 0  | 0     |  |
| 800 mg/kg                      |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
|                                |      | EF             |   |   |    |    |     | EF           |               |   |    |       |  |
|                                |      | Bilirubin      |   |   |    |    |     | Occult blood |               |   |    |       |  |
| Test article                   | Dose | -              | ± | + | 2+ | 3+ | 0   | -            | ±             | + | 2+ | 3+    |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | -            | 4             | 1 | 0  | 0     |  |
| 0 mg/kg                        |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 4            | 1             | 0 | 0  | 0     |  |
| 50 mg/kg                       |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 5            | 0             | 0 | 0  | 0     |  |
| 200 mg/kg                      |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
| PTSA Monohydrate               | n    | -              | 5 | 0 | 0  | 0  | 0   | 4            | 0             | 0 | 1  | 0     |  |
| 800 mg/kg                      |      |                |   |   |    |    |     |              |               |   |    | 0     |  |
|                                |      | EF             |   |   |    |    |     | EF           |               |   |    |       |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 3

Study No. : SR15146

| Urinary findings<br>Sex : Male |      | Stage : Week 4 |   |   |   | Species : Rat |
|--------------------------------|------|----------------|---|---|---|---------------|
|                                |      | Color          |   |   |   |               |
| Test article                   | Dose | A              | B | C | D |               |
| PTSA Monohydrate               | n    | 5              | 0 | 0 | 0 |               |
| 0 mg/kg                        |      |                |   |   |   |               |
| PTSA Monohydrate               | n    | 5              | 0 | 0 | 0 |               |
| 50 mg/kg                       |      |                |   |   |   |               |
| PTSA Monohydrate               | n    | 5              | 0 | 0 | 0 |               |
| 200 mg/kg                      |      |                |   |   |   |               |
| PTSA Monohydrate               | n    | 5              | 0 | 0 | 0 |               |
| 800 mg/kg                      |      |                |   |   |   |               |

EF

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 4

Study No. : SR15146

| Urinary findings<br>Sex : Male |      | Stage : Week 4 | Species : Rat |
|--------------------------------|------|----------------|---------------|
| Urine volume                   |      |                |               |
| Test article                   |      | mL/21hr        |               |
| Dose                           |      |                |               |
| PTSA Monohydrate               | n    | 5              |               |
| 0 mg/kg                        | Mean | 14.20          |               |
|                                | S.D. | 2.41           |               |
| PTSA Monohydrate               | n    | 5              |               |
| 50 mg/kg                       | Mean | 14.60          |               |
|                                | S.D. | 3.07           |               |
| PTSA Monohydrate               | n    | 5              |               |
| 200 mg/kg                      | Mean | 18.60          |               |
|                                | S.D. | 7.66           |               |
| PTSA Monohydrate               | n    | 5              |               |
| 800 mg/kg                      | Mean | 16.70          |               |
|                                | S.D. | 6.02           |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 5

Study No. : SR15146

| Urinary findings<br>Sex : Male |   | Stage : Week 4   |   |   |   |   |   |   | Species : Rat |  |
|--------------------------------|---|------------------|---|---|---|---|---|---|---------------|--|
|                                |   | Specific gravity |   |   |   |   |   |   |               |  |
| <b>Test article</b>            |   |                  |   |   |   |   |   |   |               |  |
| Dose                           |   | 0                | 1 | 2 | 3 | 4 | 5 |   |               |  |
| PTSA Monohydrate               | n | 0                | 0 | 0 | 0 | 0 | 5 | 0 |               |  |
| 0 mg/kg                        |   |                  |   |   |   |   |   |   |               |  |
| PTSA Monohydrate               | n | 0                | 0 | 0 | 2 | 2 | 2 | 1 |               |  |
| 50 mg/kg                       |   |                  |   |   |   |   |   |   |               |  |
| PTSA Monohydrate               | n | 0                | 0 | 1 | 2 | 2 | 2 | 0 |               |  |
| 200 mg/kg                      |   |                  |   |   |   |   |   |   |               |  |
| PTSA Monohydrate               | n | 0                | 0 | 1 | 1 | 1 | 1 | 2 |               |  |
| 800 mg/kg                      |   |                  |   |   |   |   |   |   |               |  |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050&lt;

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 6

Study No. : SR15146

| Urinary findings<br>Sex : Male  |   | Stage : Week 4 |   |   |    |    |  | Species : Rat |   |   |    |    |  |
|---|---|----------------|---|---|----|----|--|---------------|---|---|----|----|--|
|   |   | RBC            |   |   |    |    |  | WBC           |   |   |    |    |  |
| <b>Test article</b>   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| Dose  |   | -              | ± | + | 2+ | 3+ |  | -             | ± | + | 2+ | 3+ |  |
| PTSA Monohydrate  | n | 5              | 0 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 0 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| PTSA Monohydrate  | n | 5              | 0 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 50 mg/kg  |   |                |   |   |    |    |  |               |   |   |    |    |  |
| PTSA Monohydrate  | n | 5              | 0 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 200 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| PTSA Monohydrate  | n | 4              | 0 | 0 | 1  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 800 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| <b>EF</b>   |   |                |   |   |    |    |  |               |   |   |    |    |  |
|   |   |                |   |   |    |    |  |               |   |   |    |    |  |
|   |   | Squamous       |   |   |    |    |  | Round         |   |   |    |    |  |
| Dose  |   | -              | ± | + | 2+ | 3+ |  | -             | ± | + | 2+ | 3+ |  |
| PTSA Monohydrate  | n | 4              | 1 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 0 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| PTSA Monohydrate  | n | 5              | 0 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 50 mg/kg  |   |                |   |   |    |    |  |               |   |   |    |    |  |
| PTSA Monohydrate  | n | 5              | 0 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 200 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| PTSA Monohydrate  | n | 3              | 2 | 0 | 0  | 0  |  | 5             | 0 | 0 | 0  | 0  |  |
| 800 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| <b>EF</b>   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| Not significantly different from PTSA Monohydrate 0 mg/kg   |   |                |   |   |    |    |  |               |   |   |    |    |  |
| EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.) |   |                |   |   |    |    |  |               |   |   |    |    |  |

Table 10 - 7

Study No. : SR15146

| Test article<br>Dose          | Sex : Male | Urinary findings |   |   |    |    |   | Stage : Week 4 |   |   |    |    |   | Species : Rat |   |   |   |
|-------------------------------|------------|------------------|---|---|----|----|---|----------------|---|---|----|----|---|---------------|---|---|---|
|                               |            | Small round      |   |   |    |    |   | Cast           |   |   |    |    |   |               |   |   |   |
|                               | n          | -                | ± | + | 2+ | 3+ | 0 | -              | ± | + | 2+ | 3+ | 0 | 0             | 0 | 0 | 0 |
| PTSA Monohydrate<br>0 mg/kg   |            |                  |   |   |    |    |   |                |   |   |    |    |   |               |   |   |   |
| PTSA Monohydrate<br>50 mg/kg  | n          | 5                | 0 | 0 | 0  | 0  | 0 | 5              | 0 | 0 | 0  | 0  | 0 |               |   |   |   |
| PTSA Monohydrate<br>200 mg/kg | n          | 5                | 0 | 0 | 0  | 0  | 0 | 5              | 0 | 0 | 0  | 0  | 0 |               |   |   |   |
| PTSA Monohydrate<br>800 mg/kg | n          | 5                | 0 | 0 | 0  | 0  | 0 | 5              | 0 | 0 | 0  | 0  | 0 |               |   |   |   |
|                               |            | EF               |   |   |    |    |   | EF             |   |   |    |    |   |               |   |   |   |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 8

Study No. : SR15146

| Urinary findings         |   | Stage : Week 4 |     |     |     |     |     |     |    | Species : Rat |   |  |  |  |  |  |  |  |  |  |  |
|--------------------------|---|----------------|-----|-----|-----|-----|-----|-----|----|---------------|---|--|--|--|--|--|--|--|--|--|--|
| Sex : Female (satellite) |   | pH             |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b>      |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>              |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate         | n | 5.0            | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |    |               |   |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg                  |   | 0              | 0   | 0   | 0   | 0   | 2   | 3   |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate         | n | 0              | 2   | 0   | 0   | 0   | 1   | 1   |    |               |   |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg                |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Protein</b>           |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Glucose</b>           |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b>      |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>              |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate         | n | -              | ±   | +   | 2+  | 3+  | -   | +   | 2+ | 3+            |   |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg                  |   | 4              | 1   | 0   | 0   | 0   | 5   | 0   | 0  | 0             |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate         | n | 2              | 0   | 0   | 1   | 1   | 3   | 0   | 0  | 1             |   |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg                |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Ketone body</b>       |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Urobilinogen</b>      |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b>      |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>              |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate         | n | -              | ±   | +   | 2+  | 3+  | 0.1 | 1   | 2  | 4             | 8 |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg                  |   | 5              | 0   | 0   | 0   | 0   | 5   | 0   | 0  | 0             | 0 |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate         | n | 4              | 0   | 0   | 0   | 0   | 4   | 0   | 0  | 0             | 0 |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg                |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>EF</b>                |   |                |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 9

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |      | Stage : Week 4 |   |    |    |   |              |   |   |   |    | Species : Rat |   |
|--|------|----------------|---|----|----|---|--------------|---|---|---|----|---------------|---|
|  |      | Bilirubin      |   |    |    |   | Occult blood |   |   |   |    |               |   |
| Test article                                 | Dose | -              | + | 2+ | 3+ | 0 | -            | ± | 0 | + | 2+ | 3+            | 0 |
| PTSA Monohydrate                             | n    | -              | 5 | 0  | 0  | 0 | -            | 5 | 0 | 0 | 0  | 0             | 0 |
| 0 mg/kg                                      |      |                |   |    |    |   |              |   |   |   |    |               |   |
| PTSA Monohydrate                             | n    | 4              | 0 | 0  | 0  | 0 | 2            | 1 | 1 | 0 | 0  | 0             | 0 |
| 800 mg/kg                                    |      |                |   |    |    |   |              |   |   |   |    |               |   |
| EF   |      |                |   |    |    |   |              |   |   |   |    |               |   |
| Color  |      |                |   |    |    |   |              |   |   |   |    |               |   |
| Test article                                 | Dose | A              | B | C  | D  | 0 |              |   |   |   |    |               |   |
| PTSA Monohydrate                             | n    | 5              | 0 | 0  | 0  | 0 |              |   |   |   |    |               |   |
| 0 mg/kg                                      |      |                |   |    |    |   |              |   |   |   |    |               |   |
| PTSA Monohydrate                             | n    | 4              | 0 | 0  | 0  | 0 |              |   |   |   |    |               |   |
| 800 mg/kg                                    |      |                |   |    |    |   |              |   |   |   |    |               |   |
| EF   |      |                |   |    |    |   |              |   |   |   |    |               |   |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 10

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |      | Stage : Week 4 | Species : Rat |
|--|------|----------------|---------------|
| Urine volume                                 |      |                |               |
| Test article                                 |      | mL/21hr        |               |
| Dose   |      |                |               |
| PTSA Monohydrate                             | n    | 5              |               |
| 0 mg/kg                                      | Mean | 11.20          |               |
|  | S.D. | 6.30           |               |
| PTSA Monohydrate                             | n    | 4              |               |
| 800 mg/kg                                    | Mean | 17.75          |               |
|  | S.D. | 5.69           |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 11

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |      | Stage : Week 4   |   |   |   |   |   |   | Species : Rat |  |
|--|------|------------------|---|---|---|---|---|---|---------------|--|
|  |      | Specific gravity |   |   |   |   |   |   |               |  |
| Test article                                 | Dose | 0                | 1 | 2 | 3 | 4 | 5 |   |               |  |
| PTSA Monohydrate                             | n    | 0                | 0 | 0 | 1 | 2 | 4 | 1 | 1             |  |
| 0 mg/kg                                      |      |                  |   |   |   |   |   |   |               |  |
| PTSA Monohydrate                             | n    | 0                | 1 | 0 | 3 | 0 | 0 | 0 | 0             |  |
| 800 mg/kg                                    |      |                  |   |   |   |   |   |   |               |  |

0:1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<  
Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 12

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |   | Stage : Week 4 |   |   |    |    |      | Species : Rat |   |   |    |    |  |  |  |  |  |  |  |  |
|--|---|----------------|---|---|----|----|------|---------------|---|---|----|----|--|--|--|--|--|--|--|--|
|  |   | RBC            |   |   |    |    |      | WBC           |   |   |    |    |  |  |  |  |  |  |  |  |
| <b>Test article</b>                          |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| Dose   |   | -              | ± | + | 2+ | 3+ |      | -             | ± | + | 2+ | 3+ |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 5              | 0 | 0 | 0  | 0  |      | 5             | 0 | 0 | 0  | 0  |  |  |  |  |  |  |  |  |
| 0 mg/kg                                      |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 4              | 0 | 0 | 0  | 0  |      | 4             | 0 | 0 | 0  | 0  |  |  |  |  |  |  |  |  |
| 800 mg/kg                                    |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| EF   |   |                |   |   |    |    | EF   |               |   |   |    |    |  |  |  |  |  |  |  |  |
| <b>Squamous</b>                              |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| <b>Round</b>                                 |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| Dose   |   | -              | ± | + | 2+ | 3+ |      | -             | ± | + | 2+ | 3+ |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 3              | 2 | 0 | 0  | 0  |      | 5             | 0 | 0 | 0  | 0  |  |  |  |  |  |  |  |  |
| 0 mg/kg                                      |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 2              | 2 | 0 | 0  | 0  |      | 4             | 0 | 0 | 0  | 0  |  |  |  |  |  |  |  |  |
| 800 mg/kg                                    |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| EF   |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| Small round                                  |   |                |   |   |    |    | Cast |               |   |   |    |    |  |  |  |  |  |  |  |  |
| <b>Cast</b>                                  |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| Dose   |   | -              | ± | + | 2+ | 3+ |      | -             | ± | + | 2+ | 3+ |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 5              | 0 | 0 | 0  | 0  |      | 5             | 0 | 0 | 0  | 0  |  |  |  |  |  |  |  |  |
| 0 mg/kg                                      |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 3              | 1 | 0 | 0  | 0  |      | 4             | 0 | 0 | 0  | 0  |  |  |  |  |  |  |  |  |
| 800 mg/kg                                    |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |
| EF   |   |                |   |   |    |    |      |               |   |   |    |    |  |  |  |  |  |  |  |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 13

Study No. : SR15146

| Urinary findings    |   | Stage : Recovery Week 2 |     |     |     |     |     |     |    | Species : Rat |   |  |  |  |  |  |  |  |  |  |  |
|---------------------|---|-------------------------|-----|-----|-----|-----|-----|-----|----|---------------|---|--|--|--|--|--|--|--|--|--|--|
| Sex : Male          |   | pH                      |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b> |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>         |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate    | n | 5.0                     | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |    |               |   |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg             |   | 0                       | 0   | 0   | 0   | 0   | 0   | 5   |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate    | n | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 5  |               |   |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>EF</b>           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b> |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>         |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate    | n | -                       | ±   | +   | 2+  | 3+  | -   | +   | 2+ | 3+            |   |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg             |   | 0                       | 1   | 4   | 0   | 0   | 5   | 0   | 0  | 0             |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate    | n | 0                       | 0   | 4   | 1   | 0   | 5   | 0   | 0  | 0             |   |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>EF</b>           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b> |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>         |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate    | n | -                       | ±   | +   | 2+  | 3+  | 0.1 | 1   | 2  | 4             | 8 |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg             |   | 5                       | 0   | 0   | 0   | 0   | 5   | 0   | 0  | 0             | 0 |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate    | n | 5                       | 0   | 0   | 0   | 0   | 5   | 0   | 0  | 0             | 0 |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>EF</b>           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
|                     |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 14

Study No. : SR15146

| Urinary findings<br>Sex : Male |      | Stage : Recovery Week 2 |   |    |    |   |              |   |    |    |   | Species : Rat |   |
|--------------------------------|------|-------------------------|---|----|----|---|--------------|---|----|----|---|---------------|---|
|                                |      | Bilirubin               |   |    |    |   | Occult blood |   |    |    |   |               |   |
| Test article                   | Dose | -                       | + | 2+ | 3+ | 0 | -            | + | 2+ | 3+ | 0 | -             | 0 |
| PTSA Monohydrate               | n    | -                       | 5 | 0  | 0  | 0 | -            | 4 | 1  | 0  | 0 | -             | 0 |
| 0 mg/kg                        |      |                         |   |    |    |   |              |   |    |    |   |               |   |
| PTSA Monohydrate               | n    | 5                       | 0 | 0  | 0  | 0 | 5            | 0 | 0  | 0  | 0 | 0             | 0 |
| 800 mg/kg                      |      |                         |   |    |    |   |              |   |    |    |   |               |   |
| EF                             |      |                         |   |    |    |   |              |   |    |    |   |               |   |
| Color                          |      |                         |   |    |    |   |              |   |    |    |   |               |   |
| Test article                   | Dose | A                       | B | C  | D  | 0 | 0            | 0 | 0  | 0  | 0 | 0             | 0 |
| PTSA Monohydrate               | n    | 5                       | 0 | 0  | 0  | 0 | 0            | 0 | 0  | 0  | 0 | 0             | 0 |
| 0 mg/kg                        |      |                         |   |    |    |   |              |   |    |    |   |               |   |
| PTSA Monohydrate               | n    | 5                       | 0 | 0  | 0  | 0 | 0            | 0 | 0  | 0  | 0 | 0             | 0 |
| 800 mg/kg                      |      |                         |   |    |    |   |              |   |    |    |   |               |   |
| EF                             |      |                         |   |    |    |   |              |   |    |    |   |               |   |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 15

Study No. : SR15146

| Urinary findings<br>Sex : Male |      | Stage : Recovery Week 2 | Species : Rat |
|--------------------------------|------|-------------------------|---------------|
| Urine volume                   |      |                         |               |
| Test article                   |      | mL/21hr                 |               |
| Dose                           |      |                         |               |
| PTSA Monohydrate               | n    | 5                       |               |
| 0 mg/kg                        | Mean | 11.40                   |               |
|                                | S.D. | 2.68                    |               |
| PTSA Monohydrate               | n    | 5                       |               |
| 800 mg/kg                      | Mean | 14.50                   |               |
|                                | S.D. | 3.32                    |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 16

Study No. : SR15146

| Urinary findings |      | Stage : Recovery Week 2 |   |   |   |   |   |   | Species : Rat |  |
|------------------|------|-------------------------|---|---|---|---|---|---|---------------|--|
| Sex : Male       |      | Specific gravity        |   |   |   |   |   |   |               |  |
| Test article     | Dose | 0                       | 1 | 2 | 3 | 4 | 5 |   |               |  |
| PTSA Monohydrate | n    | 0                       | 0 | 0 | 0 | 0 | 2 | 3 |               |  |
| 0 mg/kg          |      |                         |   |   |   |   |   |   |               |  |
| PTSA Monohydrate | n    | 0                       | 0 | 1 | 0 | 3 | 1 |   |               |  |
| 800 mg/kg        |      |                         |   |   |   |   |   |   |               |  |

0:1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<  
Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 17

Study No. : SR15146

| Urinary findings<br>Sex : Male |   | Stage : Recovery Week 2 |   |   |    |    |       |   |   |    |    | Species : Rat |  |
|--------------------------------|---|-------------------------|---|---|----|----|-------|---|---|----|----|---------------|--|
|                                |   | RBC                     |   |   |    |    | WBC   |   |   |    |    |               |  |
| Test article                   |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| Dose                           |   | -                       | ± | + | 2+ | 3+ | -     | ± | + | 2+ | 3+ |               |  |
| PTSA Monohydrate               | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 0 mg/kg                        |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| PTSA Monohydrate               | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 800 mg/kg                      |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| EF                             |   |                         |   |   |    |    |       |   |   |    |    |               |  |
|                                |   | Squamous                |   |   |    |    | Round |   |   |    |    |               |  |
| Test article                   |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| Dose                           |   | -                       | ± | + | 2+ | 3+ | -     | ± | + | 2+ | 3+ |               |  |
| PTSA Monohydrate               | n | 1                       | 4 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 0 mg/kg                        |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| PTSA Monohydrate               | n | 4                       | 1 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 800 mg/kg                      |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| EF                             |   |                         |   |   |    |    |       |   |   |    |    |               |  |
|                                |   | Small round             |   |   |    |    | Cast  |   |   |    |    |               |  |
| Test article                   |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| Dose                           |   | -                       | ± | + | 2+ | 3+ | -     | ± | + | 2+ | 3+ |               |  |
| PTSA Monohydrate               | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 0 mg/kg                        |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| PTSA Monohydrate               | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 800 mg/kg                      |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| EF                             |   |                         |   |   |    |    |       |   |   |    |    |               |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 18

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |   | Stage : Recovery Week 2 |     |     |     |     |     |     |    | Species : Rat |   |  |  |  |  |  |  |  |  |  |  |
|--|---|-------------------------|-----|-----|-----|-----|-----|-----|----|---------------|---|--|--|--|--|--|--|--|--|--|--|
|  |   | pH                      |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b>                          |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>                                  |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 5.0                     | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |    |               |   |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg                                      |   | 0                       | 0   | 1   | 0   | 1   | 1   | 2   |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 0                       | 0   | 0   | 0   | 1   | 0   | 3   |    |               |   |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg                                    |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <br><b>Protein</b>                           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <br><b>Glucose</b>                           |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b>                          |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>                                  |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | -                       | ±   | +   | 2+  | 3+  | -   | +   | 2+ | 3+            |   |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg                                      |   | 2                       | 1   | 2   | 0   | 0   | 5   | 0   | 0  | 0             |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 1                       | 0   | 3   | 0   | 0   | 4   | 0   | 0  | 0             |   |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg                                    |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <br><b>Ketone body</b>                       |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <br><b>Urobilinogen</b>                      |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Test article</b>                          |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <b>Dose</b>                                  |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | -                       | ±   | +   | 2+  | 3+  | 0.1 | 1   | 2  | 4             | 8 |  |  |  |  |  |  |  |  |  |  |
| 0 mg/kg                                      |   | 5                       | 0   | 0   | 0   | 0   | 5   | 0   | 0  | 0             | 0 |  |  |  |  |  |  |  |  |  |  |
| PTSA Monohydrate                             | n | 4                       | 0   | 0   | 0   | 0   | 4   | 0   | 0  | 0             | 0 |  |  |  |  |  |  |  |  |  |  |
| 800 mg/kg                                    |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |
| <br><b>EF</b>                                |   |                         |     |     |     |     |     |     |    |               |   |  |  |  |  |  |  |  |  |  |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 19

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |      | Stage : Recovery Week 2 |   |    |    |   |              |   |   |   |    | Species : Rat |    |   |
|--|------|-------------------------|---|----|----|---|--------------|---|---|---|----|---------------|----|---|
|  |      | Bilirubin               |   |    |    |   | Occult blood |   |   |   |    |               |    |   |
| Test article                                 | Dose | -                       | + | 2+ | 3+ | 0 | -            | ± | 1 | + | 2+ | 0             | 3+ | 0 |
| PTSA Monohydrate<br>0 mg/kg                  | n    | 5                       | 0 | 0  | 0  | 0 | 4            | 1 | 0 | 0 | 0  | 0             | 0  |   |
| PTSA Monohydrate<br>800 mg/kg                | n    | 4                       | 0 | 0  | 0  | 0 | 4            | 0 | 0 | 0 | 0  | 0             | 0  |   |
| EF   |      |                         |   |    |    |   |              |   |   |   |    |               |    |   |
| Color  |      |                         |   |    |    |   |              |   |   |   |    |               |    |   |
| Test article                                 | Dose | A                       | B | C  | D  | 0 | 0            | 0 | 0 | 0 | 0  | 0             | 0  |   |
| PTSA Monohydrate<br>0 mg/kg                  | n    | 5                       | 0 | 0  | 0  | 0 | 0            | 0 | 0 | 0 | 0  | 0             | 0  |   |
| PTSA Monohydrate<br>800 mg/kg                | n    | 4                       | 0 | 0  | 0  | 0 | 0            | 0 | 0 | 0 | 0  | 0             | 0  |   |
| EF   |      |                         |   |    |    |   |              |   |   |   |    |               |    |   |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 10 - 20

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |      | Stage : Recovery Week 2 | Species : Rat |
|--|------|-------------------------|---------------|
| Urine volume                                 |      |                         |               |
| Test article                                 |      | mL/21hr                 |               |
| Dose   |      |                         |               |
| PTSA Monohydrate                             | n    | 5                       |               |
| 0 mg/kg                                      | Mean | 12.00                   |               |
|  | S.D. | 2.92                    |               |
| PTSA Monohydrate                             | n    | 4                       |               |
| 800 mg/kg                                    | Mean | 10.00                   |               |
|  | S.D. | 4.04                    |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 21

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |      | Stage : Recovery Week 2 |   |   |   |   |   | Species : Rat |   |
|--|------|-------------------------|---|---|---|---|---|---------------|---|
|  |      | Specific gravity        |   |   |   |   |   |               |   |
| Test article                                 | Dose | 0                       | 1 | 2 | 3 | 4 | 5 |               |   |
| PTSA Monohydrate                             | n    | 0                       | 0 | 0 | 0 | 1 | 3 | 3             | 1 |
| 0 mg/kg                                      |      |                         |   |   |   |   |   |               |   |
| PTSA Monohydrate                             | n    | 0                       | 0 | 0 | 0 | 1 | 2 | 2             | 1 |
| 800 mg/kg                                    |      |                         |   |   |   |   |   |               |   |

0:1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<  
Not significantly different from PTSA Monohydrate 0 mg/kg

Table 10 - 22

Study No. : SR15146

| Urinary findings<br>Sex : Female (satellite) |   | Stage : Recovery Week 2 |   |   |    |    |       |   |   |    |    | Species : Rat |  |
|--|---|-------------------------|---|---|----|----|-------|---|---|----|----|---------------|--|
|  |   | RBC                     |   |   |    |    | WBC   |   |   |    |    |               |  |
| Test article                                 |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| Dose   |   | -                       | ± | + | 2+ | 3+ | -     | ± | + | 2+ | 3+ |               |  |
| PTSA Monohydrate                             | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 0 mg/kg                                      |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| PTSA Monohydrate                             | n | 4                       | 0 | 0 | 0  | 0  | 4     | 0 | 0 | 0  | 0  |               |  |
| 800 mg/kg                                    |   |                         |   |   |    |    |       |   |   |    |    |               |  |
|  |   | EF                      |   |   |    |    | EF    |   |   |    |    |               |  |
|  |   | Squamous                |   |   |    |    | Round |   |   |    |    |               |  |
| Test article                                 |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| Dose   |   | -                       | ± | + | 2+ | 3+ | -     | ± | + | 2+ | 3+ |               |  |
| PTSA Monohydrate                             | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 0 mg/kg                                      |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| PTSA Monohydrate                             | n | 3                       | 1 | 0 | 0  | 0  | 4     | 0 | 0 | 0  | 0  |               |  |
| 800 mg/kg                                    |   |                         |   |   |    |    |       |   |   |    |    |               |  |
|  |   | EF                      |   |   |    |    | EF    |   |   |    |    |               |  |
|  |   | Small round             |   |   |    |    | Cast  |   |   |    |    |               |  |
| Test article                                 |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| Dose   |   | -                       | ± | + | 2+ | 3+ | -     | ± | + | 2+ | 3+ |               |  |
| PTSA Monohydrate                             | n | 5                       | 0 | 0 | 0  | 0  | 5     | 0 | 0 | 0  | 0  |               |  |
| 0 mg/kg                                      |   |                         |   |   |    |    |       |   |   |    |    |               |  |
| PTSA Monohydrate                             | n | 4                       | 0 | 0 | 0  | 0  | 4     | 0 | 0 | 0  | 0  |               |  |
| 800 mg/kg                                    |   |                         |   |   |    |    |       |   |   |    |    |               |  |
|  |   | EF                      |   |   |    |    | EF    |   |   |    |    |               |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 11 - 1

Study No. : SR15146

|                  | Hematological findings |       | Stage : Day 29      |                     |                     |                     |       |       | Species : Rat |                     |                     |                     |
|------------------|------------------------|-------|---------------------|---------------------|---------------------|---------------------|-------|-------|---------------|---------------------|---------------------|---------------------|
|                  | Sex : Male             |       | RBC                 | HGB                 | HCT                 | MCV                 | MCH   | MCHC  | Reticulocyte  | Platelet            | WBC                 | Neutrophil          |
| Test article     |                        |       | 10 <sup>4</sup> /µL | g/dL                | %                   | fL                  | pg    | g/dL  | %             | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| Dose             |                        |       |                     |                     |                     |                     |       |       |               |                     |                     |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
| 0 mg/kg          | Mean                   | 851.0 | 15.22               | 42.88               | 50.46               | 17.90               | 35.50 | 3.110 | 106.06        | 67.92               | 12.94               |                     |
|                  | S.D.                   | 41.2  | 0.51                | 1.09                | 2.13                | 0.38                | 0.79  | 0.453 | 11.85         | 22.13               | 3.96                |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
| 50 mg/kg         | Mean                   | 868.2 | 15.72               | 43.96               | 50.64               | 18.12               | 35.80 | 2.826 | 110.52        | 57.14               | 12.12               |                     |
|                  | S.D.                   | 7.4   | 0.37                | 1.21                | 1.69                | 0.47                | 0.51  | 0.449 | 9.75          | 16.09               | 7.47                |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
| 200 mg/kg        | Mean                   | 875.4 | 15.92               | 44.42               | 50.74               | 18.20               | 35.84 | 3.102 | 111.22        | 67.92               | 10.76               |                     |
|                  | S.D.                   | 27.1  | 0.47                | 1.45                | 2.07                | 0.56                | 0.42  | 0.165 | 14.94         | 23.89               | 3.82                |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
| 800 mg/kg        | Mean                   | 856.4 | 15.22               | 42.68               | 49.84               | 17.76               | 35.66 | 3.242 | 126.92        | 61.46               | 12.14               |                     |
|                  | S.D.                   | 6.5   | 0.29                | 1.20                | 1.45                | 0.36                | 0.59  | 0.650 | 11.29         | 10.83               | 6.57                |                     |
|                  |                        |       |                     |                     |                     |                     |       |       | DT *          |                     |                     |                     |
|                  |                        |       | Lymphocyte          | Monocyte            | Eosinophil          | Basophil            | PT    | APTT  |               |                     |                     |                     |
| Test article     |                        |       | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |               |                     |                     |                     |
| Dose             |                        |       |                     |                     |                     |                     |       |       |               |                     |                     |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
| 0 mg/kg          | Mean                   | 51.90 | 2.40                | 0.68                | 0.00                | 20.62               | 21.56 |       |               |                     |                     |                     |
|                  | S.D.                   | 19.85 | 1.17                | 0.29                | 0.00                | 3.28                | 3.15  |       |               |                     |                     |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
| 50 mg/kg         | Mean                   | 42.30 | 1.74                | 0.96                | 0.02                | 30.24               | 25.00 |       |               |                     |                     |                     |
|                  | S.D.                   | 9.10  | 0.95                | 0.21                | 0.04                | 7.25                | 2.67  |       |               |                     |                     |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
| 200 mg/kg        | Mean                   | 54.22 | 2.02                | 0.92                | 0.00                | 27.42               | 25.70 |       |               |                     |                     |                     |
|                  | S.D.                   | 19.75 | 0.91                | 0.41                | 0.00                | 5.54                | 2.02  |       |               |                     |                     |                     |
| PTSA Monohydrate | n                      | 5     | 5                   | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
| 800 mg/kg        | Mean                   | 46.30 | 1.80                | 1.22                | 0.00                | 19.30               | 22.28 |       |               |                     |                     |                     |
|                  | S.D.                   | 9.66  | 0.44                | 0.76                | 0.00                | 3.18                | 0.65  |       |               |                     |                     |                     |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

DT : Dunnett test (two-side)

Table 11 - 2

Study No. : SR15146

| Sex : Female     | Hematological findings |                     |          |                     |            |                     |              | Stage : Lactation Day 5 |                     |                     | Species : Rat |
|------------------|------------------------|---------------------|----------|---------------------|------------|---------------------|--------------|-------------------------|---------------------|---------------------|---------------|
|                  | RBC                    | HGB                 | HCT      | MCV                 | MCH        | MCHC                | Reticulocyte | Platelet                | WBC                 | Neutrophil          |               |
| Test article     | 10 <sup>4</sup> /µL    | g/dL                | %        | fL                  | pg         | g/dL                | %            | 10 <sup>4</sup> /µL     | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |               |
| Dose             |                        |                     |          |                     |            |                     |              |                         |                     |                     |               |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 0 mg/kg          | Mean                   | 740.4               | 14.18    | 40.56               | 54.80      | 19.14               | 34.96        | 5.408                   | 129.52              | 80.84               | 34.54         |
|                  | S.D.                   | 26.6                | 0.63     | 1.47                | 0.53       | 0.23                | 0.53         | 0.833                   | 20.91               | 11.65               | 9.66          |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 50 mg/kg         | Mean                   | 725.4               | 13.92    | 40.26               | 55.64      | 19.24               | 34.56        | 8.588                   | 133.02              | 90.04               | 29.90         |
|                  | S.D.                   | 45.0                | 0.52     | 1.39                | 3.28       | 1.00                | 0.31         | 2.240                   | 15.13               | 9.47                | 6.35          |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 200 mg/kg        | Mean                   | 659.6               | 13.04    | 38.40               | 58.60      | 19.86               | 33.94        | 10.216                  | 116.84              | 77.20               | 29.98         |
|                  | S.D.                   | 78.1                | 1.03     | 2.05                | 4.15       | 0.91                | 1.04         | 3.654                   | 9.49                | 25.28               | 9.40          |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 800 mg/kg        | Mean                   | 717.4               | 13.30    | 38.48               | 53.66      | 18.56               | 34.54        | 6.800                   | 121.12              | 97.24               | 33.50         |
|                  | S.D.                   | 30.9                | 0.60     | 1.58                | 1.94       | 0.47                | 0.55         | 0.633                   | 10.81               | 43.36               | 8.85          |
|                  |                        |                     |          |                     |            |                     |              |                         |                     |                     |               |
|                  | Lymphocyte             | 10 <sup>2</sup> /µL | Monocyte | 10 <sup>2</sup> /µL | Eosinophil | 10 <sup>2</sup> /µL | Basophil     | PT                      | APTT                |                     |               |
| Test article     |                        |                     |          |                     |            |                     |              | sec                     | sec                 |                     |               |
| Dose             |                        |                     |          |                     |            |                     |              |                         |                     |                     |               |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 0 mg/kg          | Mean                   | 42.38               | 2.98     | 0.94                | 0.00       | 17.00               | 16.46        |                         |                     |                     |               |
|                  | S.D.                   | 11.94               | 0.42     | 0.43                | 0.00       | 0.40                | 0.64         |                         |                     |                     |               |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 50 mg/kg         | Mean                   | 57.28               | 2.28     | 0.58                | 0.00       | 17.68               | 16.78        |                         |                     |                     |               |
|                  | S.D.                   | 6.01                | 0.64     | 0.15                | 0.00       | 0.74                | 0.91         |                         |                     |                     |               |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 200 mg/kg        | Mean                   | 44.56               | 2.10     | 0.56                | 0.00       | 16.98               | 17.12        |                         |                     |                     |               |
|                  | S.D.                   | 17.47               | 0.97     | 0.41                | 0.00       | 1.13                | 1.22         |                         |                     |                     |               |
| PTSA Monohydrate | n                      | 5                   | 5        | 5                   | 5          | 5                   | 5            | 5                       | 5                   | 5                   |               |
| 800 mg/kg        | Mean                   | 60.78               | 2.04     | 0.90                | 0.02       | 17.50               | 16.78        |                         |                     |                     |               |
|                  | S.D.                   | 37.46               | 0.94     | 0.54                | 0.04       | 0.59                | 1.35         |                         |                     |                     |               |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

ST : Steel test (two-side)

Table 11 - 3

Study No. : SR15146

| Hematological findings<br>Sex : Female (satellite) |                     | Stage : Day 29 |                     |                     |                     |       |       |              | Species : Rat |       |            |
|--|---------------------|----------------|---------------------|---------------------|---------------------|-------|-------|--------------|---------------|-------|------------|
|  |                     | RBC            | HGB                 | HCT                 | MCV                 | MCH   | MCHC  | Reticulocyte | Platelet      | WBC   | Neutrophil |
| Test article                                       | 10 <sup>4</sup> /µL |                |                     |                     |                     |       |       |              |               |       |            |
| Dose   |                     |                |                     |                     |                     |       |       |              |               |       |            |
| PTSA Monohydrate                                   | n                   | 5              | 5                   | 5                   | 5                   | 5     | 5     | 5            | 5             | 5     | 5          |
| 0 mg/kg  | Mean                | 827.8          | 15.12               | 41.94               | 50.68               | 18.24 | 36.06 | 3.132        | 127.90        | 33.80 | 6.64       |
|  | S.D.                | 25.0           | 0.54                | 1.61                | 1.14                | 0.47  | 0.25  | 0.574        | 17.44         | 3.99  | 2.54       |
| PTSA Monohydrate                                   | n                   | 5              | 5                   | 5                   | 5                   | 5     | 5     | 5            | 5             | 5     | 5          |
| 800 mg/kg  | Mean                | 783.8          | 14.58               | 40.92               | 52.24               | 18.58 | 35.62 | 3.596        | 128.64        | 46.14 | 8.42       |
|  | S.D.                | 56.9           | 0.88                | 2.65                | 1.66                | 0.52  | 0.30  | 0.512        | 16.78         | 16.07 | 4.08       |
|  |                     |                |                     |                     |                     |       |       | T2 *         |               |       |            |
|  |                     | Lymphocyte     | Monocyte            | Eosinophil          | Basophil            | PT    | APTT  |              |               |       |            |
| Test article                                       | 10 <sup>2</sup> /µL |                | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |              |               |       |            |
| Dose   |                     |                |                     |                     |                     |       |       |              |               |       |            |
| PTSA Monohydrate                                   | n                   | 5              | 5                   | 5                   | 5                   | 5     | 5     |              |               |       |            |
| 0 mg/kg  | Mean                | 25.38          | 1.16                | 0.62                | 0.00                | 16.88 | 14.86 |              |               |       |            |
|  | S.D.                | 1.46           | 0.47                | 0.29                | 0.00                | 1.01  | 0.99  |              |               |       |            |
| PTSA Monohydrate                                   | n                   | 5              | 5                   | 5                   | 5                   | 5     | 5     |              |               |       |            |
| 800 mg/kg  | Mean                | 35.40          | 1.58                | 0.74                | 0.00                | 15.56 | 16.54 |              |               |       |            |
|  | S.D.                | 14.22          | 0.53                | 0.56                | 0.00                | 0.58  | 1.61  |              |               |       |            |
|  |                     |                |                     |                     | EF                  |       | T2 *  |              |               |       |            |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

T2 : Student t-test (two-side)

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 11 - 4

Study No. : SR15146

|                            | Hematological findings |       | Stage : Recovery Day 15 |                     |                     |                     |       |       | Species : Rat |                     |                     |                     |
|----------------------------|------------------------|-------|-------------------------|---------------------|---------------------|---------------------|-------|-------|---------------|---------------------|---------------------|---------------------|
|                            | Sex : Male             |       | RBC                     | HGB                 | HCT                 | MCV                 | MCH   | MCHC  | Reticulocyte  | Platelet            | WBC                 | Neutrophil          |
| Test article Dose          |                        |       | 10 <sup>4</sup> /µL     | g/dL                | %                   | fL                  | pg    | g/dL  | %             | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| PTSA Monohydrate 0 mg/kg   | n                      | 5     | 5                       | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
|                            | Mean                   | 923.6 | 16.06                   | 45.02               | 48.76               | 17.40               | 35.68 | 2.890 | 120.74        | 67.08               | 15.06               |                     |
|                            | S.D.                   | 44.7  | 0.82                    | 2.31                | 1.39                | 0.43                | 0.38  | 0.505 | 10.62         | 14.34               | 3.96                |                     |
| PTSA Monohydrate 800 mg/kg | n                      | 5     | 5                       | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
|                            | Mean                   | 886.4 | 15.80                   | 44.48               | 50.20               | 17.84               | 35.54 | 3.054 | 124.68        | 81.30               | 16.94               |                     |
|                            | S.D.                   | 23.3  | 0.39                    | 1.14                | 1.65                | 0.51                | 0.18  | 0.113 | 11.91         | 26.18               | 8.16                |                     |
|                            |                        |       | Lymphocyte              | Monocyte            | Eosinophil          | Basophil            | PT    | APTT  |               |                     |                     |                     |
| Test article Dose          |                        |       | 10 <sup>2</sup> /µL     | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |               |                     |                     |                     |
| PTSA Monohydrate 0 mg/kg   | n                      | 5     | 5                       | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
|                            | Mean                   | 47.58 | 2.98                    | 1.46                | 0.00                | 23.64               | 23.90 |       |               |                     |                     |                     |
|                            | S.D.                   | 12.93 | 0.83                    | 0.55                | 0.00                | 3.87                | 1.96  |       |               |                     |                     |                     |
| PTSA Monohydrate 800 mg/kg | n                      | 5     | 5                       | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
|                            | Mean                   | 59.12 | 3.42                    | 1.80                | 0.02                | 24.64               | 24.86 |       |               |                     |                     |                     |
|                            | S.D.                   | 18.51 | 1.17                    | 0.40                | 0.04                | 3.38                | 1.74  |       |               |                     |                     |                     |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 11 - 5

Study No. : SR15146

|  |            | Stage : Recovery Day 15 |                     |                     |                     |       |       | Species : Rat |                     |                     |                     |
|--|------------|-------------------------|---------------------|---------------------|---------------------|-------|-------|---------------|---------------------|---------------------|---------------------|
| Hematological findings<br>Sex : Female (satellite) |            | RBC                     | HGB                 | HCT                 | MCV                 | MCH   | MCHC  | Reticulocyte  | Platelet            | WBC                 | Neutrophil          |
| Test article                                       |            | 10 <sup>4</sup> /µL     | g/dL                | %                   | fL                  | pg    | g/dL  | %             | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| Dose   |            |                         |                     |                     |                     |       |       |               |                     |                     |                     |
| PTSA Monohydrate                                   | n          | 5                       | 5                   | 5                   | 5                   | 5     | 5     | 5             | 5                   | 5                   | 5                   |
| 0 mg/kg  | Mean       | 840.2                   | 15.64               | 44.28               | 52.74               | 18.64 | 35.34 | 2.544         | 119.80              | 52.82               | 6.64                |
|  | S.D.       | 43.4                    | 0.79                | 2.48                | 2.29                | 0.66  | 0.57  | 0.663         | 12.41               | 15.74               | 3.36                |
| PTSA Monohydrate                                   | n          | 4                       | 4                   | 4                   | 4                   | 4     | 4     | 4             | 4                   | 4                   | 4                   |
| 800 mg/kg  | Mean       | 849.0                   | 15.30               | 42.75               | 50.40               | 18.03 | 35.78 | 2.798         | 120.68              | 53.75               | 7.15                |
|  | S.D.       | 33.7                    | 0.42                | 1.45                | 1.52                | 0.51  | 0.26  | 0.543         | 8.32                | 16.42               | 3.06                |
| <hr/>  |            |                         |                     |                     |                     |       |       |               |                     |                     |                     |
|  | Lymphocyte | 10 <sup>2</sup> /µL     | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   | APTT          |                     |                     |                     |
| Test article                                       |            |                         |                     |                     |                     |       |       |               |                     |                     |                     |
| Dose   |            |                         |                     |                     |                     |       |       |               |                     |                     |                     |
| PTSA Monohydrate                                   | n          | 5                       | 5                   | 5                   | 5                   | 5     | 5     |               |                     |                     |                     |
| 0 mg/kg  | Mean       | 43.48                   | 1.72                | 0.98                | 0.00                | 14.84 | 16.68 |               |                     |                     |                     |
|  | S.D.       | 14.20                   | 0.66                | 0.45                | 0.00                | 0.45  | 2.14  |               |                     |                     |                     |
| PTSA Monohydrate                                   | n          | 4                       | 4                   | 4                   | 4                   | 4     | 4     |               |                     |                     |                     |
| 800 mg/kg  | Mean       | 44.23                   | 1.50                | 0.88                | 0.00                | 15.63 | 15.30 |               |                     |                     |                     |
|  | S.D.       | 16.38                   | 0.54                | 0.21                | 0.00                | 1.59  | 1.29  |               |                     |                     |                     |
|  |            |                         |                     | EF                  |                     |       |       |               |                     |                     |                     |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 12 - 1

Study No. : SR15146

|                  | Biochemical findings |       | Stage : Day 29 |       |       |       |        |       | Species : Rat |         |         |
|------------------|----------------------|-------|----------------|-------|-------|-------|--------|-------|---------------|---------|---------|
|                  | Sex : Male           |       | AST            | ALT   | ALP   | γ-GTP | T-Bil  | TBA   | Glucose       | T-Cho   | TG      |
|                  |                      | IU/L  | IU/L           | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL | mg/dL         | mg/dL   | g/dL    |
| Test article     |                      |       |                |       |       |       |        |       |               |         |         |
| Dose             |                      |       |                |       |       |       |        |       |               |         |         |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 0 mg/kg          | Mean                 | 59.6  | 27.2           | 423.6 | 0.28  | 0.056 | 9.40   | 145.8 | 45.8          | 35.6    | 5.04    |
|                  | S.D.                 | 6.7   | 2.7            | 75.0  | 0.23  | 0.015 | 6.72   | 9.4   | 11.0          | 20.7    | 0.17    |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 50 mg/kg         | Mean                 | 77.8  | 29.4           | 486.8 | 0.24  | 0.056 | 6.36   | 141.2 | 39.0          | 24.0    | 5.08    |
|                  | S.D.                 | 34.3  | 3.8            | 123.1 | 0.15  | 0.009 | 5.05   | 7.7   | 9.5           | 10.5    | 0.15    |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 200 mg/kg        | Mean                 | 74.6  | 31.4           | 463.4 | 0.22  | 0.058 | 5.58   | 147.6 | 45.4          | 42.8    | 5.10    |
|                  | S.D.                 | 17.7  | 1.5            | 25.8  | 0.08  | 0.019 | 1.34   | 9.9   | 8.9           | 19.8    | 0.28    |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 800 mg/kg        | Mean                 | 74.6  | 39.4           | 485.6 | 0.54  | 0.060 | 7.68   | 138.0 | 56.8          | 33.4    | 4.96    |
|                  | S.D.                 | 14.2  | 13.7           | 119.2 | 0.38  | 0.007 | 5.57   | 8.2   | 10.4          | 7.4     | 0.09    |
| <hr/>            |                      |       |                |       |       |       |        |       |               |         |         |
|                  |                      | UN    | Crea           | Na    | K     | Cl    | Ca     | IP    | A/G           | Albumin | Albumin |
|                  |                      | mg/dL | mg/dL          | mEq/L | mEq/L | mEq/L | mg/dL  | mg/dL |               | g/dL    | %       |
| Test article     |                      |       |                |       |       |       |        |       |               |         |         |
| Dose             |                      |       |                |       |       |       |        |       |               |         |         |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 0 mg/kg          | Mean                 | 14.88 | 0.310          | 144.8 | 4.124 | 105.8 | 9.40   | 7.84  | 1.056         | 2.584   | 51.28   |
|                  | S.D.                 | 2.70  | 0.035          | 1.1   | 0.130 | 1.9   | 0.32   | 0.82  | 0.122         | 0.165   | 3.01    |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 50 mg/kg         | Mean                 | 13.90 | 0.282          | 145.4 | 4.054 | 106.4 | 9.26   | 7.38  | 1.026         | 2.572   | 50.58   |
|                  | S.D.                 | 0.57  | 0.024          | 1.5   | 0.090 | 1.1   | 0.11   | 0.47  | 0.044         | 0.120   | 1.11    |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 200 mg/kg        | Mean                 | 13.88 | 0.294          | 145.0 | 4.144 | 106.0 | 9.30   | 7.74  | 1.062         | 2.618   | 51.40   |
|                  | S.D.                 | 0.64  | 0.027          | 1.6   | 0.229 | 1.2   | 0.19   | 0.34  | 0.082         | 0.094   | 1.97    |
| PTSA Monohydrate | n                    | 5     | 5              | 5     | 5     | 5     | 5      | 5     | 5             | 5       | 5       |
| 800 mg/kg        | Mean                 | 14.54 | 0.264          | 144.4 | 4.298 | 106.4 | 9.28   | 7.62  | 1.104         | 2.604   | 52.48   |
|                  | S.D.                 | 1.62  | 0.018          | 1.3   | 0.212 | 0.9   | 0.22   | 0.41  | 0.030         | 0.065   | 0.75    |
|                  | DT *                 |       |                |       |       |       |        |       |               |         |         |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

DT : Dunnett test (two-side)

Table 12 - 2

Study No. : SR15146

| Sex : Male       | Biochemical findings |              |            |             | Stage : Day 29 | Species : Rat |
|------------------|----------------------|--------------|------------|-------------|----------------|---------------|
|                  | $\alpha$ 1-G         | $\alpha$ 2-G | $\beta$ -G | $\gamma$ -G |                |               |
| Test article     |                      | %            | %          | %           | %              |               |
| Dose             |                      |              |            |             |                |               |
| PTSA Monohydrate | n                    | 5            | 5          | 5           | 5              |               |
| 0 mg/kg          | Mean                 | 21.24        | 7.28       | 16.24       | 3.96           |               |
|                  | S.D.                 | 3.88         | 0.79       | 0.67        | 0.43           |               |
| PTSA Monohydrate | n                    | 5            | 5          | 5           | 5              |               |
| 50 mg/kg         | Mean                 | 22.52        | 7.04       | 15.56       | 4.30           |               |
|                  | S.D.                 | 1.74         | 0.59       | 1.39        | 0.64           |               |
| PTSA Monohydrate | n                    | 5            | 5          | 5           | 5              |               |
| 200 mg/kg        | Mean                 | 20.84        | 7.62       | 16.28       | 3.86           |               |
|                  | S.D.                 | 3.06         | 0.48       | 1.06        | 0.71           |               |
| PTSA Monohydrate | n                    | 5            | 5          | 5           | 5              |               |
| 800 mg/kg        | Mean                 | 18.88        | 8.08       | 16.92       | 3.64           |               |
|                  | S.D.                 | 1.56         | 0.29       | 0.96        | 0.47           |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 12 - 3

Study No. : SR15146

| Sex : Female     |      | Stage : Lactation Day 5 |       |       |       |       |        |         | Species : Rat |         |         |
|------------------|------|-------------------------|-------|-------|-------|-------|--------|---------|---------------|---------|---------|
|                  |      | AST                     | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho         | TG      | TP      |
| Test article     |      | IU/L                    | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL         | mg/dL   | g/dL    |
| Dose             |      |                         |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 0 mg/kg          | Mean | 102.4                   | 52.4  | 218.8 | 0.20  | 0.056 | 11.38  | 127.8   | 52.2          | 42.0    | 5.60    |
|                  | S.D. | 40.2                    | 6.7   | 43.7  | 0.17  | 0.011 | 7.22   | 6.6     | 11.1          | 14.2    | 0.25    |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 50 mg/kg         | Mean | 114.4                   | 74.4  | 241.2 | 0.38  | 0.078 | 14.32  | 134.8   | 65.0          | 43.8    | 5.68    |
|                  | S.D. | 54.7                    | 42.5  | 38.9  | 0.48  | 0.024 | 5.01   | 13.1    | 10.6          | 19.3    | 0.31    |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 200 mg/kg        | Mean | 87.4                    | 47.0  | 257.6 | 0.32  | 0.062 | 9.26   | 128.2   | 52.6          | 38.6    | 5.46    |
|                  | S.D. | 15.7                    | 8.1   | 67.4  | 0.22  | 0.008 | 3.77   | 12.8    | 10.6          | 10.7    | 0.11    |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 800 mg/kg        | Mean | 83.8                    | 51.4  | 269.0 | 0.22  | 0.056 | 13.14  | 128.6   | 53.4          | 54.2    | 5.40    |
|                  | S.D. | 13.6                    | 7.8   | 87.4  | 0.22  | 0.005 | 5.64   | 8.0     | 4.2           | 29.7    | 0.16    |
| <hr/>            |      |                         |       |       |       |       |        |         |               |         |         |
|                  |      | UN                      | Crea  | Na    | K     | Cl    | Ca     | IP      | A/G           | Albumin | Albumin |
| Test article     |      | mg/dL                   | mg/dL | mEq/L | mEq/L | mEq/L | mg/dL  | mg/dL   |               | g/dL    | %       |
| Dose             |      |                         |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 0 mg/kg          | Mean | 20.68                   | 0.364 | 142.8 | 4.220 | 104.2 | 10.34  | 10.22   | 1.040         | 2.852   | 50.92   |
|                  | S.D. | 2.17                    | 0.024 | 0.4   | 0.262 | 0.8   | 0.21   | 0.79    | 0.086         | 0.169   | 1.94    |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 50 mg/kg         | Mean | 19.42                   | 0.362 | 142.6 | 4.418 | 103.8 | 10.00  | 7.98    | 1.062         | 2.924   | 51.48   |
|                  | S.D. | 2.99                    | 0.038 | 0.9   | 0.412 | 1.1   | 0.19   | 0.72    | 0.042         | 0.179   | 0.95    |
|                  |      |                         |       |       |       |       |        | DT **   |               |         |         |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 200 mg/kg        | Mean | 18.52                   | 0.352 | 142.4 | 4.214 | 105.4 | 9.98   | 9.34    | 1.002         | 2.732   | 50.02   |
|                  | S.D. | 1.84                    | 0.023 | 0.5   | 0.221 | 0.5   | 0.28   | 1.30    | 0.047         | 0.047   | 1.14    |
| PTSA Monohydrate | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 800 mg/kg        | Mean | 17.82                   | 0.332 | 143.0 | 4.052 | 105.8 | 10.04  | 8.40    | 1.048         | 2.760   | 51.12   |
|                  | S.D. | 2.73                    | 0.029 | 1.4   | 0.181 | 1.5   | 0.46   | 0.87    | 0.091         | 0.164   | 2.32    |
|                  |      |                         |       |       |       |       |        | DT *    |               |         |         |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05, \*\* P&lt;0.01

DT : Dunnett test (two-side)

Table 12 - 4

Study No. : SR15146

|                  | Biochemical findings    |              |            |             | Species : Rat |
|------------------|-------------------------|--------------|------------|-------------|---------------|
|                  | Stage : Lactation Day 5 |              |            |             |               |
| Sex : Female     | $\alpha$ 1-G            | $\alpha$ 2-G | $\beta$ -G | $\gamma$ -G |               |
| Test article     |                         | %            | %          | %           | %             |
| Dose             |                         |              |            |             |               |
| PTSA Monohydrate | n                       | 5            | 5          | 5           | 5             |
| 0 mg/kg          | Mean                    | 20.08        | 7.74       | 16.90       | 4.36          |
|                  | S.D.                    | 3.01         | 1.31       | 0.66        | 0.97          |
| PTSA Monohydrate | n                       | 5            | 5          | 5           | 5             |
| 50 mg/kg         | Mean                    | 20.12        | 7.16       | 16.98       | 4.26          |
|                  | S.D.                    | 1.51         | 0.93       | 1.05        | 0.32          |
| PTSA Monohydrate | n                       | 5            | 5          | 5           | 5             |
| 200 mg/kg        | Mean                    | 20.24        | 6.84       | 17.70       | 5.20          |
|                  | S.D.                    | 1.77         | 0.86       | 0.81        | 0.94          |
| PTSA Monohydrate | n                       | 5            | 5          | 5           | 5             |
| 800 mg/kg        | Mean                    | 18.98        | 7.54       | 17.54       | 4.82          |
|                  | S.D.                    | 1.52         | 0.84       | 0.72        | 0.83          |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 12 - 5

Study No. : SR15146

| Biochemical findings<br>Sex : Female (satellite) |      | Stage : Day 29 |       |       |       |       |        |         | Species : Rat |         |         |
|--|------|----------------|-------|-------|-------|-------|--------|---------|---------------|---------|---------|
|  |      | AST            | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho         | TG      | TP      |
| Test article                                     |      | IU/L           | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL         | mg/dL   | g/dL    |
| Dose   |      |                |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate                                 | n    | 5              | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 0 mg/kg  | Mean | 58.2           | 24.4  | 286.6 | 0.50  | 0.072 | 6.48   | 128.8   | 52.8          | 15.0    | 5.60    |
|  | S.D. | 7.2            | 4.2   | 57.9  | 0.34  | 0.008 | 1.58   | 18.4    | 10.8          | 6.1     | 0.25    |
| PTSA Monohydrate                                 | n    | 5              | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 800 mg/kg  | Mean | 72.0           | 26.0  | 224.8 | 0.50  | 0.050 | 6.90   | 127.6   | 55.8          | 24.6    | 5.22    |
|  | S.D. | 31.8           | 14.2  | 50.7  | 0.28  | 0.012 | 4.60   | 7.1     | 10.3          | 13.9    | 0.33    |
|  |      |                |       |       |       | T2 *  |        |         |               |         |         |
|  |      | UN             | Crea  | Na    | K     | Cl    | Ca     | IP      | A/G           | Albumin | Albumin |
| Test article                                     |      | mg/dL          | mg/dL | mEq/L | mEq/L | mEq/L | mg/dL  | mg/dL   |               | g/dL    | %       |
| Dose   |      |                |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate                                 | n    | 5              | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 0 mg/kg  | Mean | 13.80          | 0.316 | 144.8 | 4.324 | 107.4 | 9.84   | 7.48    | 1.214         | 3.076   | 54.82   |
|  | S.D. | 0.97           | 0.023 | 0.8   | 0.249 | 0.5   | 0.21   | 0.35    | 0.095         | 0.247   | 1.91    |
| PTSA Monohydrate                                 | n    | 5              | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 800 mg/kg  | Mean | 14.66          | 0.338 | 144.6 | 4.070 | 108.0 | 9.62   | 7.86    | 1.126         | 2.764   | 52.88   |
|  | S.D. | 1.73           | 0.026 | 1.1   | 0.224 | 1.4   | 0.13   | 0.55    | 0.098         | 0.289   | 2.21    |
|  |      | α1-G           | α2-G  | β-G   | γ-G   |       |        |         |               |         |         |
| Test article                                     |      | %              | %     | %     | %     |       |        |         |               |         |         |
| Dose   |      |                |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate                                 | n    | 5              | 5     | 5     | 5     |       |        |         |               |         |         |
| 0 mg/kg  | Mean | 16.48          | 7.16  | 15.76 | 5.78  |       |        |         |               |         |         |
|  | S.D. | 1.04           | 0.35  | 0.85  | 0.85  |       |        |         |               |         |         |
| PTSA Monohydrate                                 | n    | 5              | 5     | 5     | 5     |       |        |         |               |         |         |
| 800 mg/kg  | Mean | 18.30          | 7.48  | 15.62 | 5.72  |       |        |         |               |         |         |
|  | S.D. | 1.45           | 0.48  | 1.20  | 1.66  |       |        |         |               |         |         |

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

T2 : Student t-test (two-side)

Table 12 - 6

Study No. : SR15146

| Biochemical findings<br>Sex : Male |      | Stage : Recovery Day 15 |       |       |       |       |        |         | Species : Rat |         |         |
|------------------------------------|------|-------------------------|-------|-------|-------|-------|--------|---------|---------------|---------|---------|
|                                    |      | AST                     | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose |               |         |         |
| Test article                       |      | IU/L                    | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL         | mg/dL   | g/dL    |
| Dose                               |      |                         |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate                   | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 0 mg/kg                            | Mean | 69.4                    | 30.2  | 348.4 | 0.32  | 0.066 | 5.80   | 137.0   | 52.8          | 28.8    | 5.02    |
|                                    | S.D. | 10.1                    | 3.8   | 35.1  | 0.27  | 0.011 | 1.42   | 7.9     | 5.5           | 7.9     | 0.27    |
| PTSA Monohydrate                   | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 800 mg/kg                          | Mean | 74.0                    | 29.2  | 316.8 | 0.24  | 0.060 | 8.72   | 136.0   | 46.6          | 26.6    | 5.06    |
|                                    | S.D. | 8.0                     | 2.9   | 42.8  | 0.09  | 0.007 | 3.85   | 9.1     | 6.6           | 7.2     | 0.15    |
| <hr/>                              |      |                         |       |       |       |       |        |         |               |         |         |
|                                    |      | UN                      | Crea  | Na    | K     | Cl    | Ca     | IP      | A/G           | Albumin | Albumin |
| Test article                       |      | mg/dL                   | mg/dL | mEq/L | mEq/L | mEq/L | mg/dL  | mg/dL   |               | g/dL    | %       |
| Dose                               |      |                         |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate                   | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 0 mg/kg                            | Mean | 14.94                   | 0.262 | 144.4 | 4.508 | 105.6 | 9.52   | 8.16    | 1.020         | 2.532   | 50.42   |
|                                    | S.D. | 1.65                    | 0.019 | 1.5   | 0.310 | 1.5   | 0.11   | 0.57    | 0.068         | 0.145   | 1.52    |
| PTSA Monohydrate                   | n    | 5                       | 5     | 5     | 5     | 5     | 5      | 5       | 5             | 5       | 5       |
| 800 mg/kg                          | Mean | 13.14                   | 0.268 | 144.2 | 4.638 | 106.2 | 9.40   | 8.10    | 1.044         | 2.580   | 51.00   |
|                                    | S.D. | 1.51                    | 0.038 | 0.8   | 0.147 | 0.4   | 0.16   | 0.48    | 0.092         | 0.101   | 2.16    |
| <hr/>                              |      |                         |       |       |       |       |        |         |               |         |         |
|                                    |      | α1-G                    | α2-G  | β-G   | γ-G   |       |        |         |               |         |         |
| Test article                       |      | %                       | %     | %     | %     |       |        |         |               |         |         |
| Dose                               |      |                         |       |       |       |       |        |         |               |         |         |
| PTSA Monohydrate                   | n    | 5                       | 5     | 5     | 5     |       |        |         |               |         |         |
| 0 mg/kg                            | Mean | 22.00                   | 7.28  | 16.28 | 4.02  |       |        |         |               |         |         |
|                                    | S.D. | 2.11                    | 0.34  | 0.23  | 0.86  |       |        |         |               |         |         |
| PTSA Monohydrate                   | n    | 5                       | 5     | 5     | 5     |       |        |         |               |         |         |
| 800 mg/kg                          | Mean | 21.28                   | 7.14  | 16.58 | 4.00  |       |        |         |               |         |         |
|                                    | S.D. | 1.64                    | 0.39  | 0.36  | 0.67  |       |        |         |               |         |         |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 12 - 7

Study No. : SR15146

|                  |      | Biochemical findings<br>Sex : Female (satellite) |       |       |       |       |        | Stage : Recovery day 15 |       |         | Species : Rat |  |
|------------------|------|--|-------|-------|-------|-------|--------|-------------------------|-------|---------|---------------|--|
|                  |      | AST  | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose                 | T-Cho | TG      | TP            |  |
| Test article     |      | IU/L   | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL                   | mg/dL | mg/dL   | g/dL          |  |
| Dose             |      |  |       |       |       |       |        |                         |       |         |               |  |
| PTSA Monohydrate | n    | 5  | 5     | 5     | 5     | 5     | 5      | 5                       | 5     | 5       | 5             |  |
| 0 mg/kg          | Mean | 53.4   | 22.0  | 196.2 | 0.42  | 0.068 | 9.34   | 144.0                   | 51.6  | 20.6    | 5.80          |  |
|                  | S.D. | 7.6  | 4.0   | 60.4  | 0.49  | 0.008 | 3.52   | 16.9                    | 17.7  | 8.3     | 0.44          |  |
| PTSA Monohydrate | n    | 4  | 4     | 4     | 4     | 4     | 4      | 4                       | 4     | 4       | 4             |  |
| 800 mg/kg        | Mean | 61.5   | 20.5  | 232.5 | 0.43  | 0.075 | 11.53  | 129.8                   | 60.5  | 17.3    | 5.63          |  |
|                  | S.D. | 4.8  | 3.8   | 85.4  | 0.29  | 0.017 | 3.90   | 16.5                    | 19.9  | 12.0    | 0.25          |  |
|                  |      | UN   | Crea  | Na    | K     | Cl    | Ca     | IP                      | A/G   | Albumin | Albumin       |  |
| Test article     |      | mg/dL  | mg/dL | mEq/L | mEq/L | mEq/L | mg/dL  | mg/dL                   |       | g/dL    | %             |  |
| Dose             |      |  |       |       |       |       |        |                         |       |         |               |  |
| PTSA Monohydrate | n    | 5  | 5     | 5     | 5     | 5     | 5      | 5                       | 5     | 5       | 5             |  |
| 0 mg/kg          | Mean | 13.90  | 0.306 | 143.4 | 3.970 | 104.4 | 10.02  | 8.26                    | 1.268 | 3.240   | 55.74         |  |
|                  | S.D. | 2.94   | 0.030 | 0.5   | 0.189 | 1.1   | 0.38   | 0.33                    | 0.173 | 0.406   | 3.42          |  |
| PTSA Monohydrate | n    | 4  | 4     | 4     | 4     | 4     | 4      | 4                       | 4     | 4       | 4             |  |
| 800 mg/kg        | Mean | 15.13  | 0.335 | 143.3 | 4.478 | 105.8 | 9.85   | 7.90                    | 1.308 | 3.185   | 56.63         |  |
|                  | S.D. | 2.06   | 0.024 | 1.7   | 0.447 | 1.0   | 0.40   | 1.02                    | 0.069 | 0.162   | 1.35          |  |
|                  |      | α1-G   | α2-G  | β-G   | γ-G   |       |        |                         |       |         |               |  |
| Test article     |      | %  | %     | %     | %     |       |        |                         |       |         |               |  |
| Dose             |      |  |       |       |       |       |        |                         |       |         |               |  |
| PTSA Monohydrate | n    | 5  | 5     | 5     | 5     |       |        |                         |       |         |               |  |
| 0 mg/kg          | Mean | 16.52  | 7.56  | 14.38 | 5.80  |       |        |                         |       |         |               |  |
|                  | S.D. | 1.60   | 0.30  | 1.34  | 1.19  |       |        |                         |       |         |               |  |
| PTSA Monohydrate | n    | 4  | 4     | 4     | 4     |       |        |                         |       |         |               |  |
| 800 mg/kg        | Mean | 15.80  | 7.55  | 14.38 | 5.65  |       |        |                         |       |         |               |  |
|                  | S.D. | 1.28   | 0.37  | 1.40  | 1.08  |       |        |                         |       |         |               |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 13 - 1

Study No. : SR15146

| Necropsy findings<br>Sex : Male                           |                      | Stage : Day 29                      |                                       |  |                                       | Species : Rat |
|---|----------------------|-------------------------------------|---------------------------------------|--|---------------------------------------|---------------|
| Organ<br>Findings   | Test article<br>Dose | PTSA Monohydrate<br>0<br>mg/kg<br>7 | PTSA Monohydrate<br>50<br>mg/kg<br>12 | PTSA Monohydrate<br>200<br>mg/kg<br>12 | PTSA Monohydrate<br>800<br>mg/kg<br>7 |               |
| Stomach<br>Thickening, limiting ridge                     | Number of Animals    | <7/7>                               | <12/12>                               | <12/12>                                | <4/7>                                 |               |
| Epididymis<br>Yellowish white focus, cauda,<br>unilateral | P                    | 0                                   | 0                                     | 0                                      | 3                                     |               |
| Other organs & tissues                                    |                      | <7/7>                               | <12/12>                               | <12/12>                                | <7/7>                                 |               |

&lt;&gt; : Not remarkable/Number of animals examined

P : Non-graded change

Table 13 - 2

Study No. : SR15146

| Necropsy findings<br>Sex : Female     |                      | Stage : Lactation Day 5   |                           |                           | Species : Rat             |
|---------------------------------------|----------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Organ<br>Findings                     | Test article<br>Dose | PTSA Monohydrate<br>mg/kg | PTSA Monohydrate<br>mg/kg | PTSA Monohydrate<br>mg/kg | PTSA Monohydrate<br>mg/kg |
| Stomach<br>Thickening, limiting ridge | Number of Animals    | <11/11><br>11             | <12/12><br>12             | <12/12><br>12             | <4/10><br>10              |
| Other organs & tissues                | P                    | 0                         | 0                         | 0                         | 6                         |
|                                       |                      | <11/11>                   | <12/12>                   | <12/12>                   | <10/10>                   |

&lt;&gt; : Not remarkable/Number of animals examined

P : Non-graded change

Table 13 - 3

Study No. : SR15146

| Necropsy findings      |                            |                        | Species : Rat                        |
|------------------------|----------------------------|------------------------|--------------------------------------|
| Sex : Female           |                            | Stage : Non-pregnancy  |                                      |
| Organ                  | Findings                   | Test article<br>Dose   | PTSA Monohydrate<br>mg/kg            |
| Stomach                | Thickening, limiting ridge | Number of Animals<br>P | 0<br><1/1><br>800<br>1<br><0/1><br>1 |
| Other organs & tissues |                            | <1/1>                  |                                      |

&lt;&gt; : Not remarkable/Number of animals examined

P : Non-graded change

Table 13 - 4

Study No. : SR15146

| Necropsy findings          |                   | Stage : Died on lactation day 0 |                  | Species : Rat |
|----------------------------|-------------------|---------------------------------|------------------|---------------|
| Sex : Female               |                   | Test article                    | PTSA Monohydrate |               |
| Organ                      | Dose              |                                 | 800              |               |
| Findings                   | Number of Animals |                                 | mg/kg            |               |
| Stomach                    |                   |                                 | 1                |               |
| Thickening, limiting ridge | P                 | <0/1>                           | 1                |               |
| Other organs & tissues     |                   | <1/1>                           |                  |               |

&lt;&gt; : Not remarkable/Number of animals examined

P : Non-graded change

Table 13 - 5

Study No. : SR15146

| Necropsy findings          |                          | Stage : Day 29    |                  | Species : Rat |
|----------------------------|--------------------------|-------------------|------------------|---------------|
| Organ Findings             | Sex : Female (satellite) | Test article Dose | PTSA Monohydrate |               |
| Stomach                    |                          | Dose<br>mg/kg     | 0<br>5           | 800<br>5      |
| Thickening, limiting ridge |                          | Number of Animals | <5/5>            | <3/5>         |
|                            | P                        |                   | 0                | 2             |
| Other organs & tissues     |                          |                   | <5/5>            | <5/5>         |

&lt;&gt; : Not remarkable/Number of animals examined

P : Non-graded change

Table 13 - 6

Study No. : SR15146

| Necropsy findings                              |                   |                         |                  | Species : Rat |
|--|-------------------|-------------------------|------------------|---------------|
| Sex : Male                                     |                   | Stage : Recovery Day 15 |                  |               |
| Organ<br>Findings                              | Test article      | PTSA Monohydrate        | PTSA Monohydrate |               |
|  | Dose              | 0<br>mg/kg              | 800<br>mg/kg     |               |
| All organs & tissues                           | Number of Animals | 5                       | 5                |               |
| <> : Not remarkable/Number of animals examined |                   |                         |                  |               |

Table 13 - 7

Study No. : SR15146

| Necropsy findings                              |                   |                         |                  | Species : Rat |
|--|-------------------|-------------------------|------------------|---------------|
| Sex : Female (satellite)                       |                   | Stage : Recovery Day 15 |                  |               |
| Organ<br>Findings                              | Test article      | PTSA Monohydrate        | PTSA Monohydrate |               |
|  | Dose              | 0<br>mg/kg              | 800<br>mg/kg     |               |
| All organs & tissues                           | Number of Animals | 5                       | 4                | <4/4>         |
| <> : Not remarkable/Number of animals examined |                   |                         |                  |               |

Table 13 - 8

Study No. : SR15146

| Necropsy findings                                   |                      |                                      |       | Species : Rat |
|---|----------------------|--------------------------------------|-------|---------------|
| Sex : Female (satellite)                            |                      | Stage : Died on administration day 3 |       |               |
| Organ Findings                                      | Test article<br>Dose | PTSA Monohydrate<br>800 mg/kg        |       |               |
| Stomach   | Number of Animals    | 1                                    | <0/1> |               |
| Red focus, mucosa, multifocal,<br>glandular stomach | P                    | 1                                    |       |               |
| Red, mucosa, pyloric part                           | P                    | 1                                    |       |               |
| Other organs & tissues                              |                      | <1/1>                                |       |               |

&lt;&gt; : Not remarkable/Number of animals examined

P : Non-graded change

Table 14 - 1

Study No. : SR15146

|                            |           | Stage : Day 29 |            |           |            |                 |            |           |            | Species : Rat |           |
|----------------------------|-----------|----------------|------------|-----------|------------|-----------------|------------|-----------|------------|---------------|-----------|
| Organ weight<br>Sex : Male |           | Body weight    |            | Liver     |            | Kidney          |            | Heart     |            | Spleen        |           |
| Test article               | Dose      | n              | AB g       | RE g/100g | AB g       | RE g/100g       | AB g       | RE g/100g | AB mg      | RE mg/100g    |           |
| PTSA Monohydrate           | 0 mg/kg   | n              | 7          | 7         | 7          | 7               | 7          | 7         | 7          | 7             |           |
|                            | Mean      | 462.9          | 11.853     | 2.554     | 3.313      | 0.717           | 1.491      | 0.321     | 739.9      | 159.824       |           |
|                            | S.D.      | 47.2           | 1.673      | 0.152     | 0.364      | 0.068           | 0.154      | 0.019     | 108.6      | 17.904        |           |
| PTSA Monohydrate           | 50 mg/kg  | n              | 12         | 12        | 12         | 12              | 12         | 12        | 12         | 12            |           |
|                            | Mean      | 451.6          | 11.375     | 2.517     | 3.308      | 0.732           | 1.451      | 0.321     | 783.4      | 172.803       |           |
|                            | S.D.      | 24.6           | 1.223      | 0.198     | 0.332      | 0.054           | 0.157      | 0.030     | 190.3      | 37.403        |           |
| PTSA Monohydrate           | 200 mg/kg | n              | 12         | 12        | 12         | 12              | 12         | 12        | 12         | 12            |           |
|                            | Mean      | 467.7          | 11.738     | 2.505     | 3.311      | 0.708           | 1.498      | 0.321     | 830.0      | 176.680       |           |
|                            | S.D.      | 32.9           | 1.514      | 0.232     | 0.366      | 0.060           | 0.151      | 0.024     | 135.5      | 20.335        |           |
| PTSA Monohydrate           | 800 mg/kg | n              | 7          | 7         | 7          | 7               | 7          | 7         | 7          | 7             |           |
|                            | Mean      | 439.6          | 11.620     | 2.640     | 3.207      | 0.730           | 1.363      | 0.310     | 742.1      | 169.323       |           |
|                            | S.D.      | 31.8           | 1.073      | 0.076     | 0.249      | 0.054           | 0.138      | 0.023     | 68.5       | 16.873        |           |
|                            |           |                |            |           |            |                 |            |           |            |               |           |
|                            |           | Thymus         |            | Adrenal   |            | Pituitary gland |            | Thyroid   |            | Testis        |           |
| Test article               | Dose      | AB mg          | RE mg/100g | AB mg     | RE mg/100g | AB mg           | RE mg/100g | AB mg     | RE mg/100g | AB g          | RE g/100g |
| PTSA Monohydrate           | 0 mg/kg   | n              | 7          | 7         | 7          | 7               | 7          | 7         | 7          | 7             | 7         |
|                            | Mean      | 353.9          | 77.459     | 70.1      | 15.111     | 12.63           | 2.721      | 21.73     | 4.756      | 3.034         | 0.660     |
|                            | S.D.      | 91.8           | 22.280     | 10.9      | 1.297      | 2.11            | 0.262      | 4.40      | 1.214      | 0.134         | 0.059     |
| PTSA Monohydrate           | 50 mg/kg  | n              | 12         | 12        | 12         | 12              | 12         | 12        | 12         | 12            | 12        |
|                            | Mean      | 326.7          | 72.835     | 70.4      | 15.537     | 11.30           | 2.498      | 19.80     | 4.385      | 3.252         | 0.722     |
|                            | S.D.      | 57.3           | 14.731     | 13.2      | 2.396      | 1.52            | 0.246      | 3.73      | 0.779      | 0.214         | 0.045     |
| PTSA Monohydrate           | 200 mg/kg | n              | 12         | 12        | 12         | 12              | 12         | 12        | 12         | 12            | 12        |
|                            | Mean      | 356.9          | 76.571     | 69.8      | 14.937     | 12.69           | 2.739      | 21.12     | 4.521      | 3.258         | 0.698     |
|                            | S.D.      | 53.9           | 12.926     | 15.0      | 3.080      | 2.56            | 0.663      | 3.10      | 0.640      | 0.267         | 0.060     |
| PTSA Monohydrate           | 800 mg/kg | n              | 7          | 7         | 7          | 7               | 7          | 7         | 7          | 7             | 7         |
|                            | Mean      | 312.1          | 71.269     | 73.3      | 16.767     | 12.23           | 2.786      | 19.64     | 4.487      | 3.217         | 0.736     |
|                            | S.D.      | 64.8           | 14.808     | 11.1      | 2.920      | 1.88            | 0.404      | 1.69      | 0.499      | 0.257         | 0.075     |

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from PTSO Monohydrate 0 mg/kg

Table 14 - 2

Study No. : SR15146

| Test article<br>Dose | Organ weight<br>Sex : Male |              | Stage : Day 29 |               |                 |              |         |              | Species : Rat |  |
|----------------------|----------------------------|--------------|----------------|---------------|-----------------|--------------|---------|--------------|---------------|--|
|                      | Epididymis                 |              | Prostate       |               | Seminal vesicle |              | Brain   |              |               |  |
|                      | AB<br>g                    | RE<br>g/100g | AB<br>mg       | RE<br>mg/100g | AB<br>g         | RE<br>g/100g | AB<br>g | RE<br>g/100g |               |  |
| PTSA Monohydrate     | n                          | 7            | 7              | 7             | 7               | 7            | 7       | 7            |               |  |
| 0 mg/kg              | Mean                       | 1.239        | 0.267          | 685.0         | 149.150         | 2.027        | 0.443   | 2.199        | 0.481         |  |
|                      | S.D.                       | 0.102        | 0.025          | 107.0         | 25.863          | 0.237        | 0.075   | 0.080        | 0.043         |  |
| PTSA Monohydrate     | n                          | 12           | 12             | 12            | 12              | 12           | 12      | 12           |               |  |
| 50 mg/kg             | Mean                       | 1.278        | 0.284          | 759.0         | 168.221         | 2.224        | 0.495   | 2.183        | 0.484         |  |
|                      | S.D.                       | 0.083        | 0.021          | 107.1         | 23.242          | 0.242        | 0.059   | 0.095        | 0.030         |  |
| PTSA Monohydrate     | n                          | 12           | 12             | 12            | 12              | 12           | 12      | 12           |               |  |
| 200 mg/kg            | Mean                       | 1.247        | 0.267          | 733.2         | 157.204         | 2.026        | 0.435   | 2.204        | 0.473         |  |
|                      | S.D.                       | 0.125        | 0.023          | 159.1         | 34.007          | 0.354        | 0.084   | 0.082        | 0.027         |  |
| PTSA Monohydrate     | n                          | 7            | 7              | 7             | 7               | 7            | 7       | 7            |               |  |
| 800 mg/kg            | Mean                       | 1.221        | 0.277          | 782.7         | 178.777         | 2.254        | 0.514   | 2.164        | 0.497         |  |
|                      | S.D.                       | 0.073        | 0.021          | 102.4         | 26.642          | 0.331        | 0.090   | 0.056        | 0.038         |  |

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 14 - 3

Study No. : SR15146

| Organ weight<br>Sex : Female |      | Stage : Lactation Day 5 |            |         |            |                 |            |         |            | Species : Rat |            |
|------------------------------|------|-------------------------|------------|---------|------------|-----------------|------------|---------|------------|---------------|------------|
|                              |      | Body weight             |            | Liver   |            | Kidney          |            | Heart   |            |               |            |
| Test article                 | Dose | AB g                    | RE g/100g  | AB g    | RE g/100g  | AB g            | RE g/100g  | AB mg   | RE mg/100g |               |            |
| PTSA Monohydrate             | n    | 11                      | 11         | 11      | 11         | 11              | 11         | 11      | 11         |               |            |
| 0 mg/kg                      | Mean | 315.2                   | 10.539     | 3.353   | 2.272      | 0.723           | 1.046      | 0.332   | 778.7      | 246.853       |            |
|                              | S.D. | 33.0                    | 1.027      | 0.251   | 0.246      | 0.065           | 0.108      | 0.020   | 158.3      | 41.429        |            |
| PTSA Monohydrate             | n    | 12                      | 12         | 12      | 12         | 12              | 12         | 12      | 12         |               |            |
| 50 mg/kg                     | Mean | 314.8                   | 10.273     | 3.263   | 2.228      | 0.708           | 1.052      | 0.334   | 760.4      | 241.754       |            |
|                              | S.D. | 21.9                    | 1.090      | 0.253   | 0.212      | 0.053           | 0.144      | 0.029   | 138.8      | 41.909        |            |
| PTSA Monohydrate             | n    | 12                      | 12         | 12      | 12         | 12              | 12         | 12      | 12         |               |            |
| 200 mg/kg                    | Mean | 320.5                   | 10.414     | 3.253   | 2.203      | 0.690           | 1.054      | 0.328   | 812.6      | 255.144       |            |
|                              | S.D. | 26.2                    | 0.875      | 0.197   | 0.201      | 0.059           | 0.097      | 0.022   | 170.8      | 56.925        |            |
| PTSA Monohydrate             | n    | 9                       | 9          | 9       | 9          | 9               | 9          | 9       | 9          |               |            |
| 800 mg/kg                    | Mean | 325.7                   | 10.633     | 3.260   | 2.461      | 0.760           | 1.076      | 0.331   | 729.7      | 222.850       |            |
|                              | S.D. | 42.2                    | 1.679      | 0.196   | 0.270      | 0.084           | 0.113      | 0.028   | 157.7      | 27.998        |            |
|                              |      |                         |            |         |            |                 |            |         |            |               |            |
|                              |      | Thymus                  |            | Adrenal |            | Pituitary gland |            | Thyroid |            | Ovary         |            |
| Test article                 | Dose | AB mg                   | RE mg/100g | AB mg   | RE mg/100g | AB mg           | RE mg/100g | AB mg   | RE mg/100g | AB mg         | RE mg/100g |
| PTSA Monohydrate             | n    | 11                      | 11         | 11      | 11         | 11              | 11         | 11      | 11         | 11            | 11         |
| 0 mg/kg                      | Mean | 234.0                   | 74.215     | 80.1    | 25.475     | 17.47           | 5.547      | 16.52   | 5.253      | 112.8         | 35.758     |
|                              | S.D. | 37.8                    | 8.961      | 14.6    | 4.218      | 3.01            | 0.807      | 2.38    | 0.655      | 19.4          | 4.579      |
| PTSA Monohydrate             | n    | 12                      | 12         | 12      | 12         | 12              | 12         | 12      | 12         | 12            | 12         |
| 50 mg/kg                     | Mean | 240.8                   | 76.532     | 77.7    | 24.744     | 18.18           | 5.794      | 18.19   | 5.779      | 112.8         | 35.788     |
|                              | S.D. | 49.8                    | 14.484     | 14.3    | 4.524      | 2.40            | 0.776      | 2.70    | 0.751      | 22.0          | 6.195      |
| PTSA Monohydrate             | n    | 12                      | 12         | 12      | 12         | 12              | 12         | 12      | 12         | 12            | 12         |
| 200 mg/kg                    | Mean | 286.3                   | 88.839     | 79.2    | 24.762     | 16.51           | 5.149      | 16.73   | 5.228      | 101.7         | 31.831     |
|                              | S.D. | 62.7                    | 15.279     | 11.8    | 3.472      | 2.14            | 0.512      | 3.33    | 1.024      | 13.2          | 4.325      |
| PTSA Monohydrate             | n    | 9                       | 9          | 9       | 9          | 9               | 9          | 9       | 9          | 9             | 9          |
| 800 mg/kg                    | Mean | 235.6                   | 72.410     | 79.8    | 24.627     | 18.28           | 5.680      | 16.03   | 4.979      | 112.7         | 34.850     |
|                              | S.D. | 60.7                    | 16.355     | 7.4     | 1.701      | 1.63            | 0.712      | 2.28    | 0.858      | 15.0          | 4.797      |

AB : Absolute weight, RE : Relative weight by body weight

Significantly different from PTS A Monohydrate 0 mg/kg: \* P&lt;0.05

DT : Dunnett test (two-side)

Table 14 - 4

Study No. : SR15146

| Organ weight<br>Sex : Female  |      | Stage : Lactation Day 5 |               |         |              | Species : Rat |
|-------------------------------|------|-------------------------|---------------|---------|--------------|---------------|
| Test article<br>Dose          |      | Uterus                  |               | Brain   |              |               |
|                               |      | AB<br>mg                | RE<br>mg/100g | AB<br>g | RE<br>g/100g |               |
| PTSA Monohydrate<br>0 mg/kg   | n    | 11                      | 11            | 11      | 11           |               |
|                               | Mean | 710.5                   | 226.811       | 2.084   | 0.665        |               |
|                               | S.D. | 81.6                    | 28.957        | 0.086   | 0.055        |               |
| PTSA Monohydrate<br>50 mg/kg  | n    | 12                      | 12            | 12      | 12           |               |
|                               | Mean | 686.2                   | 218.963       | 2.081   | 0.665        |               |
|                               | S.D. | 110.4                   | 37.271        | 0.045   | 0.041        |               |
| PTSA Monohydrate<br>200 mg/kg | n    | 12                      | 12            | 12      | 12           |               |
|                               | Mean | 679.2                   | 212.379       | 2.037   | 0.638        |               |
|                               | S.D. | 101.7                   | 30.624        | 0.078   | 0.054        |               |
| PTSA Monohydrate<br>800 mg/kg | n    | 9                       | 9             | 9       | 9            |               |
|                               | Mean | 700.7                   | 216.318       | 2.054   | 0.637        |               |
|                               | S.D. | 78.1                    | 20.109        | 0.070   | 0.067        |               |

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 14 - 5

Study No. : SR15146

|  |             | Stage : Day 29 |         |         |         |                 |         |         |         | Species : Rat |         |
|--|-------------|----------------|---------|---------|---------|-----------------|---------|---------|---------|---------------|---------|
| Organ weight<br>Sex : Female (satellite) |             | Liver          |         | Kidney  |         | Heart           |         | Spleen  |         |               |         |
| Test article                             | Body weight | AB             | RE      | AB      | RE      | AB              | RE      | AB      | RE      |               |         |
| Dose                                     | g           | g              | g/100g  | g       | g/100g  | g               | g/100g  | g       | g/100g  | mg            | mg/100g |
| PTSA Monohydrate                         | n           | 5              | 5       | 5       | 5       | 5               | 5       | 5       | 5       | 5             | 5       |
| 0 mg/kg                                  | Mean        | 262.6          | 6.830   | 2.592   | 1.872   | 0.712           | 0.908   | 0.344   | 491.2   | 187.708       |         |
|  | S.D.        | 13.2           | 1.131   | 0.330   | 0.156   | 0.055           | 0.105   | 0.030   | 58.0    | 27.229        |         |
| PTSA Monohydrate                         | n           | 5              | 5       | 5       | 5       | 5               | 5       | 5       | 5       | 5             | 5       |
| 800 mg/kg                                | Mean        | 257.6          | 7.150   | 2.774   | 2.040   | 0.790           | 0.904   | 0.352   | 525.2   | 203.566       |         |
|  | S.D.        | 8.8            | 0.669   | 0.206   | 0.399   | 0.142           | 0.087   | 0.031   | 104.4   | 37.719        |         |
| <hr/>                                    |             |                |         |         |         |                 |         |         |         |               |         |
|  |             | Thymus         |         | Adrenal |         | Pituitary gland |         | Thyroid |         | Ovary         |         |
| Test article                             | Dose        | AB             | RE      | AB      | RE      | AB              | RE      | AB      | RE      | AB            | RE      |
|  |             | mg             | mg/100g | mg      | mg/100g | mg              | mg/100g | mg      | mg/100g | mg            | mg/100g |
| PTSA Monohydrate                         | n           | 5              | 5       | 5       | 5       | 5               | 5       | 5       | 5       | 5             | 5       |
| 0 mg/kg                                  | Mean        | 364.0          | 138.926 | 78.0    | 29.778  | 14.44           | 5.508   | 17.92   | 6.896   | 105.2         | 40.180  |
|  | S.D.        | 36.5           | 15.938  | 12.8    | 5.086   | 1.33            | 0.575   | 5.21    | 2.283   | 15.0          | 6.198   |
| PTSA Monohydrate                         | n           | 5              | 5       | 5       | 5       | 5               | 5       | 5       | 5       | 5             | 5       |
| 800 mg/kg                                | Mean        | 342.0          | 132.082 | 75.6    | 29.374  | 15.96           | 6.198   | 17.22   | 6.656   | 108.0         | 41.784  |
|  | S.D.        | 90.8           | 32.323  | 7.8     | 3.145   | 2.16            | 0.817   | 3.60    | 1.205   | 20.8          | 6.905   |
| <hr/>                                    |             |                |         |         |         |                 |         |         |         |               |         |
|  |             | Uterus         |         | Brain   |         |                 |         |         |         |               |         |
| Test article                             | Dose        | AB             | RE      | AB      | RE      |                 |         |         |         |               |         |
|  |             | mg             | mg/100g | g       | g/100g  |                 |         |         |         |               |         |
| PTSA Monohydrate                         | n           | 5              | 5       | 5       | 5       |                 |         |         |         |               |         |
| 0 mg/kg                                  | Mean        | 780.0          | 296.618 | 1.918   | 0.728   |                 |         |         |         |               |         |
|  | S.D.        | 220.5          | 81.729  | 0.028   | 0.033   |                 |         |         |         |               |         |
| PTSA Monohydrate                         | n           | 5              | 5       | 5       | 5       |                 |         |         |         |               |         |
| 800 mg/kg                                | Mean        | 657.8          | 254.922 | 1.998   | 0.776   |                 |         |         |         |               |         |
|  | S.D.        | 115.6          | 40.699  | 0.057   | 0.034   |                 |         |         |         |               |         |
|  |             | T2 *           |         |         |         |                 |         |         |         |               |         |

AB : Absolute weight, RE : Relative weight by body weight

Significantly different from PTSA Monohydrate 0 mg/kg: \* P&lt;0.05

T2 : Student t-test (two-side)

Table 14 - 6

Study No. : SR15146

|                            |      | Stage : Recovery Day 15 |               |          |               |                 |               |          |               | Species : Rat |               |
|----------------------------|------|-------------------------|---------------|----------|---------------|-----------------|---------------|----------|---------------|---------------|---------------|
| Organ weight<br>Sex : Male |      | Body weight             |               | Liver    |               | Kidney          |               | Heart    |               | Spleen        |               |
| Test article               | Dose | AB<br>g                 | RE<br>g/100g  | AB<br>g  | RE<br>g/100g  | AB<br>g         | RE<br>g/100g  | AB<br>g  | RE<br>g/100g  | AB<br>mg      | RE<br>mg/100g |
| PTSA Monohydrate           | n    | 5                       | 5             | 5        | 5             | 5               | 5             | 5        | 5             | 5             | 5             |
| 0 mg/kg                    | Mean | 486.2                   | 11.840        | 2.436    | 3.340         | 0.688           | 1.526         | 0.312    | 713.2         | 147.190       |               |
|                            | S.D. | 26.0                    | 0.946         | 0.144    | 0.100         | 0.028           | 0.177         | 0.028    | 51.2          | 15.311        |               |
| PTSA Monohydrate           | n    | 5                       | 5             | 5        | 5             | 5               | 5             | 5        | 5             | 5             | 5             |
| 800 mg/kg                  | Mean | 489.4                   | 11.710        | 2.386    | 3.266         | 0.666           | 1.492         | 0.306    | 806.8         | 165.130       |               |
|                            | S.D. | 18.3                    | 1.384         | 0.197    | 0.396         | 0.062           | 0.094         | 0.011    | 93.2          | 20.499        |               |
| <hr/>                      |      |                         |               |          |               |                 |               |          |               |               |               |
|                            |      | Thymus                  |               | Adrenal  |               | Pituitary gland |               | Thyroid  |               | Testis        |               |
| Test article               | Dose | AB<br>mg                | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>g       | RE<br>g/100g  |
| PTSA Monohydrate           | n    | 5                       | 5             | 5        | 5             | 5               | 5             | 5        | 5             | 5             | 5             |
| 0 mg/kg                    | Mean | 357.4                   | 73.126        | 70.4     | 14.584        | 12.88           | 2.650         | 23.74    | 4.890         | 3.400         | 0.702         |
|                            | S.D. | 73.6                    | 11.789        | 13.7     | 3.265         | 1.30            | 0.245         | 4.39     | 0.931         | 0.140         | 0.064         |
| PTSA Monohydrate           | n    | 5                       | 5             | 5        | 5             | 5               | 5             | 5        | 5             | 5             | 5             |
| 800 mg/kg                  | Mean | 338.0                   | 69.332        | 66.8     | 13.708        | 11.82           | 2.416         | 19.02    | 3.888         | 3.592         | 0.734         |
|                            | S.D. | 104.4                   | 22.145        | 11.7     | 2.759         | 1.95            | 0.400         | 1.99     | 0.406         | 0.327         | 0.051         |
| <hr/>                      |      |                         |               |          |               |                 |               |          |               |               |               |
|                            |      | Epididymis              |               | Prostate |               | Seminal vesicle |               | Brain    |               |               |               |
| Test article               | Dose | AB<br>g                 | RE<br>g/100g  | AB<br>mg | RE<br>mg/100g | AB<br>g         | RE<br>g/100g  | AB<br>g  | RE<br>g/100g  |               |               |
| PTSA Monohydrate           | n    | 5                       | 5             | 5        | 5             | 5               | 5             | 5        | 5             |               |               |
| 0 mg/kg                    | Mean | 1.346                   | 0.278         | 767.6    | 157.744       | 2.208           | 0.456         | 2.246    | 0.460         |               |               |
|                            | S.D. | 0.056                   | 0.015         | 146.8    | 28.018        | 0.300           | 0.065         | 0.047    | 0.028         |               |               |
| PTSA Monohydrate           | n    | 5                       | 5             | 5        | 5             | 5               | 5             | 5        | 5             |               |               |
| 800 mg/kg                  | Mean | 1.336                   | 0.274         | 725.8    | 148.786       | 2.164           | 0.442         | 2.258    | 0.460         |               |               |
|                            | S.D. | 0.140                   | 0.023         | 228.3    | 47.923        | 0.281           | 0.051         | 0.128    | 0.031         |               |               |

AB : Absolute weight, RE : Relative weight by body weight  
 Not significantly different from PTSO Monohydrate 0 mg/kg

Table 14 - 7

Study No. : SR15146

| Organ weight<br>Sex : Female (satellite) |           |             |       | Stage : Recovery Day 15 |           |        |           |            |           |        |            | Species : Rat |   |
|--|-----------|-------------|-------|-------------------------|-----------|--------|-----------|------------|-----------|--------|------------|---------------|---|
| Test article                             | Dose      | Body weight |       | Liver                   |           | Kidney |           | Heart      |           | Spleen |            |               |   |
|  |           | n           | g     | AB g                    | RE g/100g | AB g   | RE g/100g | AB g       | RE g/100g | AB mg  | RE mg/100g |               |   |
| PTSA Monohydrate                         | 0 mg/kg   | n           | 5     | 5                       | 5         | 5      | 5         | 5          | 5         | 5      | 5          |               |   |
|  |           | Mean        | 277.0 | 7.106                   | 2.566     | 1.894  | 0.684     | 0.950      | 0.344     | 485.6  | 175.066    |               |   |
|  |           | S.D.        | 8.4   | 0.793                   | 0.274     | 0.144  | 0.048     | 0.100      | 0.029     | 49.1   | 13.672     |               |   |
| PTSA Monohydrate                         | 800 mg/kg | n           | 4     | 4                       | 4         | 4      | 4         | 4          | 4         | 4      | 4          |               |   |
|  |           | Mean        | 274.8 | 6.965                   | 2.538     | 2.025  | 0.745     | 0.880      | 0.320     | 532.0  | 194.748    |               |   |
|  |           | S.D.        | 33.5  | 0.945                   | 0.208     | 0.215  | 0.108     | 0.079      | 0.012     | 49.6   | 18.822     |               |   |
|  |           |             |       |                         |           |        |           |            |           |        |            |               |   |
| Thymus                                   |           |             |       |                         |           |        |           |            |           |        |            |               |   |
| Test article                             | Dose      | AB mg       |       | RE mg/100g              |           | AB mg  |           | RE mg/100g |           | AB mg  |            | RE mg/100g    |   |
|  |           | n           | 5     | 5                       | 5         | 5      | 5         | 5          | 5         | 5      | 5          | 5             | 5 |
| PTSA Monohydrate                         | 0 mg/kg   | Mean        | 286.6 | 103.496                 | 74.6      | 26.962 | 17.22     | 6.216      | 13.44     | 4.858  | 76.4       | 27.572        |   |
|  |           | S.D.        | 45.5  | 16.391                  | 16.7      | 6.077  | 2.76      | 0.976      | 1.72      | 0.632  | 19.3       | 6.798         |   |
| PTSA Monohydrate                         | 800 mg/kg | n           | 4     | 4                       | 4         | 4      | 4         | 4          | 4         | 4      | 4          | 4             | 4 |
|  |           | Mean        | 282.3 | 99.395                  | 68.8      | 25.063 | 17.98     | 6.500      | 15.18     | 5.560  | 72.3       | 26.353        |   |
|  |           | S.D.        | 137.9 | 37.698                  | 7.5       | 1.035  | 3.76      | 0.697      | 2.84      | 1.084  | 22.1       | 7.015         |   |
|  |           |             |       |                         |           |        |           |            |           |        |            |               |   |
| Uterus                                   |           |             |       |                         |           |        |           |            |           |        |            |               |   |
| Test article                             | Dose      | AB mg       |       | RE mg/100g              |           | AB g   |           | RE g/100g  |           |        |            |               |   |
|  |           | n           | 5     | 5                       | 5         | 5      | 5         | 5          | 5         |        |            |               |   |
| PTSA Monohydrate                         | 0 mg/kg   | Mean        | 621.0 | 225.072                 | 2.040     | 0.736  |           |            |           |        |            |               |   |
|  |           | S.D.        | 81.9  | 36.864                  | 0.091     | 0.029  |           |            |           |        |            |               |   |
| PTSA Monohydrate                         | 800 mg/kg | n           | 4     | 4                       | 4         | 4      | 4         | 4          | 4         |        |            |               |   |
|  |           | Mean        | 733.5 | 268.690                 | 2.120     | 0.780  |           |            |           |        |            |               |   |
|  |           | S.D.        | 106.0 | 40.977                  | 0.058     | 0.096  |           |            |           |        |            |               |   |

AB : Absolute weight, RE : Relative weight by body weight

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 15 - 1

Study No. : SR15146

| Histopathological findings                    |                                   |                      |                                   |     |    |    |                                    |      |    | Species : Rat |                                     |      |    |         |     |   |   |
|---|-----------------------------------|----------------------|-----------------------------------|-----|----|----|------------------------------------|------|----|---------------|-------------------------------------|------|----|---------|-----|---|---|
| Sex : Male                                    |                                   | Stage : Day 29       |                                   |     |    |    |                                    |      |    |               |                                     |      |    |         |     |   |   |
| Organ<br>Findings                             | Number of Animals<br>Grade        | Test article<br>Dose | PTSA<br>Monohydrate<br>0<br>mg/kg |     |    |    | PTSA<br>Monohydrate<br>50<br>mg/kg |      |    |               | PTSA<br>Monohydrate<br>200<br>mg/kg |      |    |         |     |   |   |
|   |                                   |                      | -                                 | 1+  | 2+ | 3+ | -                                  | 1+   | 2+ | 3+            | -                                   | 1+   | 2+ | 3+      |     |   |   |
| Lung  |                                   |                      | 7                                 | <7> |    |    | 12                                 | <0>  |    |               | 12                                  | <0>  |    | 7       |     |   |   |
|   | Aggregation, macrophage, alveolar |                      | 5                                 | 2   | 0  | 0  | 0                                  | 0    | 0  | 0             | 0                                   | 0    | 1  | 0       | 0   | 0 |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      | 6  |         |     |   |   |
| Trachea                                       |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |
| Submandibular gland                           |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |
| Esophagus                                     |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |
| Stomach                                       |                                   |                      |                                   | <7> |    |    |                                    | <12> |    |               |                                     | <12> |    |         | <7> |   |   |
| Hyperplasia, squamous cell,<br>limiting ridge |                                   |                      | 7                                 | 0   | 0  | 0  | 0                                  | 0    | 12 | 0             | 0                                   | 0    | 0  | 1       | 6   | 0 | 0 |
|   |                                   |                      |                                   |     |    |    | EF                                 |      |    |               | EF                                  |      |    | FT \$\$ |     |   |   |
| Duodenum                                      |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |
| Jejunum                                       |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |
| Ileum   |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |
| Cecum   |                                   |                      | 7                                 | <7> |    |    | 0                                  | <0>  |    |               | 0                                   | <0>  |    | 7       | <7> |   |   |
|   |                                   |                      |                                   |     |    |    | ED                                 |      |    |               | ED                                  |      |    | EF      |     |   |   |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Significantly different from PTSAMonohydrate 0 mg/kg: \$\$ P&lt;0.01

FT : Fisher's exact test (two-side)

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 2

Study No. : SR15146

| Histopathological findings |                            |                                 |                                   |    |    |    |                                    |    |    | Species : Rat |                                     |    |    |     |
|----------------------------|----------------------------|---------------------------------|-----------------------------------|----|----|----|------------------------------------|----|----|---------------|-------------------------------------|----|----|-----|
| Sex : Male                 |                            | Stage : Day 29                  |                                   |    |    |    |                                    |    |    |               |                                     |    |    |     |
| Organ<br>Findings          | Number of Animals<br>Grade | Test article<br>Dose            | PTSA<br>Monohydrate<br>0<br>mg/kg |    |    |    | PTSA<br>Monohydrate<br>50<br>mg/kg |    |    |               | PTSA<br>Monohydrate<br>200<br>mg/kg |    |    |     |
|                            |                            |                                 | -                                 | 1+ | 2+ | 3+ | -                                  | 1+ | 2+ | 3+            | -                                   | 1+ | 2+ | 3+  |
|                            |                            |                                 | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    |     |
| Colon                      |                            |                                 | 7                                 |    |    |    | 0                                  |    |    |               | 0                                   |    |    | 7   |
|                            |                            |                                 |                                   |    |    |    | ED                                 |    |    |               | ED                                  |    |    | EF  |
| Rectum                     |                            |                                 | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 7                                 |    |    |    | 0                                  |    |    |               | 0                                   |    |    | 7   |
| Pancreas                   |                            | Atrophy, acinar cell, focal     | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 6                                 | 1  | 0  | 0  | 0                                  | 0  | 0  | 0             | 0                                   | 0  | 0  | 6   |
| Liver                      |                            | Microgranuloma                  | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 5                                 | 2  | 0  | 0  | 0                                  | 0  | 0  | 0             | 0                                   | 0  | 0  | 6   |
| Heart                      |                            | Cardiomyopathy, focal           | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 6                                 | 1  | 0  | 0  | 0                                  | 0  | 0  | 0             | 0                                   | 0  | 0  | 6   |
| Kidney                     |                            | Basophilic change, renal tubule | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 5                                 | 2  | 0  | 0  | 0                                  | 0  | 0  | 0             | 0                                   | 0  | 0  | 5   |
| Urinary bladder            |                            |                                 | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 7                                 |    |    |    | 0                                  |    |    |               | 0                                   |    |    | EF  |
| Testis                     |                            |                                 | <7>                               |    |    |    | <0>                                |    |    |               | <0>                                 |    |    | <7> |
|                            |                            |                                 | 7                                 |    |    |    | 0                                  |    |    |               | 0                                   |    |    | EF  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 3

Study No. : SR15146

| Histopathological findings |                            |                |                          |   |     |    |                           |    |   | Species : Rat |                            |    |    |     |
|----------------------------|----------------------------|----------------|--------------------------|---|-----|----|---------------------------|----|---|---------------|----------------------------|----|----|-----|
| Sex : Male                 |                            | Stage : Day 29 |                          |   |     |    |                           |    |   |               |                            |    |    |     |
| Organ                      | Findings                   | Test article   | PTSA Monohydrate 0 mg/kg |   |     |    | PTSA Monohydrate 50 mg/kg |    |   |               | PTSA Monohydrate 200 mg/kg |    |    |     |
|                            |                            |                | Dose                     | 7 | 1+  | 2+ | 3+                        | 4+ | - | 1+            | 2+                         | 3+ | 4+ | 7   |
| Number of Animals          | Grade                      |                |                          |   |     |    |                           |    |   |               |                            |    |    |     |
| Epididymis                 | Granuloma, spermatic       |                |                          | 7 | 0   | 0  | 0                         | 0  | 0 | 0             | 0                          | 0  | 0  | 6   |
|                            |                            |                |                          |   | <7> |    |                           |    |   | <0>           |                            |    |    | 1   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 0   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 0   |
| Prostate                   | Inflammation, interstitium |                |                          | 4 | 3   | 0  | 0                         | 0  | 0 | 0             | 0                          | 0  | 0  | 3   |
|                            |                            |                |                          |   | <7> |    |                           |    |   | <0>           |                            |    |    | 4   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 0   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 0   |
| Seminal vesicle            |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |
| Coagulating gland          |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |
| Cerebrum                   |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |
| Cerebellum                 |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |
| Pons                       |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |
| Spinal cord                |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |
| Sciatic nerve              |                            |                |                          | 7 | <7> |    |                           |    |   | <0>           |                            |    |    | <7> |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | 7   |
|                            |                            |                |                          |   |     |    |                           |    |   |               |                            |    |    | EF  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 4

Study No. : SR15146

| Histopathological findings      |          |                |                          |     |    |     |                           |    |     | Species : Rat |                            |    |     |     |    |    |    |
|---------------------------------|----------|----------------|--------------------------|-----|----|-----|---------------------------|----|-----|---------------|----------------------------|----|-----|-----|----|----|----|
| Sex : Male                      |          | Stage : Day 29 |                          |     |    |     |                           |    |     |               |                            |    |     |     |    |    |    |
| Organ                           | Findings | Test article   | PTSA Monohydrate 0 mg/kg |     |    |     | PTSA Monohydrate 50 mg/kg |    |     |               | PTSA Monohydrate 200 mg/kg |    |     |     |    |    |    |
|                                 |          |                | Dose                     | 0   | 50 | 200 | 0                         | 50 | 200 | 800           | 0                          | 50 | 200 | 800 |    |    |    |
| Number of Animals               | Grade    |                | -                        | 1+  | 2+ | 3+  | 4+                        | -  | 1+  | 2+            | 3+                         | 4+ | -   | 1+  | 2+ | 3+ | 4+ |
| Spleen                          |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Thymus                          |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Bone marrow, femur              |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Submandibular lymph node        |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Mesenteric lymph node           |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Peyer's patch                   |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Pituitary gland                 |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Thyroid<br>Ultimobranchial body |          |                | 6                        | 1   | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |
| Parathyroid                     |          |                | 7                        | <7> | 0  | 0   | 0                         | 0  | <0> | 0             | 0                          | 0  | 7   | <7> | 0  | 0  | 0  |
|                                 |          |                |                          |     | ED | ED  | ED                        | ED |     | ED            | ED                         | ED | EF  |     | ED | ED | ED |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 5

Study No. : SR15146

|                   |              | Histopathological findings |                                   |       |   |     |                                    |    |    |   |                                     |               |    |    |                                     |     |    |    |    |     |   |     |
|-------------------|--------------|----------------------------|-----------------------------------|-------|---|-----|------------------------------------|----|----|---|-------------------------------------|---------------|----|----|-------------------------------------|-----|----|----|----|-----|---|-----|
|                   |              | Sex : Male                 |                                   |       |   |     | Stage : Day 29                     |    |    |   |                                     | Species : Rat |    |    |                                     |     |    |    |    |     |   |     |
| Organ<br>Findings | Test article | Dose                       | PTSA<br>Monohydrate<br>0<br>mg/kg |       |   |     | PTSA<br>Monohydrate<br>50<br>mg/kg |    |    |   | PTSA<br>Monohydrate<br>200<br>mg/kg |               |    |    | PTSA<br>Monohydrate<br>800<br>mg/kg |     |    |    |    |     |   |     |
|                   |              |                            | Number of Animals                 | Grade | - | 1+  | 2+                                 | 3+ | 4+ | - | 1+                                  | 2+            | 3+ | 4+ | -                                   | 1+  | 2+ | 3+ | 4+ |     |   |     |
|                   |              |                            |                                   |       |   | 7   |                                    |    |    |   | 7                                   |               |    |    |                                     | 7   |    |    |    |     |   |     |
| Adrenal           |              |                            |                                   |       | 7 | <7> |                                    |    |    |   | 0                                   | ED            |    |    |                                     | 0   | ED |    |    |     | 7 | EF  |
|                   |              |                            |                                   |       |   |     |                                    |    |    |   |                                     |               |    |    |                                     |     |    |    |    |     |   |     |
| Eyeball           |              |                            |                                   |       | 7 | <7> |                                    |    |    |   | 0                                   | ED            |    |    |                                     | <0> |    |    |    | <0> |   | <7> |
|                   |              |                            |                                   |       |   |     |                                    |    |    |   |                                     |               |    |    |                                     |     |    |    |    |     |   |     |
| Harderian gland   |              |                            |                                   |       | 7 | <7> |                                    |    |    |   | 0                                   | ED            |    |    |                                     | <0> |    |    |    | <0> |   | <7> |
|                   |              |                            |                                   |       |   |     |                                    |    |    |   |                                     |               |    |    |                                     |     |    |    |    |     |   |     |
| Skeletal muscle   |              |                            |                                   |       | 7 | <7> |                                    |    |    |   | 0                                   | ED            |    |    |                                     | <0> |    |    |    | <0> |   | <7> |
|                   |              |                            |                                   |       |   |     |                                    |    |    |   |                                     |               |    |    |                                     |     |    |    |    |     |   |     |
| Femur             |              |                            |                                   |       | 7 | <7> |                                    |    |    |   | 0                                   | ED            |    |    |                                     | <0> |    |    |    | <0> |   | <7> |
|                   |              |                            |                                   |       |   |     |                                    |    |    |   |                                     |               |    |    |                                     |     |    |    |    |     |   |     |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 6

Study No. : SR15146

| Histopathological findings                 |                                   |                         |                          |    |      |    |                           |      |    | Species : Rat |                            |      |    |         |    |    |    |
|--|-----------------------------------|-------------------------|--------------------------|----|------|----|---------------------------|------|----|---------------|----------------------------|------|----|---------|----|----|----|
| Sex : Female                               |                                   | Stage : Lactation Day 5 |                          |    |      |    |                           |      |    |               |                            |      |    |         |    |    |    |
| Organ                                      | Findings                          | Test article            | PTSA Monohydrate 0 mg/kg |    |      |    | PTSA Monohydrate 50 mg/kg |      |    |               | PTSA Monohydrate 200 mg/kg |      |    |         |    |    |    |
|  |                                   |                         | Dose                     | 11 | 12   | 12 | 11                        | 12   | 12 | 10            | 10                         | 10   | 10 |         |    |    |    |
| Number of Animals                          | Grade                             |                         | -                        | 1+ | 2+   | 3+ | 4+                        | -    | 1+ | 2+            | 3+                         | 4+   | -  | 1+      | 2+ | 3+ | 4+ |
| Lung                                       | Aggregation, macrophage, alveolar |                         | 10                       | 1  | 0    | 0  | 0                         | 0    | 0  | 0             | 0                          | 0    | 10 | 0       | 0  | 0  | 0  |
|  |                                   |                         |                          |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |
| Trachea                                    |                                   |                         | 11                       |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |
| Submandibular gland                        |                                   |                         | 11                       |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |
| Esophagus                                  |                                   |                         | 11                       |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |
| Stomach                                    |                                   |                         |                          |    | <11> |    |                           | <12> |    | <12>          |                            | <12> |    | <10>    |    |    |    |
| Hyperplasia, squamous cell, limiting ridge |                                   |                         | 11                       | 0  | 0    | 0  | 0                         | 0    | 12 | 0             | 0                          | 0    | 0  | 3       | 7  | 0  | 0  |
|  |                                   |                         |                          |    |      | EF |                           |      | EF |               |                            |      |    | FT \$\$ |    |    |    |
| Hyperkeratosis, limiting ridge             |                                   |                         | 11                       | 0  | 0    | 0  | 0                         | 0    | 12 | 0             | 0                          | 0    | 0  | 7       | 3  | 0  | 0  |
|  |                                   |                         |                          |    |      | EF |                           |      | EF |               |                            |      |    |         |    |    |    |
| Duodenum                                   |                                   |                         | 11                       |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |
| Jejunum                                    |                                   |                         | 11                       |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |
| Ileum                                      |                                   |                         | 11                       |    | <11> |    |                           | <0>  |    | <0>           |                            | <0>  |    | <10>    |    |    |    |
|  |                                   |                         |                          |    |      | 0  | ED                        |      | 0  | ED            |                            | 0    | ED | 10      | EF |    |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Significantly different from PTSAMonohydrate 0 mg/kg: \$\$ P&lt;0.01

FT : Fisher's exact test (two-side)

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 7

Study No. : SR15146

|  |                            | Histopathological findings |   |   |      |  |                         |   |      |   |    |               |         |
|--|----------------------------|----------------------------|---|---|------|--|-------------------------|---|------|---|----|---------------|---------|
|  |                            | Sex : Female               |   |   |      |  | Stage : Lactation Day 5 |   |      |   |    | Species : Rat |         |
| Organ<br>Findings                      | Number of Animals<br>Grade | Test article               |   | PTSA<br>Monohydrate<br>0<br>mg/kg<br>11 |      | PTSA<br>Monohydrate<br>50<br>mg/kg<br>12 |                         | PTSA<br>Monohydrate<br>200<br>mg/kg<br>12 |      | PTSA<br>Monohydrate<br>800<br>mg/kg<br>10 |    |               |         |
|  |                            | Dose                       |   |   |      |  |                         |   |      |   |    |               |         |
| Cecum                                  |                            |                            |   | -                                       | 1+   | 2+                                       | 3+                      | 4+  | -    | 1+  | 2+ | 3+            | 4+      |
|  |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
|  |                            | 11                         |   |   |      | 0  |                         |   | 0    |   |    |               | 10      |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               | EF      |
| Colon                                  |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
|  |                            | 11                         |   |   |      | 0  |                         |   | 0    |   |    |               | 10      |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               | EF      |
| Rectum                                 |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
|  |                            | 11                         |   |   |      | 0  |                         |   | 0    |   |    |               | 10      |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               | EF      |
| Pancreas                               |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
|  |                            | 11                         |   |   |      | 0  |                         |   | 0    |   |    |               | 10      |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               | EF      |
| Liver                                  |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
| Vacuolation, hepatocyte,<br>periportal |                            | 11                         | 0 | 0                                       | 0    | 0  | 0                       | 0   | 0    | 0   | 0  | 0             | 0       |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               |         |
| Microgranuloma                         |                            | 9                          | 2 | 0                                       | 0    | 0  | 0                       | 0   | 0    | 0   | 0  | 0             | 0       |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               |         |
| Heart                                  |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
|  |                            | 11                         |   |   |      | 0  |                         |   | 0    |   |    |               | 10      |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               | EF      |
| Kidney                                 |                            |                            |   |   | <11> |  |                         |   | <12> |   |    |               | <10>    |
| Basophilic change, renal tubule        |                            | 10                         | 1 | 0                                       | 0    | 0  | 0                       | 0   | 12   | 0   | 0  | 0             | FT \$\$ |
|  |                            |                            |   |   |      |  |                         |   |      | 9   | 3  | 0             | 0       |
| Urinary bladder                        |                            |                            |   |   | <11> |  |                         |   | <0>  |   |    |               | <10>    |
|  |                            | 11                         |   |   |      | 0  |                         |   | 0    |   |    |               | 10      |
|  |                            |                            |   |   |      | ED                                       |                         |   | ED   |   |    |               | EF      |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Significantly different from PTSAMonohydrate 0 mg/kg: \$\$ P&lt;0.01

FT : Fisher's exact test (two-side)

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 8

Study No. : SR15146

| Sex : Female<br>Histopathological findings |                         | Stage : Lactation Day 5 |    |                          |    |    |    |                           |    |    |    |                            |    | Species : Rat |    |                            |    |
|--|-------------------------|-------------------------|----|--------------------------|----|----|----|---------------------------|----|----|----|----------------------------|----|---------------|----|----------------------------|----|
|  |                         | Test article            |    | PTSA Monohydrate 0 mg/kg |    |    |    | PTSA Monohydrate 50 mg/kg |    |    |    | PTSA Monohydrate 200 mg/kg |    |               |    | PTSA Monohydrate 800 mg/kg |    |
| Organ Findings                             | Number of Animals Grade | Dose                    | -  | 1+                       | 2+ | 3+ | 4+ | -                         | 1+ | 2+ | 3+ | 4+                         | -  | 1+            | 2+ | 3+                         | 4+ |
| Ovary                                      |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Uterine horn                               |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Uterine cervix                             |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Vagina                                     |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Cerebrum                                   |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Cerebellum                                 |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Pons                                       |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Spinal cord                                |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |
| Sciatic nerve                              |                         |                         | 11 | <11>                     | 0  | ED |    | <0>                       | 0  | ED |    | <0>                        | 10 | EF            |    | <10>                       |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

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EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 9

Study No. : SR15146

| Histopathological findings      |          |                         |                          |    |      |    |                           |    |     | Species : Rat |                            |    |     |    |    |      |    |    |
|---------------------------------|----------|-------------------------|--------------------------|----|------|----|---------------------------|----|-----|---------------|----------------------------|----|-----|----|----|------|----|----|
| Sex : Female                    |          | Stage : Lactation Day 5 |                          |    |      |    |                           |    |     |               |                            |    |     |    |    |      |    |    |
| Organ                           | Findings | Test article            | PTSA Monohydrate 0 mg/kg |    |      |    | PTSA Monohydrate 50 mg/kg |    |     |               | PTSA Monohydrate 200 mg/kg |    |     |    |    |      |    |    |
|                                 |          |                         | Dose                     | 1+ | 2+   | 3+ | 4+                        | 1+ | 2+  | 3+            | 4+                         | 1+ | 2+  | 3+ | 4+ |      |    |    |
| Number of Animals               | Grade    |                         |                          | -  | 1+   | 2+ | 3+                        | 4+ | -   | 1+            | 2+                         | 3+ | 4+  | -  | 1+ | 2+   | 3+ | 4+ |
| Spleen                          |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Thymus                          |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Bone marrow, femur              |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Submandibular lymph node        |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Mesenteric lymph node           |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Peyer's patch                   |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Pituitary gland                 |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |
| Thyroid<br>Ultimobranchial body |          |                         |                          | 9  | <11> | 0  | ED                        | 0  | <0> | 0             | ED                         | 0  | <0> | 9  | EF | <10> |    |    |
| Parathyroid                     |          |                         |                          | 11 | <11> | 0  | ED                        |    | <0> | 0             | ED                         |    | <0> | 10 | EF | <10> |    |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

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EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 10

Study No. : SR15146

| Sex : Female      |          | Histopathological findings |                          |    |    |                         |                           |    |    |    |                            |     |    | Species : Rat |                            |    |
|-------------------|----------|----------------------------|--------------------------|----|----|-------------------------|---------------------------|----|----|----|----------------------------|-----|----|---------------|----------------------------|----|
|                   |          | Test article               |                          |    |    | Stage : Lactation Day 5 |                           |    |    |    |                            |     |    |               |                            |    |
| Organ             | Findings | Dose                       | PTSA Monohydrate 0 mg/kg |    |    |                         | PTSA Monohydrate 50 mg/kg |    |    |    | PTSA Monohydrate 200 mg/kg |     |    |               | PTSA Monohydrate 800 mg/kg |    |
|                   |          |                            | -                        | 1+ | 2+ | 3+                      | -                         | 1+ | 2+ | 3+ | 4+                         | -   | 1+ | 2+            | 3+                         | 4+ |
| Number of Animals | Grade    |                            |                          |    |    |                         |                           |    |    |    |                            |     |    |               |                            |    |
| Adrenal           |          |                            |                          |    |    |                         |                           |    |    |    |                            |     |    |               |                            |    |
|                   |          |                            | 11                       |    |    |                         | <11>                      |    | 0  |    |                            | 0   |    | 10            |                            |    |
|                   |          |                            |                          |    |    |                         |                           |    | ED |    |                            | ED  |    | EF            |                            |    |
| Eyeball           |          |                            |                          |    |    |                         | <11>                      |    |    |    |                            | <0> |    |               | <0>                        |    |
|                   |          |                            | 11                       |    |    |                         |                           |    | 0  |    |                            | 0   |    | 10            |                            |    |
|                   |          |                            |                          |    |    |                         |                           |    | ED |    |                            | ED  |    | EF            |                            |    |
| Harderian gland   |          |                            |                          |    |    |                         | <11>                      |    |    |    |                            | <0> |    |               | <0>                        |    |
|                   |          |                            | 11                       |    |    |                         |                           |    | 0  |    |                            | 0   |    | 10            |                            |    |
|                   |          |                            |                          |    |    |                         |                           |    | ED |    |                            | ED  |    | EF            |                            |    |
| Skeletal muscle   |          |                            |                          |    |    |                         | <11>                      |    |    |    |                            | <0> |    |               | <0>                        |    |
|                   |          |                            | 11                       |    |    |                         |                           |    | 0  |    |                            | 0   |    | 10            |                            |    |
|                   |          |                            |                          |    |    |                         |                           |    | ED |    |                            | ED  |    | EF            |                            |    |
| Femur             |          |                            |                          |    |    |                         | <11>                      |    |    |    |                            | <0> |    |               | <0>                        |    |
|                   |          |                            | 11                       |    |    |                         |                           |    | 0  |    |                            | 0   |    | 10            |                            |    |
|                   |          |                            |                          |    |    |                         |                           |    | ED |    |                            | ED  |    | EF            |                            |    |
| Mammary gland     |          |                            |                          |    |    |                         | <11>                      |    |    |    |                            | <0> |    |               | <0>                        |    |
|                   |          |                            | 11                       |    |    |                         |                           |    | 0  |    |                            | 0   |    | 10            |                            |    |
|                   |          |                            |                          |    |    |                         |                           |    | ED |    |                            | ED  |    | EF            |                            |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

ED : The number of samples of a treated group is less than 2.

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 11

Study No. : SR15146

| Histopathological findings                    |              | Species : Rat         |             |     |             |    |      |   |       |    |               |    |  |  |
|---|--------------|-----------------------|-------------|-----|-------------|----|------|---|-------|----|---------------|----|--|--|
| Sex : Female                                  |              | Stage : Non-pregnancy |             |     |             |    |      |   |       |    |               |    |  |  |
| Organ<br>Findings                             | Test article | Dose                  | PTSA        |     |             |    | PTSA |   |       |    | Species : Rat |    |  |  |
|   |              |                       | Monohydrate |     | Monohydrate |    | 800  |   | mg/kg |    |               |    |  |  |
|   |              |                       | 0           | 1   | 1           | 1  | 0    | 1 | 1     | 4+ |               |    |  |  |
| Number of Animals                             | Grade        |                       | -           | 1+  | 2+          | 3+ | 4+   | - | 1+    | 2+ | 3+            | 4+ |  |  |
|   |              |                       |             |     |             |    |      |   |       |    |               |    |  |  |
| Lung  |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Trachea                                       |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Submandibular gland                           |              |                       |             | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Esophagus                                     |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Stomach                                       |              |                       |             | <1> |             |    |      |   | <1>   |    |               |    |  |  |
| Hyperplasia, squamous cell,<br>limiting ridge |              |                       | 1           | 0   | 0           | 0  | 0    | 0 | 1     | 0  | 0             | 0  |  |  |
| Duodenum                                      |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Jejunum                                       |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Ileum   |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Cecum   |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Colon   |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Rectum  |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Pancreas                                      |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Liver   |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |
| Heart   |              |                       | 1           | <1> |             |    |      | 1 | <1>   |    |               |    |  |  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 12

Study No. : SR15146

| Histopathological findings      |              | Species : Rat         |                     |       |     |     |                     |       |   |     |               |    |    |
|---------------------------------|--------------|-----------------------|---------------------|-------|-----|-----|---------------------|-------|---|-----|---------------|----|----|
| Sex : Female                    |              | Stage : Non-pregnancy |                     |       |     |     |                     |       |   |     |               |    |    |
| Organ<br>Findings               | Test article | Dose                  | PTSA<br>Monohydrate |       |     |     | PTSA<br>Monohydrate |       |   |     | Species : Rat |    |    |
|                                 |              |                       | 0                   | mg/kg | 1   | <1> | 800                 | mg/kg | 1 | <1> | Species : Rat |    |    |
|                                 |              |                       | -                   |       | 1+  | 2+  | 3+                  | 4+    | - | 1+  | 2+            | 3+ | 4+ |
| Kidney                          |              |                       |                     |       |     |     |                     |       |   |     |               |    |    |
| Basophilic change, renal tubule |              |                       | 0                   | 1     | 0   | 0   | 0                   | 0     | 0 | 0   | 1             | 0  | 0  |
| Cast, hyaline                   |              |                       | 1                   | 0     | 0   | 0   | 0                   | 0     | 0 | 1   | 0             | 0  | 0  |
| Urinary bladder                 |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Ovary                           |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Uterine horn                    |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Uterine cervix                  |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Vagina                          |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Cerebrum                        |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Cerebellum                      |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Pons                            |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Spinal cord                     |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Sciatic nerve                   |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Spleen                          |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |
| Thymus                          |              |                       |                     |       | <1> |     |                     |       |   | <1> |               |    |    |
|                                 |              |                       | 1                   |       |     |     |                     |       |   | 1   |               |    |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 13

Study No. : SR15146

| Organ<br>Findings                      | Sex : Female<br>Number of Animals<br>Grade | Histopathological findings |                                   |     |    |    |                                     |           |     | Species : Rat |  |
|--|--|----------------------------|-----------------------------------|-----|----|----|-------------------------------------|-----------|-----|---------------|--|
|  |  | Test article<br>Dose       | PTSA<br>Monohydrate<br>0<br>mg/kg |     |    |    | PTSA<br>Monohydrate<br>800<br>mg/kg |           |     |               |  |
|  |  |                            | -                                 | 1+  | 2+ | 3+ | 4+                                  | -         | 1+  | 2+            |  |
| Bone marrow, femur                     |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Submandibular lymph node               |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Mesenteric lymph node                  |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Peyer's patch                          |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Pituitary gland<br>Cyst, pars distalis |  | 0 1 0 0 0                  | <1>                               |     |    |    |                                     | 1 0 0 0 0 | <1> |               |  |
| Thyroid                                |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Parathyroid                            |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Adrenal                                |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Eyeball                                |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Harderian gland                        |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Skeletal muscle                        |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Femur                                  |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |
| Mammary gland                          |  |                            | 1                                 | <1> |    |    |                                     | 1         | <1> |               |  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 14

Study No. : SR15146

| Histopathological findings |   | Stage : Died on lactation day 0 |                             |   |    |    | Species : Rat |    |
|----------------------------|---|---------------------------------|-----------------------------|---|----|----|---------------|----|
| Sex : Female               |   | Test article                    |                             |   |    |    |               |    |
| Organ                      | Findings                                      | Dose                            | PTSA                        |   |    |    |               |    |
|                            |   |                                 | Monohydrate<br>800<br>mg/kg | 1 | 1+ | 2+ | 3+            | 4+ |
| Number of Animals          | Grade   | -                               | <1>                         |   |    |    |               |    |
| Lung                       | Necrosis, bronchial epithelial                | 0                               | 0                           | 0 | 1  | 0  |               |    |
|                            | Edema, alveolar                               | 0                               | 0                           | 0 | 1  | 0  |               |    |
|                            | Edema, perivascular                           | 0                               | 0                           | 1 | 0  | 0  |               |    |
|                            | Infiltration, neutrophil                      | 0                               | 0                           | 1 | 0  | 0  |               |    |
| Trachea                    |   | 1                               | <1>                         |   |    |    |               |    |
| Submandibular gland        |   | 1                               | <1>                         |   |    |    |               |    |
| Esophagus                  |   | 1                               | <1>                         |   |    |    |               |    |
| Stomach                    |   |                                 | <1>                         |   |    |    |               |    |
|                            | Hyperplasia, squamous cell,<br>limiting ridge | 0                               | 1                           | 0 | 0  | 0  |               |    |
| Duodenum                   |   | 1                               | <1>                         |   |    |    |               |    |
| Jejunum                    |   | 1                               | <1>                         |   |    |    |               |    |
| Ileum                      |   | 1                               | <1>                         |   |    |    |               |    |
| Cecum                      |   | 1                               | <1>                         |   |    |    |               |    |
| Colon                      |   | 1                               | <1>                         |   |    |    |               |    |
| Rectum                     |   | 1                               | <1>                         |   |    |    |               |    |
| Pancreas                   |   | 1                               | <1>                         |   |    |    |               |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 15

Study No. : SR15146

| Histopathological findings |              | Stage : Died on lactation day 0 |             |     |       |    | Species : Rat |               |
|----------------------------|--------------|---------------------------------|-------------|-----|-------|----|---------------|---------------|
| Organ Findings             | Sex : Female | Test article                    | PTSA        |     |       |    |               | Species : Rat |
|                            | Dose         |                                 | Monohydrate | 800 | mg/kg | 1  | <1>           |               |
| Number of Animals          | Grade        | -                               | 1+          | 2+  | 3+    | 4+ |               |               |
| Liver                      |              |                                 | 1           |     |       |    |               |               |
| Heart                      |              |                                 | <1>         |     |       |    |               |               |
| Kidney                     |              |                                 | <1>         |     |       |    |               |               |
| Urinary bladder            |              |                                 | <1>         |     |       |    |               |               |
| Ovary                      |              |                                 | <1>         |     |       |    |               |               |
| Uterine horn               |              |                                 | <1>         |     |       |    |               |               |
| Uterine cervix             |              |                                 | <1>         |     |       |    |               |               |
| Vagina                     |              |                                 | <1>         |     |       |    |               |               |
| Cerebrum                   |              |                                 | <1>         |     |       |    |               |               |
| Cerebellum                 |              |                                 | <1>         |     |       |    |               |               |
| Pons                       |              |                                 | <1>         |     |       |    |               |               |
| Spinal cord                |              |                                 | <1>         |     |       |    |               |               |
| Sciatic nerve              |              |                                 | <1>         |     |       |    |               |               |
| Spleen                     |              |                                 | <1>         |     |       |    |               |               |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 16

Study No. : SR15146

| Histopathological findings |              | Stage : Died on lactation day 0     |       |   |     |    | Species : Rat |    |     |
|----------------------------|--------------|-------------------------------------|-------|---|-----|----|---------------|----|-----|
| Sex : Female               | Test article | PTSA<br>Monohydrate<br>800<br>mg/kg |       |   |     |    |               |    |     |
| Organ Findings             | Dose         | Number of Animals                   | Grade | - | 1+  | 2+ | 3+            | 4+ | <1> |
| Thymus                     |              |                                     |       |   | 1   |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Bone marrow, femur         |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Submandibular lymph node   |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Mesenteric lymph node      |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Peyer's patch              |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Pituitary gland            |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Thyroid                    |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Parathyroid                |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Adrenal                    |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Eyeball                    |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Harderian gland            |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Skeletal muscle            |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Femur                      |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |
| Mammary gland              |              |                                     |       |   | <1> |    |               |    |     |
|                            |              | 1                                   |       |   |     |    |               |    |     |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 17

Study No. : SR15146

| Histopathological findings                  |              | Species : Rat  |             |     |             |    |           |      |         |    |    |    |
|---|--------------|----------------|-------------|-----|-------------|----|-----------|------|---------|----|----|----|
| Sex : Female (satellite)                    |              | Stage : Day 29 |             |     |             |    |           |      |         |    |    |    |
| Organ Findings                              | Test article | Dose           | PTSA        |     |             |    |           | PTSA |         |    |    |    |
|   |              |                | Monohydrate |     | Monohydrate |    | 800 mg/kg |      | 5 mg/kg |    |    |    |
|   |              |                | -           | 1+  | 2+          | 3+ | 4+        | -    | 1+      | 2+ | 3+ | 4+ |
| Lung  |              |                |             |     |             |    |           | <5>  |         |    |    |    |
|   |              |                | 5           |     |             |    |           |      | 5       |    |    |    |
|   |              |                |             |     |             |    |           |      | EF      |    |    |    |
| Trachea                                     |              |                |             | <5> |             |    |           |      | <5>     |    |    |    |
|   |              |                | 5           |     |             |    |           |      | 5       |    |    |    |
|   |              |                |             |     |             |    |           |      | EF      |    |    |    |
| Submandibular gland                         |              |                |             | <5> |             |    |           |      | <5>     |    |    |    |
|   |              |                | 5           |     |             |    |           |      | 5       |    |    |    |
|   |              |                |             |     |             |    |           |      | EF      |    |    |    |
| Esophagus                                   |              |                |             | <5> |             |    |           |      | <5>     |    |    |    |
|   |              |                | 5           |     |             |    |           |      | 5       |    |    |    |
|   |              |                |             |     |             |    |           |      | EF      |    |    |    |
| Stomach                                     |              |                |             | <5> |             |    |           |      | <5>     |    |    |    |
| Hyperplasia, squamous cell, limiting ridge  |              |                | 5           | 0   | 0           | 0  | 0         | 0    | 5       | 0  | 0  | 0  |
|   |              |                |             |     |             |    |           |      | FT \$\$ |    |    |    |
| Hyperkeratosis, limiting ridge              |              |                | 5           | 0   | 0           | 0  | 0         | 0    | 2       | 3  | 0  | 0  |
| Fibrosis, lamina propria, glandular stomach |              |                | 5           | 0   | 0           | 0  | 0         | 0    | 4       | 1  | 0  | 0  |
| Duodenum                                    |              |                |             | <5> |             |    |           |      | <5>     |    |    |    |
|   |              |                | 5           |     |             |    |           |      | 5       |    |    |    |
|   |              |                |             |     |             |    |           |      | EF      |    |    |    |
| Jejunum                                     |              |                |             | <5> |             |    |           |      | <5>     |    |    |    |
|   |              |                | 5           |     |             |    |           |      | 5       |    |    |    |
|   |              |                |             |     |             |    |           |      | EF      |    |    |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Significantly different from PTSA Monohydrate 0 mg/kg: \$\$ P&lt;0.01

FT : Fisher's exact test (two-side)

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 18

Study No. : SR15146

| Histopathological findings      |                   |       |                |             |      |       |             |     |       | Species : Rat |  |
|---------------------------------|-------------------|-------|----------------|-------------|------|-------|-------------|-----|-------|---------------|--|
| Sex : Female (satellite)        |                   |       | Stage : Day 29 |             |      |       |             |     |       |               |  |
| Organ<br>Findings               | Number of Animals | Grade | Test article   |             | PTSA |       | PTSA        |     |       |               |  |
|                                 |                   |       | Dose           | Monohydrate | 0    | mg/kg | Monohydrate | 800 | mg/kg |               |  |
|                                 |                   |       |                | 5           |      |       | 5           |     |       |               |  |
| Ileum                           |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
|                                 |                   | 1+    | 5              |             |      |       | 5           |     |       |               |  |
|                                 |                   | 2+    |                |             |      |       | EF          |     |       |               |  |
|                                 |                   | 3+    |                |             |      |       |             |     |       |               |  |
|                                 |                   | 4+    |                |             |      |       |             |     |       |               |  |
| Cecum                           |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
|                                 |                   | 1+    | 5              |             |      |       | 5           |     |       |               |  |
|                                 |                   | 2+    |                |             |      |       | EF          |     |       |               |  |
| Colon                           |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
|                                 |                   | 1+    | 5              |             |      |       | 5           |     |       |               |  |
|                                 |                   | 2+    |                |             |      |       | EF          |     |       |               |  |
| Rectum                          |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
|                                 |                   | 1+    | 5              |             |      |       | 5           |     |       |               |  |
|                                 |                   | 2+    |                |             |      |       | EF          |     |       |               |  |
| Pancreas                        |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
|                                 |                   | 1+    | 5              |             |      |       | 5           |     |       |               |  |
|                                 |                   | 2+    |                |             |      |       | EF          |     |       |               |  |
| Liver                           |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
| Microgranuloma                  |                   | 1+    | 3              | 2           | 0    | 0     | 0           | 4   | 1     | 0             |  |
|                                 |                   | 2+    |                |             |      |       |             | 0   | 0     | 0             |  |
| Heart                           |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
|                                 |                   | 1+    | 5              |             |      |       | 5           |     |       |               |  |
|                                 |                   | 2+    |                |             |      |       | EF          |     |       |               |  |
| Kidney                          |                   | -     |                | <5>         |      |       | <5>         |     |       |               |  |
| Basophilic change, renal tubule |                   | 1+    | 3              | 2           | 0    | 0     | 0           | 2   | 2     | 0             |  |
|                                 |                   | 2+    |                |             |      |       |             | 1   | 0     | 0             |  |
| Mineralization, cortex          |                   | -     |                | 5           | 0    | 0     | 0           | 4   | 0     | 1             |  |
|                                 |                   | 1+    |                |             |      |       |             | 0   | 0     | 0             |  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 19

Study No. : SR15146

| Histopathological findings<br>Sex : Female (satellite) |              | Stage : Day 29 |                                   |     |    |    |                                     |    |    | Species : Rat |                            |
|--|--------------|----------------|-----------------------------------|-----|----|----|-------------------------------------|----|----|---------------|----------------------------|
| Organ<br>Findings                                      | Test article | Dose           | PTSA<br>Monohydrate<br>0<br>mg/kg |     |    |    | PTSA<br>Monohydrate<br>800<br>mg/kg |    |    |               | Number of Animals<br>Grade |
|  |              |                | -                                 | 1+  | 2+ | 3+ | -                                   | 1+ | 2+ | 3+            |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | <5>                        |
| Urinary bladder  |              |                | 5                                 |     |    |    | 5                                   |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Ovary  |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Uterine horn   |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Uterine cervix   |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Vagina   |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Cerebrum   |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Cerebellum   |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Pons   |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |
| Spinal cord  |              |                | 5                                 | <5> |    |    | <5>                                 |    |    |               |                            |
|  |              |                |                                   |     |    |    |                                     |    |    |               | EF                         |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 20

Study No. : SR15146

| Histopathological findings         |                          | Stage : Day 29 |                                   |    |    |    |    |                                     |    |    |    | Species : Rat |
|------------------------------------|--------------------------|----------------|-----------------------------------|----|----|----|----|-------------------------------------|----|----|----|---------------|
| Organ<br>Findings                  | Sex : Female (satellite) | Test article   | PTSA<br>Monohydrate<br>0<br>mg/kg |    |    |    |    | PTSA<br>Monohydrate<br>800<br>mg/kg |    |    |    |               |
|                                    | Dose                     |                | -                                 | 1+ | 2+ | 3+ | 4+ | -                                   | 1+ | 2+ | 3+ | 4+            |
|                                    | Number of Animals        |                |                                   |    |    |    |    |                                     |    |    |    |               |
| Sciatic nerve                      | Grade                    |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Spleen                             |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Thymus                             |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Bone marrow, femur                 |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Submandibular lymph node           |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Mesenteric lymph node              |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Peyer's patch                      |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
|                                    |                          |                | 5                                 |    |    |    |    | 5                                   |    |    |    |               |
|                                    |                          |                |                                   |    |    |    |    | EF                                  |    |    |    |               |
| Pituitary gland                    |                          |                | <5>                               |    |    |    |    | <5>                                 |    |    |    |               |
| Craniohypophyseal tissue, aberrant |                          |                | 4                                 | 1  | 0  | 0  | 0  | 5                                   | 0  | 0  | 0  | 0             |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 21

Study No. : SR15146

| Histopathological findings<br>Sex : Female (satellite) |              | Stage : Day 29 |                                   |   |     |    |    |                                     |    |     |    | Species : Rat |
|--|--------------|----------------|-----------------------------------|---|-----|----|----|-------------------------------------|----|-----|----|---------------|
| Organ<br>Findings                                      | Test article | Dose           | PTSA<br>Monohydrate<br>0<br>mg/kg |   |     |    |    | PTSA<br>Monohydrate<br>800<br>mg/kg |    |     |    |               |
|  |              |                | -                                 |   |     |    |    | <5>                                 |    |     |    |               |
|  |              |                | <5>                               |   |     |    |    | <5>                                 |    |     |    |               |
| Thyroid  |              |                | -                                 | 4 | 1   | 0  | 0  | 0                                   | 4  | 1   | 0  | 0             |
| Ultimobranchial body                                   |              |                | 1+                                | 5 | 2+  | 3+ | 4+ |                                     | 1+ | 2+  | 3+ | 4+            |
| Parathyroid  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |
| Adrenal  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |
| Eyeball  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |
| Harderian gland  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |
| Skeletal muscle  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |
| Femur  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |
| Mammary gland  |              |                |                                   | 5 | <5> |    |    |                                     |    | <5> |    |               |
|  |              |                |                                   |   |     |    |    |                                     |    | 5   | EF |               |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 22

Study No. : SR15146

| Histopathological findings                    |                   |                         |    |             |               |               |
|---|-------------------|-------------------------|----|-------------|---------------|---------------|
| Sex : Male                                    |                   | Stage : Recovery Day 15 |    |             | Species : Rat |               |
| Organ<br>Findings                             | Test article      | PTSA                    |    | PTSA        |               | Species : Rat |
|   | Dose              | Monohydrate             | 0  | Monohydrate | 800           |               |
|   | Number of Animals | mg/kg                   | 5  | mg/kg       | 5             |               |
| Grade   | -                 | 1+                      | 2+ | 3+          | 4+            |               |
| Stomach                                       |                   | <5>                     |    | <5>         |               |               |
| Hyperplasia, squamous cell,<br>limiting ridge |                   | 5                       | 0  | 0           | 0             | 0             |
|   |                   | 3                       | 2  | 0           | 0             | 0             |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

Table 15 - 23

Study No. : SR15146

| Histopathological findings |                                 | Stage : Recovery Day 15  |       |              |             |       |             |       |   |   |   | Species : Rat |  |
|----------------------------|---------------------------------|--------------------------|-------|--------------|-------------|-------|-------------|-------|---|---|---|---------------|--|
| Organ                      | Findings                        | Sex : Female (satellite) |       | Test article |             | PTSA  |             | PTSA  |   |   |   |               |  |
|                            |                                 | Number of Animals        | Grade | Dose         | Monohydrate |       | Monohydrate |       |   |   |   |               |  |
|                            |                                 |                          |       |              | 0           | mg/kg | 800         | mg/kg |   |   |   |               |  |
| Stomach                    |                                 |                          |       | 5            |             |       | 4           |       |   |   |   |               |  |
|                            |                                 |                          |       | <5>          |             |       | <4>         |       |   |   |   |               |  |
| Kidney                     |                                 |                          |       |              | 5           | 0     | 0           | 0     | 2 | 2 | 0 | 0             |  |
|                            | Basophilic change, renal tubule |                          |       |              |             |       |             |       |   |   |   |               |  |
|                            |                                 |                          |       |              |             |       |             |       |   |   |   |               |  |
|                            | Hyperplasia, tubular epithelium |                          |       |              | 5           | 0     | 0           | 0     | 3 | 1 | 0 | 0             |  |
|                            |                                 |                          |       |              |             |       |             |       |   |   |   |               |  |
| Cyst                       |                                 |                          |       |              | 5           | 0     | 0           | 0     | 3 | 1 | 0 | 0             |  |
|                            |                                 |                          |       |              |             |       |             |       |   |   |   |               |  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Not significantly different from PTSAMonohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 15 - 24

Study No. : SR15146

| Histopathological findings<br>Sex : Female (satellite) |                      | Stage : Died on administration day 3 |       |   |    |    | Species : Rat |    |
|--|----------------------|--------------------------------------|-------|---|----|----|---------------|----|
| Organ<br>Findings                                      | Test article<br>Dose | PTSA<br>Monohydrate<br>800<br>mg/kg  |       |   |    |    |               |    |
|  |                      | Number of Animals                    | Grade | - | 1+ | 2+ | 3+            | 4+ |
| Lung   |                      |                                      |       | 1 |    |    |               |    |
|  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Trachea  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Submandibular gland                                    |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Esophagus  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Stomach  |                      |                                      | <1>   |   |    |    |               |    |
| Erosion, glandular stomach                             |                      | 0                                    | 1     | 0 | 0  | 0  |               |    |
| Necrosis, mucosa, pyloric part                         |                      | 0                                    | 0     | 0 | 1  | 0  |               |    |
| Duodenum   |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Jejunum  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Ileum  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Cecum  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Colon  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Rectum   |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Pancreas   |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |
| Liver  |                      |                                      | <1>   |   |    |    |               |    |
|  |                      | 1                                    |       |   |    |    |               |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 25

Study No. : SR15146

| Histopathological findings<br>Sex : Female (satellite) |                      | Stage : Died on administration day 3 |       |     |    |    | Species : Rat |    |
|--|----------------------|--------------------------------------|-------|-----|----|----|---------------|----|
| Organ<br>Findings                                      | Test article<br>Dose | PTSA<br>Monohydrate<br>800<br>mg/kg  |       |     |    |    |               |    |
|  |                      | Number of Animals                    | Grade | -   | 1+ | 2+ | 3+            | 4+ |
| Heart  |                      |                                      |       | 1   |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Kidney   |                      |                                      |       | <1> |    |    |               |    |
| Necrosis, renal tubule, cortex                         |                      | 0                                    | 0     | 0   | 0  | 1  |               |    |
| Urinary bladder  |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Ovary  |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Uterine horn   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Uterine cervix   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Vagina   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Cerebrum   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Cerebellum   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Pons   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Spinal cord  |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Sciatic nerve  |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |
| Spleen   |                      |                                      |       | <1> |    |    |               |    |
| Atrophy, white pulp                                    |                      | 0                                    | 0     | 1   | 0  | 0  |               |    |
| Thymus   |                      |                                      |       | <1> |    |    |               |    |
|  |                      | 1                                    |       |     |    |    |               |    |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 15 - 26

Study No. : SR15146

| Histopathological findings<br>Sex : Female (satellite) |                      | Stage : Died on administration day 3 |       |     |    |    | Species : Rat |    |  |
|--|----------------------|--------------------------------------|-------|-----|----|----|---------------|----|--|
| Organ<br>Findings                                      | Test article<br>Dose | PTSA<br>Monohydrate<br>800<br>mg/kg  |       |     |    |    |               |    |  |
|  |                      | Number of Animals                    | Grade | -   | 1+ | 2+ | 3+            | 4+ |  |
| Bone marrow, femur                                     |                      |                                      |       |     | 1  |    |               |    |  |
|  |                      |                                      | <1>   |     |    |    |               |    |  |
|  |                      |                                      |       | 1   |    |    |               |    |  |
| Submandibular lymph node                               |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Mesenteric lymph node                                  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Peyer's patch  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Pituitary gland<br>Cyst, pars distalis                 |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       | 0   | 1  | 0  | 0             | 0  |  |
| Thyroid  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Parathyroid  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Adrenal  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Eyeball  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Harderian gland  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Skeletal muscle  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Femur  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |
| Mammary gland  |                      |                                      |       | <1> |    |    |               |    |  |
|  |                      |                                      |       |     | 1  |    |               |    |  |

&lt;&gt; : Number of animals examined

- : Not remarkable

1+ : Slight, 2+ : Mild, 3+ : Moderate, 4+ : Severe

Table 16

Study No. : SR15146

| Estrous cycles<br>Generation : F0 |      |   |                     | Species : Rat  |
|-----------------------------------|------|---|---------------------|--|
|                                   |      | /Before mating                            |                     |  |
| Test article                      | Dose | Mean length of<br>estrous cycle<br>(Days) | Number of<br>estrus | Number of animals with acyclic or<br>irregular cycle |
| PTSA Monohydrate<br>0 mg/kg       | n    | 12  | 12                  | 12<br>(0)  |
|                                   | Mean | 4.00                                      | 3.5                 |  |
|                                   | S.D. | 0.00                                      | 0.5                 |  |
|                                   |      |   |                     | EF   |
| PTSA Monohydrate<br>50 mg/kg      | n    | 12  | 12                  | 12<br>(0)  |
|                                   | Mean | 4.00                                      | 3.8                 |  |
|                                   | S.D. | 0.00                                      | 0.5                 |  |
|                                   |      |   |                     | EF   |
| PTSA Monohydrate<br>200 mg/kg     | n    | 12  | 12                  | 12<br>(0)  |
|                                   | Mean | 4.00                                      | 3.3                 |  |
|                                   | S.D. | 0.00                                      | 0.5                 |  |
|                                   |      |   |                     | EF   |
| PTSA Monohydrate<br>800 mg/kg     | n    | 12  | 12                  | 12<br>(0)  |
|                                   | Mean | 4.08                                      | 3.5                 |  |
|                                   | S.D. | 0.19                                      | 0.5                 |  |
|                                   |      |   |                     | EF   |

() : Values in brackets represent number of animals with acyclic or irregular cycle.

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 17 - 1

Study No. : SR15146

| Test article<br>Dose          | Reproductive performance |                   | Species : Rat          |                        |                      |                     |                      |                     |       |  |
|-------------------------------|--------------------------|-------------------|------------------------|------------------------|----------------------|---------------------|----------------------|---------------------|-------|--|
|                               | Generation : F0          |                   | Sex : Male             |                        | 1st mating           |                     | 2nd mating           |                     | Total |  |
|                               | Number of pairs          | Day of conceiving | Copulation index (%)   | Fertility index (%)    | Copulation index (%) | Fertility index (%) | Copulation index (%) | Fertility index (%) |       |  |
| PTSA Monohydrate<br>0 mg/kg   | n<br>Mean<br>S.D.        | 12<br>3.2<br>2.1  | 12<br>(12/12)<br>100.0 | 12<br>(11/12)<br>91.7  |                      |                     | (12/12)<br>100.0     | (11/12)<br>91.7     |       |  |
| PTSA Monohydrate<br>50 mg/kg  | n<br>Mean<br>S.D.        | 12<br>3.3<br>1.2  | 12<br>(12/12)<br>100.0 | 12<br>(12/12)<br>100.0 |                      |                     | (12/12)<br>100.0     | (12/12)<br>100.0    |       |  |
| PTSA Monohydrate<br>200 mg/kg | n<br>Mean<br>S.D.        | 12<br>3.0<br>3.6  | 12<br>(12/12)<br>100.0 | 12<br>(12/12)<br>100.0 |                      |                     | (12/12)<br>100.0     | (12/12)<br>100.0    |       |  |
| PTSA Monohydrate<br>800 mg/kg | n<br>Mean<br>S.D.        | 12<br>2.6<br>1.4  | 12<br>(12/12)<br>100.0 | 12<br>(11/12)<br>91.7  |                      |                     | (12/12)<br>100.0     | (11/12)<br>91.7     |       |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 17 - 2

Study No. : SR15146

| Test article<br>Dose          | Reproductive performance |                   | Species : Rat          |                        |                      |                     |                      |                     |       |  |
|-------------------------------|--------------------------|-------------------|------------------------|------------------------|----------------------|---------------------|----------------------|---------------------|-------|--|
|                               | Generation : F0          |                   | Sex : Female           |                        | 1st mating           |                     | 2nd mating           |                     | Total |  |
|                               | Number of pairs          | Day of conceiving | Copulation index (%)   | Fertility index (%)    | Copulation index (%) | Fertility index (%) | Copulation index (%) | Fertility index (%) |       |  |
| PTSA Monohydrate<br>0 mg/kg   | n<br>Mean<br>S.D.        | 12<br>3.2<br>2.1  | 12<br>(12/12)<br>100.0 | 12<br>(11/12)<br>91.7  |                      |                     | (12/12)<br>100.0     | (11/12)<br>91.7     |       |  |
| PTSA Monohydrate<br>50 mg/kg  | n<br>Mean<br>S.D.        | 12<br>3.3<br>1.2  | 12<br>(12/12)<br>100.0 | 12<br>(12/12)<br>100.0 |                      |                     | (12/12)<br>100.0     | (12/12)<br>100.0    |       |  |
| PTSA Monohydrate<br>200 mg/kg | n<br>Mean<br>S.D.        | 12<br>3.0<br>3.6  | 12<br>(12/12)<br>100.0 | 12<br>(12/12)<br>100.0 |                      |                     | (12/12)<br>100.0     | (12/12)<br>100.0    |       |  |
| PTSA Monohydrate<br>800 mg/kg | n<br>Mean<br>S.D.        | 12<br>2.6<br>1.4  | 12<br>(12/12)<br>100.0 | 12<br>(11/12)<br>91.7  |                      |                     | (12/12)<br>100.0     | (11/12)<br>91.7     |       |  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 18 - 1

Study No. : SR15146

| Test article<br>Dose          | Delivery data<br>Generation : F0 |                           |                       |                        |                            | Species : Rat    |                   |                                |                            |                  |                           |
|-------------------------------|----------------------------------|---------------------------|-----------------------|------------------------|----------------------------|------------------|-------------------|--------------------------------|----------------------------|------------------|---------------------------|
|                               | Gestation<br>period<br>(day)     | Number of<br>implantation | Birth<br>index<br>(%) | Number of<br>offspring | Number of<br>live newborns |                  |                   | Sex rate<br>(offspring)<br>(%) | Number of<br>dead newborns |                  | Gestation<br>index<br>(%) |
|                               |                                  |                           |                       |                        | M                          | F                | Total             |                                | Dead                       | Cannibalism      |                           |
| PTSA Monohydrate<br>0 mg/kg   | n<br>Mean<br>S.D.                | 11<br>22.09<br>0.30       | 11<br>15.7<br>1.8     | 11<br>90.00<br>14.2    | 11<br>6.6<br>2.2           | 11<br>7.5<br>2.3 | 11<br>14.1<br>2.8 | 73/155<br>47.1                 | 11<br>0.1<br>0.3           | 11<br>0.0<br>0.0 | 11/11<br>100.0<br>0.00    |
| PTSA Monohydrate<br>50 mg/kg  | n<br>Mean<br>S.D.                | 12<br>22.25<br>0.45       | 12<br>15.8<br>1.4     | 12<br>92.75<br>14.8    | 12<br>6.7<br>2.0           | 12<br>8.0<br>2.0 | 12<br>14.7<br>1.8 | 80/176<br>45.5                 | 12<br>0.2<br>0.6           | 12<br>0.0<br>0.6 | 12/12<br>100.0<br>0.00    |
| PTSA Monohydrate<br>200 mg/kg | n<br>Mean<br>S.D.                | 12<br>22.08<br>0.29       | 12<br>15.8<br>1.5     | 12<br>91.61<br>14.3    | 12<br>7.3<br>2.1           | 12<br>7.1<br>1.9 | 12<br>14.3<br>1.6 | 87/172<br>50.6                 | 12<br>0.0<br>0.0           | 12<br>0.0<br>0.0 | 12/12<br>100.0<br>0.00    |
| PTSA Monohydrate<br>800 mg/kg | n<br>Mean<br>S.D.                | 11<br>22.18<br>0.40       | 11<br>15.5<br>2.1     | 11<br>91.61<br>14.4    | 11<br>6.9<br>2.3           | 11<br>7.4<br>2.5 | 11<br>14.3<br>2.4 | 76/157<br>48.4                 | 11<br>0.1<br>0.3           | 11<br>0.0<br>0.3 | 11/11<br>100.0<br>0.00    |
|                               |                                  |                           |                       |                        |                            |                  |                   |                                | EF                         | EF               | EF                        |

M : Male, F : Female

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 18 - 2

Study No. : SR15146

| Delivery data<br>Generation : F0 |      |                               |                              | Species : Rat           |
|----------------------------------|------|-------------------------------|------------------------------|-------------------------|
| Test article                     |      | Number of<br>corpora<br>lutea | Implantation<br>index<br>(%) | Nursing<br>index<br>(%) |
| PTSA Monohydrate                 | n    | 11                            | 11                           | 11/11                   |
| 0 mg/kg                          | Mean | 15.8                          | 99.44                        | 100.0                   |
|                                  | S.D. | 1.8                           | 1.87                         |                         |
| PTSA Monohydrate                 | n    | 12                            | 12                           | 12/12                   |
| 50 mg/kg                         | Mean | 16.2                          | 97.94                        | 100.0                   |
|                                  | S.D. | 1.3                           | 3.95                         |                         |
| PTSA Monohydrate                 | n    | 12                            | 12                           | 12/12                   |
| 200 mg/kg                        | Mean | 15.8                          | 100.00                       | 100.0                   |
|                                  | S.D. | 1.5                           | 0.00                         |                         |
| PTSA Monohydrate                 | n    | 11                            | 11                           | 9/9                     |
| 800 mg/kg                        | Mean | 15.8                          | 98.15                        | 100.0                   |
|                                  | S.D. | 1.8                           | 4.35                         |                         |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 18 - 3

Study No. : SR15146

| Delivery data (external examination of offspring)     |                     |                     |                     | Day after birth : 0 |
|---|---------------------|---------------------|---------------------|---------------------|
| Generation : F0                                       |                     |                     |                     | Species : Rat       |
|   | PTSA<br>Monohydrate | PTSA<br>Monohydrate | PTSA<br>Monohydrate | PTSA<br>Monohydrate |
| Test article  |                     |                     |                     |                     |
| Dose  | 0                   | 50                  | 200                 | 800                 |
| Dose unit   | mg/kg               | mg/kg               | mg/kg               | mg/kg               |
| Number of dams  | 11                  | 12                  | 12                  | 11                  |
| Number of offspring                                   | 155                 | 176                 | 172                 | 157                 |
| Number of dams with anomalous offspring (incidence %) | 0(0.00)             | 0(0.00)             | 0(0.00)             | 0(0.00)             |
|   |                     | EF                  | EF                  | EF                  |
| Number of offspring with any anomaly (incidence %)    | 0(0.00)             | 0(0.00)             | 0(0.00)             | 0(0.00)             |
|   |                     | EF                  | EF                  | EF                  |

Not significantly different from PTSA Monohydrate 0 mg/kg

EF : The averages of all groups are same and all data is 0 in frequency. (all data of all groups is identical.)

Table 19

Study No. : SR15146

| Clinical sign of offspring<br>Generation : F0 |   | Species : Rat |                 |     |     |     |     |   |
|---|---|---------------|-----------------|-----|-----|-----|-----|---|
| Test article                                  | Dose                                    |               | Day after birth | 0   | 1   | 2   | 3   | 4 |
|   | Clinical signs                          | Time          | 1               | 1   | 1   | 1   | 1   | 1 |
| PTSA Monohydrate                              | Number of dams examined                 |               | 11              | 11  | 11  | 11  | 11  |   |
| 0 mg/kg                                       | Number of offspring                     |               | 155             | 155 | 155 | 155 | 154 |   |
|   | Number of dams with anomalous offspring |               | 0               | 0   | 0   | 0   | 0   |   |
| PTSA Monohydrate                              | Number of dams examined                 |               | 12              | 12  | 12  | 12  | 12  |   |
| 50 mg/kg                                      | Number of offspring                     |               | 176             | 176 | 176 | 176 | 173 |   |
|   | Number of dams with anomalous offspring |               | 0               | 0   | 0   | 0   | 0   |   |
| PTSA Monohydrate                              | Number of dams examined                 |               | 12              | 12  | 12  | 12  | 12  |   |
| 200 mg/kg                                     | Number of offspring                     |               | 172             | 172 | 172 | 172 | 172 |   |
|   | Number of dams with anomalous offspring |               | 0               | 0   | 0   | 0   | 0   |   |
| PTSA Monohydrate                              | Number of dams examined                 |               | 10              | 10  | 10  | 10  | 9   |   |
| 800 mg/kg                                     | Number of offspring                     |               | 157             | 142 | 142 | 128 | 126 |   |
|   | Number of dams with anomalous offspring |               | 0               | 0   | 0   | 0   | 0   |   |

F0 lactation)1 : Daily examination

Table 20

Study No. : SR15146

## Litter size and viability index of offspring

Generation : F0

Species : Rat

| Test article<br>Dose          |       | /Day after birth |                |                             |                |                             | Species : Rat |
|-------------------------------|-------|------------------|----------------|-----------------------------|----------------|-----------------------------|---------------|
|                               |       | 0<br>All pups    | 0<br>Live pups | 0<br>Viability<br>index (%) | 4<br>Live pups | 4<br>Viability<br>index (%) |               |
| PTSA Monohydrate<br>0 mg/kg   | Total | 156              | 155            |                             | 154            |                             |               |
|                               | n     | 11               | 11             | 11                          | 11             | 11                          |               |
|                               | Mean  |                  |                | 99.30                       |                | 99.52                       |               |
|                               | S.D.  |                  |                | 2.32                        |                | 1.60                        |               |
| PTSA Monohydrate<br>50 mg/kg  | Total | 178              | 176            |                             | 173            |                             |               |
|                               | n     | 12               | 12             | 12                          | 12             | 12                          |               |
|                               | Mean  |                  |                | 99.02                       |                | 98.31                       |               |
|                               | S.D.  |                  |                | 3.41                        |                | 3.08                        |               |
| PTSA Monohydrate<br>200 mg/kg | Total | 172              | 172            |                             | 172            |                             |               |
|                               | n     | 12               | 12             | 12                          | 12             | 12                          |               |
|                               | Mean  |                  |                | 100.00                      |                | 100.00                      |               |
|                               | S.D.  |                  |                | 0.00                        |                | 0.00                        |               |
| PTSA Monohydrate<br>800 mg/kg | Total | 158              | 157            |                             | 126            |                             |               |
|                               | n     | 11               | 11             | 11                          | 9              | 9                           |               |
|                               | Mean  |                  |                | 99.39                       |                | 98.62                       |               |
|                               | S.D.  |                  |                | 2.02                        |                | 2.73                        |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 21

Study No. : SR15146

|                               |        | Body weight of offspring<br>Generation : F0 |       | Unit : g | Species : Rat |
|-------------------------------|--------|---|-------|----------|---------------|
| Test article                  | Dose   | /Day after birth                            |       |          |               |
|                               |        | 0   | 4     |          |               |
| PTSA Monohydrate<br>0 mg/kg   | Male   | n   | 11    | 11       |               |
|                               |        | Mean  | 6.774 | 11.289   |               |
|                               |        | S.D.  | 0.640 | 2.010    |               |
|                               | Female | n   | 11    | 11       |               |
|                               |        | Mean  | 6.331 | 10.578   |               |
|                               |        | S.D.  | 0.649 | 1.876    |               |
| PTSA Monohydrate<br>50 mg/kg  | Male   | n   | 12    | 12       |               |
|                               |        | Mean  | 6.723 | 11.185   |               |
|                               |        | S.D.  | 0.573 | 1.078    |               |
|                               | Female | n   | 12    | 12       |               |
|                               |        | Mean  | 6.305 | 10.529   |               |
|                               |        | S.D.  | 0.561 | 1.002    |               |
| PTSA Monohydrate<br>200 mg/kg | Male   | n   | 12    | 12       |               |
|                               |        | Mean  | 6.707 | 11.050   |               |
|                               |        | S.D.  | 0.540 | 0.631    |               |
|                               | Female | n   | 12    | 12       |               |
|                               |        | Mean  | 6.240 | 10.570   |               |
|                               |        | S.D.  | 0.551 | 0.883    |               |
| PTSA Monohydrate<br>800 mg/kg | Male   | n   | 11    | 9        |               |
|                               |        | Mean  | 6.765 | 11.659   |               |
|                               |        | S.D.  | 0.713 | 1.922    |               |
|                               | Female | n   | 11    | 9        |               |
|                               |        | Mean  | 6.388 | 10.681   |               |
|                               |        | S.D.  | 0.646 | 1.653    |               |

Not significantly different from PTSA Monohydrate 0 mg/kg

Table 22

Study No. : SR15146

| Test article<br>Dose<br>Dose unit                     | Necropsy findings of offspring<br>Generation : F0 |                                 |                                  |                                  | Species : Rat |
|---|---|---------------------------------|----------------------------------|----------------------------------|---------------|
|   | PTSA Monohydrate<br>0<br>mg/kg                    | PTSA Monohydrate<br>50<br>mg/kg | PTSA Monohydrate<br>200<br>mg/kg | PTSA Monohydrate<br>800<br>mg/kg |               |
| Number of dams  | 11  | 12                              | 12                               | 9                                |               |
| Number of live offspring examined on Day 4 of birth   | 154   | 173                             | 172                              | 126                              |               |
| Finding absent  | 154   | 173                             | 172                              | 125                              |               |
| Kidney: Dilatation, renal pelvis, bilateral           | 0   | 0                               | 0                                | 1                                |               |
| Number of dead offspring examined on Day 0-4 of birth | 1   | 2                               | 0                                | 1                                |               |
| Finding absent  | 1   | 2                               | 0                                | 1                                |               |

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 0 mg/kg |   |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
|-----------------------------|----------------|---|---|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Animal No.                  | Clinical signs | Day   |   | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12            | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |    |    |
|                             |                | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |    |    |
| 10101                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10102                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10103                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10104                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10105                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10106                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10107                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10108                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10109                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10110                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10111                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10112                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| Animal No.                  |                | Day   |   | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21            | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 |    |
| Animal No.                  | Clinical signs | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
|                             |                | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10101                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10102                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10103                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10104                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10105                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10106                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10107                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10108                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10109                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10110                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10111                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10112                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| Animal No.                  |                | Day   |   | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30            | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 |
| Animal No.                  | Clinical signs | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
|                             |                | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10101                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10102                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10103                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10104                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10105                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10106                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10107                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10108                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10109                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10110                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10111                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 10112                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |

Administration)1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 0 mg/kg |    |    | Species : Rat |
|-----------------------------|----------------|---|----|----|---------------|
| Animal No.                  | Clinical signs | Day   | 28 | 29 |               |
|                             |                | Time  | 1  | 2  | 3             |
| 10101                       | No abnormality | -   | -  | -  |               |
| 10102                       | No abnormality | -   | -  | -  |               |
| 10103                       | No abnormality | -   | -  | -  |               |
| 10104                       | No abnormality | -   | -  | -  |               |
| 10105                       | No abnormality | -   | -  | -  |               |
| 10106                       | No abnormality | -   | -  | -  |               |
| 10107                       | No abnormality | -   | -  | -  |               |
| 10108                       | No abnormality | -   | -  | -  |               |
| 10109                       | No abnormality | -   | -  | -  |               |
| 10110                       | No abnormality | -   | -  | -  |               |
| 10111                       | No abnormality | -   | -  | -  |               |
| 10112                       | No abnormality | -   | -  | -  |               |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

Administration)1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 50 mg/kg |    |    | Species : Rat |
|-----------------------------|----------------|--|----|----|---------------|
| Animal No.                  | Clinical signs | Day  | 28 | 29 |               |
|                             |                | Time   | 1  | 2  | 3             |
| 10201                       | No abnormality |  | -  | -  | -             |
| 10202                       | No abnormality |  | -  | -  | -             |
| 10203                       | No abnormality |  | -  | -  | -             |
| 10204                       | No abnormality |  | -  | -  | -             |
| 10205                       | No abnormality |  | -  | -  | -             |
| 10206                       | No abnormality |  | -  | -  | -             |
| 10207                       | No abnormality |  | -  | -  | -             |
| 10208                       | No abnormality |  | -  | -  | -             |
| 10209                       | No abnormality |  | -  | -  | -             |
| 10210                       | No abnormality |  | -  | -  | -             |
| 10211                       | No abnormality |  | -  | -  | -             |
| 10212                       | No abnormality |  | -  | -  | -             |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 200 mg/kg |   |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
|-----------------------------|----------------|---|---|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Animal No.                  | Clinical signs | Day   |   | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12            | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |    |    |
|                             |                | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
| 10301                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10302                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10303                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10304                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10305                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10306                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10307                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10308                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10309                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10310                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10311                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10312                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| Animal No.                  |                | Day   |   | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21            | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 |    |
| Animal No.                  | Clinical signs | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
|                             |                | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10301                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10302                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10303                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10304                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10305                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10306                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10307                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10308                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10309                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10310                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10311                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10312                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| Animal No.                  |                | Day   |   | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30            | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 |
| Animal No.                  | Clinical signs | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
|                             |                | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10301                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10302                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10303                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10304                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10305                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10306                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10307                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10308                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10309                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10310                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10311                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10312                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |

Administration)1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 200 mg/kg |    |    | Species : Rat |
|-----------------------------|----------------|---|----|----|---------------|
| Animal No.                  | Clinical signs | Day   | 28 | 29 |               |
|                             |                | Time  | 1  | 2  | 3             |
| 10301                       | No abnormality | -   | -  | -  |               |
| 10302                       | No abnormality | -   | -  | -  |               |
| 10303                       | No abnormality | -   | -  | -  |               |
| 10304                       | No abnormality | -   | -  | -  |               |
| 10305                       | No abnormality | -   | -  | -  |               |
| 10306                       | No abnormality | -   | -  | -  |               |
| 10307                       | No abnormality | -   | -  | -  |               |
| 10308                       | No abnormality | -   | -  | -  |               |
| 10309                       | No abnormality | -   | -  | -  |               |
| 10310                       | No abnormality | -   | -  | -  |               |
| 10311                       | No abnormality | -   | -  | -  |               |
| 10312                       | No abnormality | -   | -  | -  |               |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 800 mg/kg |   |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
|-----------------------------|----------------|---|---|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Animal No.                  | Clinical signs | Day   |   | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 | 12            | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |    |    |
|                             |                | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
| 10401                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10402                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10403                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10404                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10405                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10406                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10407                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10408                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10409                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10410                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10411                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10412                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| Animal No.                  |                | Day   |   | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21            | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 |    |
| Animal No.                  | Clinical signs | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
|                             |                | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10401                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10402                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10403                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10404                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10405                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10406                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10407                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10408                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10409                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10410                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10411                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10412                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| Animal No.                  |                | Day   |   | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30            | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 |
| Animal No.                  | Clinical signs | Time  |   | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
|                             |                | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10401                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10402                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10403                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10404                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10405                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10406                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10407                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10408                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10409                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10410                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10411                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |
| 10412                       | No abnormality | -   | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |

Administration)1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Male |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 800 mg/kg |    |    | Species : Rat |
|-----------------------------|----------------|---|----|----|---------------|
| Animal No.                  | Clinical signs | Day   | 28 | 29 |               |
|                             |                | Time  | 1  | 2  | 3             |
| 10401                       | No abnormality |   | -  | -  | -             |
| 10402                       | No abnormality |   | -  | -  |               |
| 10403                       | No abnormality |   | -  | -  |               |
| 10404                       | No abnormality |   | -  | -  | -             |
| 10405                       | No abnormality |   | -  | -  | -             |
| 10406                       | No abnormality |   | -  | -  | -             |
| 10407                       | No abnormality |   | -  | -  |               |
| 10408                       | No abnormality |   | -  | -  |               |
| 10409                       | No abnormality |   | -  | -  |               |
| 10410                       | No abnormality |   | -  | -  |               |
| 10411                       | No abnormality |   | -  | -  |               |
| 10412                       | No abnormality |   | -  | -  | -             |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Animal No. | Clinical signs | Period : F0 before mating Day 1-14 |   |   |   |   |   |   |   |   |   |   |   |   |   | Species : Rat |   |   |   |
|------------|----------------|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---|---|---|
|            |                | Day                                |   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 1 | 2 | 1 | 2             | 1 | 2 |   |
|            |                | Time                               |   | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1             | 2 | 1 | 2 |
| 50151      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50152      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50153      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50154      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50155      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50156      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50157      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50158      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50159      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50160      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50161      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50162      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| Animal No. | Clinical signs | Day 10-14                          |   |   |   |   |   |   |   |   |   |   |   |   |   | Species : Rat |   |   |   |
|            |                | Time                               | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2 |   |
|            |                |                                    | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2 |   |
| 50151      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50152      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50153      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50154      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50155      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50156      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50157      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50158      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50159      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50160      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50161      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50162      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |

F0 before mating)1 : Pre-dosing, 2 : Post-dosing

| Animal No. | Clinical signs | Period : F0 mating Day 15-27 |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |    |    |
|------------|----------------|------------------------------|---|----|---|----|---|----|---|----|---|----|---|---------------|----|----|
|            |                | Day 15                       |   | 16 |   | 17 |   | 18 |   | 19 |   | 20 |   | 21            | 22 | 23 |
|            |                | Time                         | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1  | 2  |
| 50153      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50154      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| 50156      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| 50157      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| 50158      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| 50159      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| 50160      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| 50162      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | -  | -  |
| Animal No. |                | Day 24 25 26 27              |   |    |   |    |   |    |   |    |   |    |   |               |    |    |
|            |                | Time                         | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  |   |    |   |               |    |    |
| 50153      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50154      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50156      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50157      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50158      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50159      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50160      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |
| 50162      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |    |    |

F0 mating1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Female |                | Period : F0 gestation Day 0-26 |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |
|-------------------------------|----------------|--------------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---------------|----|
| Animal No.                    | Clinical signs | Day 0                          |    | 1  |    | 2  |    | 3  |    | 4  |    | 5  |    | 6  |    | 7  |    | 8             |    |
|                               |                | Time                           | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  |
| 50151                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50152                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50153                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50154                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50155                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50156                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50157                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50158                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50159                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50160                         | No abnormality | -                              | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -             | \$ |
| 50161                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50162                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| Animal No.                    | Clinical signs | Day 9                          |    | 10 |    | 11 |    | 12 |    | 13 |    | 14 |    | 15 |    | 16 |    | 17            |    |
|                               |                | Time                           | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  |
| 50151                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50152                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50153                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50154                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50155                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50156                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50157                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50158                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50159                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50160                         | No abnormality | -                              | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -             | \$ |
| 50161                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50162                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| Animal No.                    | Clinical signs | Day 18                         |    | 19 |    | 20 |    | 21 |    | 22 |    | 23 |    | 24 |    | 25 |    | 26            |    |
|                               |                | Time                           | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 3  |
| 50151                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50152                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50153                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50154                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50155                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50156                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50157                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50158                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50159                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50160                         | No abnormality | -                              | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -             | \$ |
| 50161                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |
| 50162                         | No abnormality | -                              | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  |

F0 gestation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

\$ : Excepted data from calculation

| Clinical sign<br>Sex : Female |                | Period : F0 lactation Day 0-5<br>Dose : PTSA Monohydrate 0 mg/kg |   |   |   |   |   |   |   |   |   | Species : Rat |   |  |
|-------------------------------|----------------|--|---|---|---|---|---|---|---|---|---|---------------|---|--|
| Animal No.                    | Clinical signs | Day  | 0 | 1 | 2 | 3 | 4 | 5 |   |   |   |               |   |  |
|                               |                | Time   | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 3 |  |
| 50151                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50152                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50153                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50154                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50155                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50156                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50157                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50158                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50159                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50161                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50162                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |

F0 lactation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Animal No. | Clinical signs | Period : F0 before mating Day 1-14 |   |   |   |   |   |   |   |   |   |   |   |   |   | Species : Rat |   |   |   |
|------------|----------------|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---|---|---|
|            |                | Day                                |   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 1 | 2 | 1 | 2             | 1 | 2 |   |
|            |                | Time                               |   | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1             | 2 | 1 | 2 |
| 50251      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50252      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50253      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50254      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50255      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50256      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50257      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50258      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50259      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50260      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50261      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50262      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| Animal No. | Clinical signs | Day 10-14                          |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |
|            |                | Time                               | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |   |               |   |   |   |
|            |                |                                    | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |   |               |   |   |   |
| 50251      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50252      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50253      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50254      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50255      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50256      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50257      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50258      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50259      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50260      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50261      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50262      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |

F0 before mating)1 : Pre-dosing, 2 : Post-dosing

| Animal No. | Clinical signs | Period : F0 mating Day 15-27 |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |    |   |    |   |   |
|------------|----------------|------------------------------|---|----|---|----|---|----|---|----|---|----|---|---------------|---|----|---|----|---|---|
|            |                | Day                          |   | 15 |   | 16 |   | 17 |   | 18 |   | 19 |   | 20            |   | 21 |   | 22 |   |   |
|            |                | Time                         | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2  | 1 | 2  | 1 | 2 |
| 50251      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50252      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50253      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50254      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50255      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50257      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50259      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50260      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50261      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50262      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| Animal No. | Clinical signs | Day                          |   |    |   |    |   |    |   |    |   |    |   | 24 25 26 27   |   |    |   |    |   |   |
|            |                | Time                         | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2  | 1 | 2  | 1 | 2 |
|            |                | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50251      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50252      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50253      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50254      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50255      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50257      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50259      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50260      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50261      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |
| 50262      | No abnormality | -                            | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - | - |

F0 mating1 : Pre-dosing, 2 : Post-dosing

| Animal No. | Clinical signs | Period : F0 gestation Day 0-26 |   |   |   |   |   |   |   |   |   |   |   |   |   | Species : Rat |   |               |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
|------------|----------------|--------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---|---------------|---|--------|---|--------|---|--------|---|--------|---|--------|---|--------|---|---------------|
|            |                | Day 0                          |   | 1 |   | 2 |   | 3 |   | 4 |   | 5 |   | 6 |   | 7             |   | Species : Rat |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
|            |                | Time                           | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50251      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50252      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50253      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50254      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50255      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50256      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50257      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50258      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50259      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50260      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50261      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| 50262      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             |   |        |   |        |   |        |   |        |   |        |   |        |   |               |
| Animal No. | Clinical signs | Day 9                          |   |   |   |   |   |   |   |   |   |   |   |   |   | Day 10        |   | Day 11        |   | Day 12 |   | Day 13 |   | Day 14 |   | Day 15 |   | Day 16 |   | Day 17 |   | Species : Rat |
|            |                | Time                           | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2             | 1 | 2      | 1 | 2      | 1 | 2      | 1 | 2      | 1 | 2      |   |        |   |               |
| 50251      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50252      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50253      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50254      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50255      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50256      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50257      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50258      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50259      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50260      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50261      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| 50262      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      |   |               |
| Animal No. | Clinical signs | Day 18                         |   |   |   |   |   |   |   |   |   |   |   |   |   | Day 19        |   | Day 20        |   | Day 21 |   | Day 22 |   | Day 23 |   | Day 24 |   | Day 25 |   | Day 26 |   | Species : Rat |
|            |                | Time                           | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2             | 1 | 2      | 1 | 2      | 1 | 2      | 1 | 2      | 1 | 2      | 1 | 2      |   |               |
| 50251      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50252      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50253      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50254      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50255      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50256      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50257      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50258      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50259      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50260      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50261      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |
| 50262      | No abnormality | -                              | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | -             | - | -      | - | -      | - | -      | - | -      | - | -      | - | -      | - |               |

F0 gestation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Clinical sign<br>Sex : Female |                | Period : F0 lactation Day 0-5<br>Dose : PTSA Monohydrate 50 mg/kg |   |   |   |   |   |   |   |   |   | Species : Rat |   |  |
|-------------------------------|----------------|---|---|---|---|---|---|---|---|---|---|---------------|---|--|
| Animal No.                    | Clinical signs | Day   | 0 | 1 | 2 | 3 | 4 | 5 |   |   |   |               |   |  |
|                               |                | Time  | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 3 |  |
| 50251                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50252                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50253                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50254                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50255                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50256                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50257                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50258                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50259                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50260                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50261                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50262                         | No abnormality |   | - | - | - | - | - | - | - | - | - | -             | - |  |

F0 lactation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Animal No. | Clinical signs | Period : F0 before mating Day 1-14 |   |    |   |    |   |    |   |    |   |   |   |   |   | Species : Rat |   |   |   |   |   |   |   |
|------------|----------------|------------------------------------|---|----|---|----|---|----|---|----|---|---|---|---|---|---------------|---|---|---|---|---|---|---|
|            |                | Day                                |   | 1  |   | 2  |   | 3  |   | 4  |   | 5 |   | 6 |   | 7             |   | 8 |   | 9 |   |   |   |
|            |                | Time                               | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2 | 1 | 2 | 1 | 2 |   |
| 50351      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50352      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50353      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50354      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50355      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50356      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50357      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50358      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50359      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50360      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50361      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| 50362      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - |   |
| Animal No. | Clinical signs | Day                                |   |    |   |    |   |    |   |    |   |   |   |   |   | Species : Rat |   |   |   |   |   |   |   |
|            |                | 10                                 |   | 11 |   | 12 |   | 13 |   | 14 |   | 1 |   | 2 |   | 1             |   | 2 |   | 1 |   | 2 |   |
|            |                | Time                               | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 1 | 2 | 1 | 2             | 1 | 2 | 1 | 2 | 1 | 2 | 1 |
| 50351      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50352      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50353      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50354      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50355      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50356      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50357      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50358      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50359      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50360      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50361      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |
| 50362      | No abnormality | -                                  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | - | -             | - | - | - | - | - | - | - |

F0 before mating)1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Female |                | Period : F0 mating Day 15-27<br>Dose : PTSA Monohydrate 200 mg/kg |    |    |    |    |    |    |    |    |    |      |   | Species : Rat |   |   |   |   |   |   |   |   |
|-------------------------------|----------------|---|----|----|----|----|----|----|----|----|----|------|---|---------------|---|---|---|---|---|---|---|---|
| Animal No.                    | Clinical signs | Day   | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | Time | 1 | 2             | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |
| 50351                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50352                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50353                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50356                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50357                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50358                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50359                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| 50361                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - |   |
| Animal No.                    |                | Day   | 24 | 25 | 26 | 27 |    |    |    |    |    |      |   |               |   |   |   |   |   |   |   |   |
| 50351                         | No abnormality | Time  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2    | 1 | 2             | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |
| 50352                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |
| 50353                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |
| 50356                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |
| 50357                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |
| 50358                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |
| 50359                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |
| 50361                         | No abnormality |   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -    | - | -             | - | - | - | - | - | - | - | - |

F0 mating 1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Female |                | Period : F0 gestation Day 0-26<br>Dose : PTSA Monohydrate 200 mg/kg |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |    |   |    |   |
|-------------------------------|----------------|---|---|----|---|----|---|----|---|----|---|----|---|---------------|---|----|---|----|---|
| Animal No.                    | Clinical signs | Day 0   |   | 1  |   | 2  |   | 3  |   | 4  |   | 5  |   | 6             |   | 7  |   | 8  |   |
|                               |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2  | 1 | 2  | 1 |
| 50351                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50352                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50353                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50354                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50355                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50356                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50357                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50358                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50359                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50360                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50361                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50362                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| Animal No.                    | Clinical signs | Day 9   |   | 10 |   | 11 |   | 12 |   | 13 |   | 14 |   | 15            |   | 16 |   | 17 |   |
|                               |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2  | 1 | 2  | 1 |
| 50351                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50352                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50353                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50354                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50355                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50356                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50357                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50358                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50359                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50360                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50361                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50362                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| Animal No.                    | Clinical signs | Day 18  |   | 19 |   | 20 |   | 21 |   | 22 |   | 23 |   | 24            |   | 25 |   | 26 |   |
|                               |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2  | 1 | 2  | 3 |
| 50351                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50352                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50353                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50354                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50355                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50356                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50357                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50358                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50359                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50360                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50361                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |
| 50362                         | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | -             | - | -  | - | -  | - |

F0 gestation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Clinical sign<br>Sex : Female |                | Period : F0 lactation Day 0-5<br>Dose : PTSA Monohydrate 200 mg/kg |   |   |   |   |   |   |   |   |   | Species : Rat |   |  |
|-------------------------------|----------------|--|---|---|---|---|---|---|---|---|---|---------------|---|--|
| Animal No.                    | Clinical signs | Day  | 0 | 1 | 2 | 3 | 4 | 5 |   |   |   |               |   |  |
|                               |                | Time   | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2             | 3 |  |
| 50351                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50352                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50353                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50354                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50355                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50356                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50357                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50358                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50359                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50360                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50361                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |
| 50362                         | No abnormality |  | - | - | - | - | - | - | - | - | - | -             | - |  |

F0 lactation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Animal No. | Clinical signs | Period : F0 before mating Day 1-14 |   |   |   |   |   |   |   |   |   |   |   |   |   | Species : Rat |   |   |   |
|------------|----------------|------------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---------------|---|---|---|
|            |                | Day                                |   | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 1 | 2 | 1 | 2             | 1 | 2 |   |
|            |                | Time                               |   | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1             | 2 | 1 | 2 |
| 50451      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50452      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50453      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50454      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50455      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50456      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50457      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50458      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50459      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50460      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50461      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| 50462      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - | - | -             | - | - | - |
| Animal No. | Clinical signs | Day 10-14                          |   |   |   |   |   |   |   |   |   |   |   |   |   |               |   |   |   |
|            |                | Time                               | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |   |               |   |   |   |
|            |                |                                    | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 | 2 |   |               |   |   |   |
| 50451      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50452      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50453      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50454      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50455      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50456      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50457      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50458      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50459      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50460      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50461      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |
| 50462      | No abnormality | -                                  | - | - | - | - | - | - | - | - | - | - | - | - |   |               |   |   |   |

F0 before mating)1 : Pre-dosing, 2 : Post-dosing

| Animal No. | Clinical signs | Period : F0 mating Day 15-27 |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |    |   |   |
|------------|----------------|------------------------------|---|----|---|----|---|----|---|----|---|----|---|---------------|---|----|---|---|
|            |                | Day 15                       |   | 16 |   | 17 |   | 18 |   | 19 |   | 20 |   | 21            |   | 22 |   |   |
|            |                | Time                         | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2             | 1 | 2  | 1 | 2 |
| 50451      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50452      | No abnormality | -                            | - | -  | - | -  | - | -  | - |    |   |    |   |               |   |    |   |   |
| 50453      | No abnormality | -                            | - | -  | - | -  | - | -  | - |    |   |    |   |               |   |    |   |   |
| 50454      | No abnormality | -                            | - |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50458      | No abnormality | -                            | - | -  | - |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50459      | No abnormality | -                            | - | -  | - | -  | - |    |   |    |   |    |   |               |   |    |   |   |
| 50460      | No abnormality | -                            | - | -  | - | -  | - | -  | - |    |   |    |   |               |   |    |   |   |
| 50462      | No abnormality | -                            | - | -  | - | -  | - | -  | - |    |   |    |   |               |   |    |   |   |
| Animal No. | Clinical signs | Day 24                       |   |    |   |    |   |    |   |    |   |    |   | Species : Rat |   |    |   |   |
|            |                | Time                         | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  |   |               |   |    |   |   |
|            |                |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50451      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50452      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50453      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50454      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50458      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50459      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50460      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |
| 50462      | No abnormality |                              |   |    |   |    |   |    |   |    |   |    |   |               |   |    |   |   |

F0 mating1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Female |                | Period : F0 gestation Day 0-26<br>Dose : PTSA Monohydrate 800 mg/kg |    |    |    |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |    |
|-------------------------------|----------------|---|----|----|----|----|----|----|----|----|----|----|----|----|----|---------------|----|----|----|
| Animal No.                    | Clinical signs | Day 0   |    | 1  |    | 2  |    | 3  |    | 4  |    | 5  |    | 6  |    | 7             |    | 8  |    |
|                               |                | Time  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  |
| 50451                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50452                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50453                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50454                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50455                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50456                         | No abnormality | -   | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -             | \$ | -  | \$ |
| 50457                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50458                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50459                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50460                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50461                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50462                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| Animal No.                    | Clinical signs | Day 9   |    | 10 |    | 11 |    | 12 |    | 13 |    | 14 |    | 15 |    | 16            |    | 17 |    |
|                               |                | Time  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 1  |
| 50451                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50452                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50453                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50454                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50455                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50456                         | No abnormality | -   | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -             | \$ | -  | \$ |
| 50457                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50458                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50459                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50460                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50461                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50462                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| Animal No.                    | Clinical signs | Day 18  |    | 19 |    | 20 |    | 21 |    | 22 |    | 23 |    | 24 |    | 25            |    | 26 |    |
|                               |                | Time  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2             | 1  | 2  | 3  |
| 50451                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50452                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50453                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50454                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50455                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50456                         | No abnormality | -   | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -  | \$ | -             | \$ | -  | \$ |
| 50457                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50458                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50459                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50460                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50461                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |
| 50462                         | No abnormality | -   | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  |

F0 gestation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

\$ : Excepted data from calculation

| Clinical sign<br>Sex : Female |                  | Period : F0 lactation Day 0-5<br>Dose : PTSA Monohydrate 800 mg/kg |     |     |     |     |     |     |     |     |     | Species : Rat |     |
|-------------------------------|------------------|--|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------------|-----|
| Animal No.                    | Clinical signs   | Day  | 0   | 1   | 2   | 3   | 4   | 5   |     |     |     |               |     |
|                               |                  | Time   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2             | 3   |
| 50451                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50452                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50453                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50454                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50455                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50457                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50458                         | Dyspnea<br>Death | +  | ... | ... | ... | ... | ... | ... | ... | ... | ... | ...           | ... |
| 50459                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50460                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50461                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |
| 50462                         | No abnormality   | -  | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   |

F0 lactation)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

... : Not applicable

| Clinical sign<br>Sex : Female (satellite) |                | Period : Administration Day 1-29 |   |   |    |    |    |    |    |    |    |    |    |    | Species : Rat |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
|---|----------------|----------------------------------|---|---|----|----|----|----|----|----|----|----|----|----|---------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Animal No.                                | Clinical signs | Day                              |   |   | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11            | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |    |    |
|   |                | Time                             | 1 | 2 | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1             | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |    |    |
| 50551                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50552                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50553                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50554                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50555                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50556                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50557                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50558                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50559                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| 50560                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |    |    |
| Animal No.                                | Clinical signs | Day                              |   |   | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20            | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 |    |
|   |                | Time                             | 1 | 2 | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1             | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
| 50551                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50552                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50553                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50554                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50555                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50556                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50557                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50558                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50559                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| 50560                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |    |
| Animal No.                                | Clinical signs | Day                              |   |   | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29            | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 |
|   |                | Time                             | 1 | 2 | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1             | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  | 1  | 2  |    |
| 50551                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50552                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50553                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50554                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50555                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50556                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50557                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50558                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50559                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |
| 50560                                     | No abnormality | -                                | - | - | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -             | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  |

Administration)1 : Pre-dosing, 2 : Post-dosing

| Clinical sign<br>Sex : Female (satellite) |                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 0 mg/kg |    |    | Species : Rat |
|---|----------------|---|----|----|---------------|
| Animal No.                                | Clinical signs | Day   | 28 | 29 |               |
|   |                | Time  | 1  | 2  | 3             |
| 50551                                     | No abnormality | -   | -  | -  |               |
| 50552                                     | No abnormality | -   | -  | -  |               |
| 50553                                     | No abnormality | -   | -  | -  |               |
| 50554                                     | No abnormality | -   | -  | -  |               |
| 50555                                     | No abnormality | -   | -  | -  |               |
| 50556                                     | No abnormality | -   | -  | -  |               |
| 50557                                     | No abnormality | -   | -  | -  |               |
| 50558                                     | No abnormality | -   | -  | -  |               |
| 50559                                     | No abnormality | -   | -  | -  |               |
| 50560                                     | No abnormality | -   | -  | -  |               |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

| Clinical sign<br>Sex : Female (satellite) |                                | Period : Administration Day 1-29<br>Dose : PTSA Monohydrate 800 mg/kg |     |     |     |     |     |     |     |     |     |     |     | Species : Rat |     |     |     |  |
|---|--------------------------------|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------------|-----|-----|-----|--|
| Animal No.                                | Clinical signs                 | Day   |     | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 1   | 2             | 1   | 2   | 1   |  |
|   |                                | Time  |     | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1             | 2   | 1   | 2   |  |
| 50651                                     | Decrease in locomotor activity | -   | -   | -   | +   | -   | +   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Staggering gait                | -   | -   | -   | -   | -   | +   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Soil of perinasal fur          | -   | -   | -   | -   | +   | +   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Soil of perigenital fur        | -   | -   | +   | +   | +   | +   | +   | +   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50652                                     | Staggering gait                | -   | +   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50653                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50654                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50655                                     | Soil of perinasal fur          | -   | -   | -   | -   | -   | +   | +   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Soil of perigenital fur        | -   | -   | -   | -   | -   | +   | +   | +   | +   | -   | -   | -   | -             | -   | -   | -   |  |
| 50656                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50657                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50658                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50659                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50660                                     | Death                          | -   | -   | -   | -   | +   | ... | ... | ... | ... | ... | ... | ... | ...           | ... | ... | ... |  |
| Animal No.                                | Clinical signs                 | Day   |     | 10  | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  |     |               |     |     |     |  |
|   |                                | Time  |     | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1             | 2   | 1   | 2   |  |
| 50651                                     | Decrease in locomotor activity | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Staggering gait                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Soil of perinasal fur          | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Soil of perigenital fur        | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50652                                     | Staggering gait                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50653                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50654                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50655                                     | Soil of perinasal fur          | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
|   | Soil of perigenital fur        | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50656                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50657                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50658                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50659                                     | No abnormality                 | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |  |
| 50660                                     | Death                          | ...   | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ...           | ... | ... | ... |  |

Administration)1 : Pre-dosing, 2 : Post-dosing

The findings except soil of fur appeared immediately after dosing and disappeared by approximately 1 hr after dosing.

... : Not applicable

| Animal No. | Clinical sign<br>Sex : Female (satellite) | Period : Administration Day 1-29 |     |     |     |     |     |     |     |     |     |     |     |     |     | Species : Rat |     |     |     |
|------------|---|----------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------------|-----|-----|-----|
|            |   | Day 19                           |     | 20  |     | 21  |     | 22  |     | 23  |     | 24  |     | 25  |     | 26            |     | 27  |     |
|            |   | Time                             | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2   | 1   | 2             | 1   | 2   | 1   |
| 50651      | Decrease in locomotor activity            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Staggering gait                           | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Soil of perinasal fur                     | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Soil of perigenital fur                   | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50652      | Staggering gait                           | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50653      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50654      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50655      | Soil of perinasal fur                     | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Soil of perigenital fur                   | -                                | -   | -   | -   | -   | -   | +   | +   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50656      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50657      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50658      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50659      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50660      | Death                                     | ...                              | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ...           | ... | ... | ... |
| Animal No. | Clinical signs                            | Day 28                           |     | 29  |     |     |     |     |     |     |     |     |     |     |     |               |     |     |     |
|            |   | Time                             | 1   | 2   | 3   |     |     |     |     |     |     |     |     |     |     |               |     |     |     |
| 50651      | Decrease in locomotor activity            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Staggering gait                           | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Soil of perinasal fur                     | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Soil of perigenital fur                   | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50652      | Staggering gait                           | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50653      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50654      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50655      | Soil of perinasal fur                     | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
|            | Soil of perigenital fur                   | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50656      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50657      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50658      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50659      | No abnormality                            | -                                | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -   | -             | -   | -   | -   |
| 50660      | Death                                     | ...                              | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ... | ...           | ... | ... | ... |

Administration)1 : Pre-dosing, 2 : Post-dosing, 3 : Necropsy day

... : Not applicable

| Clinical sign<br>Sex : Male |                | Period : Recovery Day 1-15<br>Dose : PTSA Monohydrate 0 mg/kg |   |    |   |    |   |    |   |    |   |    |   |   |   |   | Species : Rat |   |  |
|-----------------------------|----------------|---|---|----|---|----|---|----|---|----|---|----|---|---|---|---|---------------|---|--|
| Animal No.                  | Clinical signs | Day 1   |   | 2  |   | 3  |   | 4  |   | 5  |   | 6  |   | 7 |   | 8 |               | 9 |  |
|                             |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 1 | 2 | 1             | 2 |  |
| 10103                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10104                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10105                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10106                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10111                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| Animal No.                  | Clinical signs | Day 10  |   | 11 |   | 12 |   | 13 |   | 14 |   | 15 |   |   |   |   |               |   |  |
|                             |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 3 |   |               |   |  |
| 10103                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10104                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10105                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10106                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10111                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |

Recovery)1 : AM, 2 : PM, 3 : Necropsy day

| Clinical sign<br>Sex : Male |                | Period : Recovery Day 1-15<br>Dose : PTSA Monohydrate 800 mg/kg |   |    |   |    |   |    |   |    |   |    |   |   |   |   | Species : Rat |   |  |
|-----------------------------|----------------|---|---|----|---|----|---|----|---|----|---|----|---|---|---|---|---------------|---|--|
| Animal No.                  | Clinical signs | Day 1   |   | 2  |   | 3  |   | 4  |   | 5  |   | 6  |   | 7 |   | 8 |               | 9 |  |
|                             |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 1 | 2 | 1             | 2 |  |
| 10402                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10403                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10407                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10409                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 10411                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| Animal No.                  | Clinical signs | Day 10  |   | 11 |   | 12 |   | 13 |   | 14 |   | 15 |   |   |   |   |               |   |  |
|                             |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 3 |   |               |   |  |
| 10402                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10403                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10407                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10409                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 10411                       | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |

Recovery)1 : AM, 2 : PM, 3 : Necropsy day

| Clinical sign<br>Sex : Female (satellite) |                | Period : Recovery Day 1-15<br>Dose : PTSA Monohydrate 0 mg/kg |   |    |   |    |   |    |   |    |   |    |   |   |   |   | Species : Rat |   |  |
|---|----------------|---|---|----|---|----|---|----|---|----|---|----|---|---|---|---|---------------|---|--|
| Animal No.                                | Clinical signs | Day 1   |   | 2  |   | 3  |   | 4  |   | 5  |   | 6  |   | 7 |   | 8 |               | 9 |  |
|   |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 1 | 2 | 1             | 2 |  |
| 50556                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 50557                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 50558                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 50559                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| 50560                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - | - | -             | - |  |
| Animal No.                                | Clinical signs | Day 10  |   | 11 |   | 12 |   | 13 |   | 14 |   | 15 |   |   |   |   |               |   |  |
|   |                | Time  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2  | 1 | 2 | 3 |   |               |   |  |
| 50556                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 50557                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 50558                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 50559                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |
| 50560                                     | No abnormality | -   | - | -  | - | -  | - | -  | - | -  | - | -  | - | - | - |   |               |   |  |

Recovery)1 : AM, 2 : PM, 3 : Necropsy day

| Clinical sign<br>Sex : Female (satellite) |                | Period : Recovery Day 1-15<br>Dose : PTSA Monohydrate 800 mg/kg |   |     |    |    |    |    |    |    |   |   |     |    |    |    | Species : Rat |    |   |   |  |
|---|----------------|---|---|-----|----|----|----|----|----|----|---|---|-----|----|----|----|---------------|----|---|---|--|
| Animal No.                                | Clinical signs | Day   |   | 1   | 2  | 3  | 4  | 5  | 6  | 7  | 8 | 9 | 10  | 11 | 12 | 13 | 14            | 15 |   |   |  |
|   |                | Time  |   | 1   | 2  | 1  | 2  | 1  | 2  | 1  | 2 | 1 | 2   | 1  | 2  | 1  | 2             | 1  |   |   |  |
| 50656                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| 50657                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| 50658                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| 50659                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| Animal No.                                |                | Clinical signs  |   | Day | 10 | 11 | 12 | 13 | 14 | 15 |   |   | Day |    | 1  | 2  | 1             | 2  | 3 |   |  |
| 50656                                     | No abnormality | Clinical signs  | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| 50657                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| 50658                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |
| 50659                                     | No abnormality | -   | - | -   | -  | -  | -  | -  | -  | -  | - | - | -   | -  | -  | -  | -             | -  | - | - |  |

Recovery)1 : AM, 2 : PM, 3 : Necropsy day

| Animal No. | Detailed clinical observation (in the cage) |                           |                        | Stage : Pre administration |         |                        | Species : Rat |
|------------|---|---------------------------|------------------------|----------------------------|---------|------------------------|---------------|
|            | Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion      | Rolling | Repetitive<br>circling |               |
| 10101      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10102      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10103      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10104      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10105      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10106      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10107      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10108      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10109      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10110      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10111      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10112      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| n          |   | 12                        | 12                     | 12                         | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                           |                        | Stage : Pre administration |         |                        | Species : Rat |
|------------|---|---------------------------|------------------------|----------------------------|---------|------------------------|---------------|
|            | Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion      | Rolling | Repetitive<br>circling |               |
| 10201      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10202      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10203      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10204      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10205      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10206      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10207      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10208      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10209      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10210      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10211      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10212      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| n          |   | 12                        | 12                     | 12                         | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                           |                        | Stage : Pre administration |         |                        | Species : Rat |
|------------|---|---------------------------|------------------------|----------------------------|---------|------------------------|---------------|
|            | Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion      | Rolling | Repetitive<br>circling |               |
| 10301      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10302      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10303      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10304      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10305      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10306      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10307      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10308      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10309      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10310      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10311      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10312      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| n          |   | 12                        | 12                     | 12                         | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                           |                        | Stage : Pre administration |         |                        | Species : Rat |
|------------|---|---------------------------|------------------------|----------------------------|---------|------------------------|---------------|
|            | Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion      | Rolling | Repetitive<br>circling |               |
| 10401      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10402      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10403      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10404      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10405      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10406      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10407      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10408      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10409      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10410      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10411      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 10412      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| n          |   | 12                        | 12                     | 12                         | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                            | Rolling | Repetitive<br>circling | Self biting   |
| Animal No.                                  |                           |                        |  |         |                        |               |
| 10101                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10102                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10103                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10104                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10105                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10106                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10107                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10108                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10109                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10110                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10111                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10112                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 7<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| Animal No.                                  |                           |                        |   |         |                        |               |
| 10201                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10202                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10203                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10204                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10205                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10206                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10207                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10208                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10209                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10210                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10211                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10212                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 7<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling | Self biting   |
| Animal No.                                  |                           |                        |  |         |                        |               |
| 10301                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10302                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10303                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10304                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10305                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10306                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10307                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10308                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10309                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10310                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10311                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10312                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling | Self biting   |
| Animal No.                                  |                           |                        |  |         |                        |               |
| 10401                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10402                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10403                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10404                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10405                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10406                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10407                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10408                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10409                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10410                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10411                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10412                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |   |         |                        |               |
| 10101                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10102                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10103                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10104                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10105                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10106                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10107                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10108                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10109                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10110                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10111                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10112                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |  |         |                        |               |
| 10201                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10202                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10203                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10204                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10205                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10206                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10207                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10208                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10209                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10210                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10211                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10212                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |   |         |                        |               |
| 10301                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10302                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10303                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10304                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10305                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10306                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10307                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10308                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10309                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10310                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10311                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10312                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |   |         |                        |               |
| 10401                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10402                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10403                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10404                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10405                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10406                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10407                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10408                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10409                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10410                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10411                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10412                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                       |                   | Stage : Day 21 |                     |             | Species : Rat |
|---|-----------------------|-------------------|----------------|---------------------|-------------|---------------|
| Sex : Male                                  | Respiratory pattern   | Tremor/Convulsion | Rolling        | Repetitive circling | Self biting |               |
| Animal No.                                  | Body position/Posture |                   |                |                     |             |               |
| 10101                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10102                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10103                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10104                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10105                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10106                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10107                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10108                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10109                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10110                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10111                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10112                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| n   | 12                    | 12                | 12             | 12                  | 12          | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                       |                   | Stage : Day 21 |                     |             | Species : Rat |
|---|-----------------------|-------------------|----------------|---------------------|-------------|---------------|
| Sex : Male                                  | Respiratory pattern   | Tremor/Convulsion | Rolling        | Repetitive circling | Self biting |               |
| Animal No.                                  | Body position/Posture |                   |                |                     |             |               |
| 10201                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10202                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10203                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10204                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10205                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10206                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10207                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10208                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10209                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10210                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10211                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10212                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| n   | 12                    | 12                | 12             | 12                  | 12          | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                       |                   | Stage : Day 21 |                     |             | Species : Rat |
|---|-----------------------|-------------------|----------------|---------------------|-------------|---------------|
| Sex : Male                                  | Respiratory pattern   | Tremor/Convulsion | Rolling        | Repetitive circling | Self biting |               |
| Animal No.                                  | Body position/Posture |                   |                |                     |             |               |
| 10301                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10302                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10303                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10304                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10305                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10306                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10307                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10308                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10309                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10310                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10311                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10312                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| n   | 12                    | 12                | 12             | 12                  | 12          | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                       |                   | Stage : Day 21 |                     |             | Species : Rat |
|---|-----------------------|-------------------|----------------|---------------------|-------------|---------------|
| Sex : Male                                  | Respiratory pattern   | Tremor/Convulsion | Rolling        | Repetitive circling | Self biting |               |
| Animal No.                                  | Body position/Posture |                   |                |                     |             |               |
| 10401                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10402                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10403                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10404                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10405                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10406                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10407                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10408                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10409                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10410                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10411                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10412                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| n   | 12                    | 12                | 12             | 12                  | 12          | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 28<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| Animal No.                                  |                           |                        |   |         |                        |               |
| 10101                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10102                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10103                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10104                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10105                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10106                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10107                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10108                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10109                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10110                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10111                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10112                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 28<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |  |         |                        |               |
| 10201                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10202                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10203                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10204                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10205                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10206                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10207                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10208                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10209                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10210                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10211                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10212                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                       |                   | Stage : Day 28 |                     |             | Species : Rat |
|---|-----------------------|-------------------|----------------|---------------------|-------------|---------------|
| Sex : Male                                  | Respiratory pattern   | Tremor/Convulsion | Rolling        | Repetitive circling | Self biting |               |
| Animal No.                                  | Body position/Posture |                   |                |                     |             |               |
| 10301                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10302                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10303                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10304                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10305                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10306                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10307                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10308                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10309                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10310                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10311                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10312                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| n   | 12                    | 12                | 12             | 12                  | 12          | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                       |                   | Stage : Day 28 |                     |             | Species : Rat |
|---|-----------------------|-------------------|----------------|---------------------|-------------|---------------|
| Sex : Male                                  | Respiratory pattern   | Tremor/Convulsion | Rolling        | Repetitive circling | Self biting |               |
| Animal No.                                  | Body position/Posture |                   |                |                     |             |               |
| 10401                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10402                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10403                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10404                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10405                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10406                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10407                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10408                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10409                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10410                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10411                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| 10412                                       | 1                     | 1                 | 1              | 0                   | 0           | 1             |
| n   | 12                    | 12                | 12             | 12                  | 12          | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Pre administration |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling                    | Repetitive<br>circling | Self biting |               |
| 50151      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50152      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50153      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50154      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50155      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50156      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50157      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50158      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50159      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50160      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50161      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50162      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| n          | 12  | 12                     | 12                    | 12                         | 12                     | 12          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Pre administration<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion  | Rolling | Repetitive<br>circling | Self biting   |
| 50251                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50252                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50253                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50254                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50255                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50256                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50257                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50258                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50259                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50260                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50261                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50262                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Pre administration |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling                    | Repetitive<br>circling | Self biting |               |
| 50351      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50352      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50353      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50354      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50355      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50356      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50357      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50358      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50359      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50360      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50361      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50362      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| n          | 12  | 12                     | 12                    | 12                         | 12                     | 12          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                           |                        | Stage : Pre administration |         |                        | Species : Rat |
|------------|---|---------------------------|------------------------|----------------------------|---------|------------------------|---------------|
|            | Sex : Female                                | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion      | Rolling | Repetitive<br>circling |               |
| 50451      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50452      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50453      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50454      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50455      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50456      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50457      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50458      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50459      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50460      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50461      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| 50462      |   | 1                         | 1                      | 1                          | 0       | 0                      | 1             |
| n          |   | 12                        | 12                     | 12                         | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|--|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling  | Repetitive<br>circling | Self biting |               |
| 50151      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50152      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50153      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50154      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50155      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50156      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50157      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50158      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50159      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50160      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50161      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50162      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| n          | 12  | 12                     | 12                    | 12   | 12                     | 12          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 7<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| 50251                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50252                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50253                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50254                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50255                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50256                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50257                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50258                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50259                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50260                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50261                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50262                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 7<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling | Self biting   |
| 50351                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50352                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50353                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50354                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50355                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50356                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50357                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50358                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50359                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50360                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50361                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50362                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|--|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling  | Repetitive<br>circling | Self biting |               |
| 50451      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50452      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50453      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50454      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50455      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50456      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50457      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50458      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50459      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50460      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50461      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| 50462      | 1   | 1                      | 1                     | 0  | 0                      | 1           |               |
| n          | 12  | 12                     | 12                    | 12   | 12                     | 12          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| 50151                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50152                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50153                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50154                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50155                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50156                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50157                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50158                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50159                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50160                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50161                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50162                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling | Self biting   |
| 50251                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50252                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50253                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50254                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50255                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50256                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50257                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50258                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50259                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50260                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50261                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50262                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50351                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50352                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50353                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50354                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50355                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50356                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50357                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50358                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50359                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50360                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50361                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50362                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50451                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50452                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50453                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50454                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50455                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50456                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50457                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50458                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50459                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50460                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50461                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50462                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 21<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| 50151                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50152                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50153                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50154                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50155                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50156                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50157                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50158                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50159                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50160                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50161                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50162                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 21<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling | Self biting   |
| 50251                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50252                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50253                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50254                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50255                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50256                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50257                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50258                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50259                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50260                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50261                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50262                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 21<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50351                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50352                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50353                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50354                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50355                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50356                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50357                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50358                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50359                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50360                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50361                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50362                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 21        |         |                        | Species : Rat |
|---|---------------------------|------------------------|-----------------------|---------|------------------------|---------------|
| Sex : Female                                | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |                       |         |                        |               |
| 50451                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50452                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50453                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50454                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50455                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50456                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50457                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50458                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50459                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50460                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50461                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50462                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12                    | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 28<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| 50151                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50152                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50153                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50154                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50155                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50156                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50157                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50158                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50159                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50160                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50161                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50162                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 28 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50251      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50252      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50253      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50254      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50255      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50256      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50257      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50258      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50259      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50260      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50261      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50262      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 12  | 12                     | 12                    | 12             | 12                     | 12          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 28<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50351                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50352                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50353                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50354                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50355                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50356                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50357                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50358                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50359                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50360                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50361                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50362                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 28<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50451                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50452                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50453                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50454                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50455                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50456                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50457                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50458                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50459                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50460                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50461                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50462                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 35<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                             | Rolling | Repetitive<br>circling | Self biting   |
| 50151                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50152                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50153                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50154                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50155                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50156                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50157                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50158                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50159                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50160                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50161                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50162                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 35<br>Dose : PTSA Monohydrate 50 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                              | Rolling | Repetitive<br>circling | Self biting   |
| 50251                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50252                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50253                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50254                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50255                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50256                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50257                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50258                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50259                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50260                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50261                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 50262                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12   | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                           |                        | Stage : Day 35        |         |                        | Species : Rat |
|------------|---|---------------------------|------------------------|-----------------------|---------|------------------------|---------------|
|            | Sex : Female                                | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling | Repetitive<br>circling |               |
| 50351      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50352      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50353      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50354      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50355      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50356      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50357      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50358      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50359      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50360      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50361      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50362      |   | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| n          |   | 12                        | 12                     | 12                    | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 35<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50451                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50452                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50453                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50454                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50455                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50456                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50457                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50458                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50459                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50460                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50461                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50462                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 12                        | 12                     | 12  | 12      | 12                     | 12            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |  |                           | Stage : Day 42<br>Dose : PTSA Monohydrate 0 mg/kg |                       |         | Species : Rat          |             |
|---|--|---------------------------|---|-----------------------|---------|------------------------|-------------|
| Sex : Female                                |  | Body position/<br>Posture | Respiratory<br>pattern                            | Tremor/<br>Convulsion | Rolling | Repetitive<br>circling | Self biting |
| Animal No.                                  |  |                           |   |                       |         |                        |             |
| 50153                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50154                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50156                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50157                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50158                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50159                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50160                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| 50162                                       |  | 1                         | 1   | 1                     | 0       | 0                      | 1           |
| n   |  | 8                         | 8   | 8                     | 8       | 8                      | 8           |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 42        |         |                        | Species : Rat |
|---|---------------------------|------------------------|-----------------------|---------|------------------------|---------------|
| Sex : Female                                | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |                       |         |                        |               |
| 50251                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50252                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50253                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50254                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50255                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50257                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50259                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50260                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50261                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50262                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| n   | 10                        | 10                     | 10                    | 10      | 10                     | 10            |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 42<br>Dose : PTSA Monohydrate 200 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Female                                |                           |                        |   |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                               | Rolling | Repetitive<br>circling | Self biting   |
| 50351                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50352                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50353                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50356                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50357                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50358                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50359                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 50361                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 8                         | 8                      | 8   | 8       | 8                      | 8             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Day 42        |         |                        | Species : Rat |
|---|---------------------------|------------------------|-----------------------|---------|------------------------|---------------|
| Sex : Female                                | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |                       |         |                        |               |
| 50451                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50452                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50453                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50454                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50459                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50460                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| 50462                                       | 1                         | 1                      | 1                     | 0       | 0                      | 1             |
| n   | 7                         | 7                      | 7                     | 7       | 7                      | 7             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Pre administration |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling                    | Repetitive<br>circling | Self biting |               |
| 50551      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50552      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50553      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50554      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50555      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50556      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50557      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50558      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50559      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50560      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| n          | 10  | 10                     | 10                    | 10                         | 10                     | 10          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Pre administration |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling                    | Repetitive<br>circling | Self biting |               |
| 50651      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50652      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50653      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50654      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50655      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50656      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50657      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50658      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50659      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| 50660      | 1   | 1                      | 1                     | 0                          | 0                      | 1           |               |
| n          | 10  | 10                     | 10                    | 10                         | 10                     | 10          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 7 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|---------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling       | Repetitive<br>circling | Self biting |               |
| 50551      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50552      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50553      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50554      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50555      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50556      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50557      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50558      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50559      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50560      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| n          | 10  | 10                     | 10                    | 10            | 10                     | 10          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 7 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|---------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling       | Repetitive<br>circling | Self biting |               |
| 50651      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50652      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50653      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50654      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50655      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50656      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50657      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50658      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| 50659      | 1   | 1                      | 1                     | 0             | 0                      | 1           |               |
| n          | 9   | 9                      | 9                     | 9             | 9                      | 9           |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal,rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic,systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 14 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50551      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50552      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50553      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50554      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50555      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50556      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50557      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50558      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50559      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50560      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 10  | 10                     | 10                    | 10             | 10                     | 10          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 14 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50651      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50652      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50653      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50654      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50655      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50656      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50657      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50658      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50659      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 9   | 9                      | 9                     | 9              | 9                      | 9           |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 21 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50551      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50552      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50553      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50554      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50555      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50556      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50557      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50558      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50559      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50560      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 10  | 10                     | 10                    | 10             | 10                     | 10          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 21 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50651      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50652      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50653      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50654      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50655      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50656      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50657      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50658      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50659      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 9   | 9                      | 9                     | 9              | 9                      | 9           |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal,rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic,systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 28 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50551      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50552      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50553      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50554      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50555      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50556      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50557      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50558      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50559      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50560      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 10  | 10                     | 10                    | 10             | 10                     | 10          |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the cage) |                        |                       | Stage : Day 28 |                        |             | Species : Rat |
|------------|---|------------------------|-----------------------|----------------|------------------------|-------------|---------------|
|            | Body position/<br>Posture                   | Respiratory<br>pattern | Tremor/<br>Convulsion | Rolling        | Repetitive<br>circling | Self biting |               |
| 50651      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50652      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50653      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50654      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50655      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50656      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50657      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50658      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| 50659      | 1   | 1                      | 1                     | 0              | 0                      | 1           |               |
| n          | 9   | 9                      | 9                     | 9              | 9                      | 9           |               |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  |                           |                        |   |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                                     | Rolling | Repetitive<br>circling | Self biting   |
| 10103                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10104                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10105                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10106                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10111                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 5                         | 5                      | 5   | 5       | 5                      | 5             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|---|---------|------------------------|---------------|
| Sex : Male                                  |                           |                        |   |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                                       | Rolling | Repetitive<br>circling | Self biting   |
| 10402                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10403                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10407                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10409                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| 10411                                       | 1                         | 1                      | 1   | 0       | 0                      | 1             |
| n   | 5                         | 5                      | 5   | 5       | 5                      | 5             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  |                           |                        |  |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion                                      | Rolling | Repetitive<br>circling | Self biting   |
| 10103                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10104                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10105                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10106                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10111                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 5                         | 5                      | 5  | 5       | 5                      | 5             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |         |                        | Species : Rat |
|---|---------------------------|------------------------|--|---------|------------------------|---------------|
| Sex : Male                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion  | Rolling | Repetitive<br>circling |               |
| Animal No.                                  |                           |                        |  |         |                        |               |
| 10402                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10403                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10407                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10409                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| 10411                                       | 1                         | 1                      | 1  | 0       | 0                      | 1             |
| n   | 5                         | 5                      | 5  | 5       | 5                      | 5             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 7          |         |                        | Species : Rat |
|---|---------------------------|------------------------|---------------------------------|---------|------------------------|---------------|
| Sex : Female (satellite)                    |                           |                        | Dose : PTSA Monohydrate 0 mg/kg |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion           | Rolling | Repetitive<br>circling | Self biting   |
| 50556                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50557                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50558                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50559                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50560                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| n   | 5                         | 5                      | 5                               | 5       | 5                      | 5             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 7            |         |                        | Species : Rat |
|---|---------------------------|------------------------|-----------------------------------|---------|------------------------|---------------|
| Sex : Female (satellite)                    |                           |                        | Dose : PTSA Monohydrate 800 mg/kg |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion             | Rolling | Repetitive<br>circling | Self biting   |
| 50656                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| 50657                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| 50658                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| 50659                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| n   | 4                         | 4                      | 4                                 | 4       | 4                      | 4             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal,rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic,systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 14         |         |                        | Species : Rat |
|---|---------------------------|------------------------|---------------------------------|---------|------------------------|---------------|
| Sex : Female (satellite)                    |                           |                        | Dose : PTSA Monohydrate 0 mg/kg |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion           | Rolling | Repetitive<br>circling | Self biting   |
| 50556                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50557                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50558                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50559                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| 50560                                       | 1                         | 1                      | 1                               | 0       | 0                      | 1             |
| n   | 5                         | 5                      | 5                               | 5       | 5                      | 5             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Detailed clinical observation (in the cage) |                           |                        | Stage : Recovery Day 14           |         |                        | Species : Rat |
|---|---------------------------|------------------------|-----------------------------------|---------|------------------------|---------------|
| Sex : Female (satellite)                    |                           |                        | Dose : PTSA Monohydrate 800 mg/kg |         |                        |               |
| Animal No.                                  | Body position/<br>Posture | Respiratory<br>pattern | Tremor/<br>Convulsion             | Rolling | Repetitive<br>circling | Self biting   |
| 50656                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| 50657                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| 50658                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| 50659                                       | 1                         | 1                      | 1                                 | 0       | 0                      | 1             |
| n   | 4                         | 4                      | 4                                 | 4       | 4                      | 4             |

Body position/Posture) 1;Normal (sitting, etc.), 2;Sleeping, 3;Crouching, 4;Prone, lateral, 5;Standing, jumping, 6;Cataleptic.

Respiratory pattern) 1;Normal, 2;Slightly abnormal, rapid or slow, 3;Moderately abnormal, difficult to breath, 4;Severe abnormal, labored, 5;Dyspnea.

Tremor/Convulsion) 1;Not present, 2;Irregularly only the legs, 3;Durable only the legs, 4;Clonic, systemic, 5;Tonic, systemic.

Stereotype/Rolling) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Repetitive circling) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Self biting) 1;Not present, 2;Present.

| Sex : Male                | Detailed clinical observation (on the hand)                   |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Pre administration<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10101                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10102                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10103                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10104                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10105                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10106                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10107                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10108                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10109                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10110                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10111                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10112                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10101                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10102                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10103                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10104                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10105                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10106                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10107                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10108                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10109                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10110                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10111                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10112                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12  |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male                | Detailed clinical observation (on the hand)                    |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Pre administration<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal  | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10201                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10202                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10203                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10204                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10205                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10206                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10207                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10208                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10209                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10210                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10211                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10212                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |
| <hr/>                     |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10201                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10202                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10203                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10204                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10205                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10206                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10207                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10208                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10209                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10210                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10211                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10212                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12   |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male                | Detailed clinical observation (on the hand)                     |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Pre administration<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10301                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10302                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10303                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10304                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10305                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10306                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10307                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10308                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10309                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10310                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10311                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10312                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10301                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10302                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10303                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10304                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10305                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10306                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10307                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10308                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10309                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10310                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10311                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10312                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12  |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)                     |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Pre administration<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10401      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10402      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10403      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10404      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10405      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10406      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10407      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10408      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10409      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10410      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10411      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10412      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10401      | 0                         |
| 10402      | 0                         |
| 10403      | 0                         |
| 10404      | 0                         |
| 10405      | 0                         |
| 10406      | 0                         |
| 10407      | 0                         |
| 10408      | 0                         |
| 10409      | 0                         |
| 10410      | 0                         |
| 10411      | 0                         |
| 10412      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)      |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                  | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10101      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10102      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10103      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10104      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10105      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10106      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10107      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10108      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10109      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10110      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10111      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10112      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |    |       |    |       |    |       |    |       |    |       |    |       |    |       |    |       |    |       |    |       |    |       |
|------------|---------------------------|----|-------|----|-------|----|-------|----|-------|----|-------|----|-------|----|-------|----|-------|----|-------|----|-------|----|-------|
|            | 10101                     | 0  | 10102 | 0  | 10103 | 0  | 10104 | 0  | 10105 | 0  | 10106 | 0  | 10107 | 0  | 10108 | 0  | 10109 | 0  | 10110 | 0  | 10111 | 0  | 10112 |
| n          | 12                        | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    | 12 | 12    |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10201      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10202      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10203      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10204      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10205      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10206      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10207      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10208      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10209      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10210      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10211      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10212      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10201      | 0                         |
| 10202      | 0                         |
| 10203      | 0                         |
| 10204      | 0                         |
| 10205      | 0                         |
| 10206      | 0                         |
| 10207      | 0                         |
| 10208      | 0                         |
| 10209      | 0                         |
| 10210      | 0                         |
| 10211      | 0                         |
| 10212      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male                | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Day 7<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10301                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10302                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10303                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10304                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10305                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10306                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10307                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10308                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10309                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10310                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10311                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10312                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |
| <hr/>                     |  |                  |             |              |     |      |                  |      |            |           |            |               |
| <hr/>                     |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10301                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10302                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10303                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10304                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10305                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10306                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10307                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10308                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10309                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10310                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10311                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10312                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12   |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10401      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10402      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10403      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10404      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10405      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10406      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10407      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10408      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10409      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10410      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10411      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10412      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10401      | 0                         |
| 10402      | 0                         |
| 10403      | 0                         |
| 10404      | 0                         |
| 10405      | 0                         |
| 10406      | 0                         |
| 10407      | 0                         |
| 10408      | 0                         |
| 10409      | 0                         |
| 10410      | 0                         |
| 10411      | 0                         |
| 10412      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10101      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10102      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10103      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10104      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10105      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10106      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10107      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10108      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10109      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10110      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10111      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10112      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |
|------------|---------------------------|---|-------|---|-------|---|-------|---|-------|---|-------|---|-------|---|-------|---|-------|---|-------|---|-------|---|-------|
|            | 10101                     | 0 | 10102 | 0 | 10103 | 0 | 10104 | 0 | 10105 | 0 | 10106 | 0 | 10107 | 0 | 10108 | 0 | 10109 | 0 | 10110 | 0 | 10111 | 0 | 10112 |
| n          | 12                        |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |   |       |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10201      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10202      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10203      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10204      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10205      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10206      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10207      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10208      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10209      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10210      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10211      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10212      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10201      | 0                         |
| 10202      | 0                         |
| 10203      | 0                         |
| 10204      | 0                         |
| 10205      | 0                         |
| 10206      | 0                         |
| 10207      | 0                         |
| 10208      | 0                         |
| 10209      | 0                         |
| 10210      | 0                         |
| 10211      | 0                         |
| 10212      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10301      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10302      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10303      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10304      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10305      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10306      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10307      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10308      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10309      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10310      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10311      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10312      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10301      | 0                         |
| 10302      | 0                         |
| 10303      | 0                         |
| 10304      | 0                         |
| 10305      | 0                         |
| 10306      | 0                         |
| 10307      | 0                         |
| 10308      | 0                         |
| 10309      | 0                         |
| 10310      | 0                         |
| 10311      | 0                         |
| 10312      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10401      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10402      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10403      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10404      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10405      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10406      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10407      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10408      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10409      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10410      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10411      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10412      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10401      | 0                         |
| 10402      | 0                         |
| 10403      | 0                         |
| 10404      | 0                         |
| 10405      | 0                         |
| 10406      | 0                         |
| 10407      | 0                         |
| 10408      | 0                         |
| 10409      | 0                         |
| 10410      | 0                         |
| 10411      | 0                         |
| 10412      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10101      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10102      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10103      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10104      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10105      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10106      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10107      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10108      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10109      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10110      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10111      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10112      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10101      | 0                         |
| 10102      | 0                         |
| 10103      | 0                         |
| 10104      | 0                         |
| 10105      | 0                         |
| 10106      | 0                         |
| 10107      | 0                         |
| 10108      | 0                         |
| 10109      | 0                         |
| 10110      | 0                         |
| 10111      | 0                         |
| 10112      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10201      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10202      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10203      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10204      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10205      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10206      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10207      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10208      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10209      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10210      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10211      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10212      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10201      | 0                         |
| 10202      | 0                         |
| 10203      | 0                         |
| 10204      | 0                         |
| 10205      | 0                         |
| 10206      | 0                         |
| 10207      | 0                         |
| 10208      | 0                         |
| 10209      | 0                         |
| 10210      | 0                         |
| 10211      | 0                         |
| 10212      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10301      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10302      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10303      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10304      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10305      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10306      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10307      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10308      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10309      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10310      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10311      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10312      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10301      | 0                         |
| 10302      | 0                         |
| 10303      | 0                         |
| 10304      | 0                         |
| 10305      | 0                         |
| 10306      | 0                         |
| 10307      | 0                         |
| 10308      | 0                         |
| 10309      | 0                         |
| 10310      | 0                         |
| 10311      | 0                         |
| 10312      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10401      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10402      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10403      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10404      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10405      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10406      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10407      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10408      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10409      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10410      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10411      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10412      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10401      | 0                         |
| 10402      | 0                         |
| 10403      | 0                         |
| 10404      | 0                         |
| 10405      | 0                         |
| 10406      | 0                         |
| 10407      | 0                         |
| 10408      | 0                         |
| 10409      | 0                         |
| 10410      | 0                         |
| 10411      | 0                         |
| 10412      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Day 28<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10101      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10102      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10103      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10104      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10105      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10106      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10107      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10108      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10109      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10110      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10111      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10112      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 10101      | 0                         |
| 10102      | 0                         |
| 10103      | 0                         |
| 10104      | 0                         |
| 10105      | 0                         |
| 10106      | 0                         |
| 10107      | 0                         |
| 10108      | 0                         |
| 10109      | 0                         |
| 10110      | 0                         |
| 10111      | 0                         |
| 10112      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male                | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Day 28<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10201                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10202                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10203                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10204                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10205                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10206                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10207                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10208                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10209                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10210                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10211                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10212                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |
| <hr/>                     |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10201                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10202                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10203                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10204                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10205                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10206                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10207                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10208                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10209                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10210                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10211                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 10212                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12   |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male                | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Day 28<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10301                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10302                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10303                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10304                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10305                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10306                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10307                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10308                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10309                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10310                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10311                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10312                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10301                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10302                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10303                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10304                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10305                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10306                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10307                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10308                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10309                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10310                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10311                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10312                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12  |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male                | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Day 28<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10401                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10402                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10403                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10404                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10405                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10406                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10407                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10408                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10409                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10410                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10411                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10412                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10401                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10402                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10403                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10404                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10405                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10406                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10407                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10408                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10409                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10410                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10411                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 10412                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12  |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Pre administration |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone                | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50151      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50152      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50153      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50154      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50155      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50156      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50157      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50158      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50159      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50160      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50161      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50162      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12                         | 12           | 12  | 12            | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50151      | 0                         |
| 50152      | 0                         |
| 50153      | 0                         |
| 50154      | 0                         |
| 50155      | 0                         |
| 50156      | 0                         |
| 50157      | 0                         |
| 50158      | 0                         |
| 50159      | 0                         |
| 50160      | 0                         |
| 50161      | 0                         |
| 50162      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)                    |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Pre administration<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal  | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50251        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50252        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50253        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50254        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50255        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50256        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50257        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50258        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50259        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50260        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50261        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50262        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50251      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50252      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50253      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50254      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50255      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50256      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50257      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50258      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50259      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50260      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50261      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50262      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Pre administration |              |     |      |                  | Species : Rat |            |           |            |
|------------|---|-----------------|------------------|----------------------------|--------------|-----|------|------------------|---------------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone                | Piloerection | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50351      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50352      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50353      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50354      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50355      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50356      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50357      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50358      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50359      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50360      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50361      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50362      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12                         | 12           | 12  | 12   | 12               | 12            | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50351      | 0                         |
| 50352      | 0                         |
| 50353      | 0                         |
| 50354      | 0                         |
| 50355      | 0                         |
| 50356      | 0                         |
| 50357      | 0                         |
| 50358      | 0                         |
| 50359      | 0                         |
| 50360      | 0                         |
| 50361      | 0                         |
| 50362      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Pre administration |              |     |      |                  | Species : Rat |            |           |            |
|------------|---|-----------------|------------------|----------------------------|--------------|-----|------|------------------|---------------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone                | Piloerection | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50451      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50452      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50453      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50454      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50455      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50456      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50457      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50458      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50459      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50460      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50461      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50462      |   | 1               | 1                | 2                          | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12                         | 12           | 12  | 12   | 12               | 12            | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50451      | 0                         |
| 50452      | 0                         |
| 50453      | 0                         |
| 50454      | 0                         |
| 50455      | 0                         |
| 50456      | 0                         |
| 50457      | 0                         |
| 50458      | 0                         |
| 50459      | 0                         |
| 50460      | 0                         |
| 50461      | 0                         |
| 50462      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)      |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                  | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50151        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50152        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50153        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50154        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50155        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50156        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50157        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50158        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50159        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50160        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50161        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50162        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50151      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50152      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50153      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50154      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50155      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50156      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50157      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50158      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50159      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50160      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50161      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50162      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female              | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Day 7<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50251                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50252                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50253                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50254                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50255                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50256                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50257                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50258                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50259                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50260                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50261                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50262                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |   |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50251                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50252                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50253                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50254                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50255                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50256                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50257                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50258                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50259                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50260                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50261                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| 50262                     | 0   |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12  |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 7<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50351        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50352        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50353        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50354        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50355        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50356        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50357        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50358        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50359        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50360        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50361        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50362        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50351      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50352      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50353      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50354      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50355      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50356      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50357      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50358      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50359      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50360      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50361      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50362      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50451        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50452        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50453        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50454        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50455        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50456        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50457        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50458        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50459        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50460        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50461        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50462        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50451      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50452      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50453      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50454      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50455      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50456      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50457      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50458      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50459      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50460      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50461      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50462      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50151        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50152        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50153        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50154        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50155        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50156        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50157        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50158        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50159        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50160        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50161        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50162        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50151      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50152      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50153      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50154      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50155      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50156      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50157      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50158      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50159      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50160      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50161      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50162      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 14<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50251        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50252        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50253        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50254        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50255        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50256        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50257        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50258        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50259        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50260        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50261        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50262        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50251      | 0                         |
| 50252      | 0                         |
| 50253      | 0                         |
| 50254      | 0                         |
| 50255      | 0                         |
| 50256      | 0                         |
| 50257      | 0                         |
| 50258      | 0                         |
| 50259      | 0                         |
| 50260      | 0                         |
| 50261      | 0                         |
| 50262      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Species : Rat |              |     |      |                  |      |            |           |            |
|------------|---|-----------------|------------------|---------------|--------------|-----|------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone   | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50351      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50352      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50353      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50354      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50355      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50356      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50357      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50358      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50359      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50360      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50361      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50362      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12            | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50351      | 0                         |
| 50352      | 0                         |
| 50353      | 0                         |
| 50354      | 0                         |
| 50355      | 0                         |
| 50356      | 0                         |
| 50357      | 0                         |
| 50358      | 0                         |
| 50359      | 0                         |
| 50360      | 0                         |
| 50361      | 0                         |
| 50362      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Species : Rat |              |     |      |                  |      |            |           |            |
|------------|---|-----------------|------------------|---------------|--------------|-----|------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone   | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50451      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50452      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50453      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50454      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50455      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50456      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50457      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50458      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50459      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50460      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50461      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50462      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12            | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50451      | 0                         |
| 50452      | 0                         |
| 50453      | 0                         |
| 50454      | 0                         |
| 50455      | 0                         |
| 50456      | 0                         |
| 50457      | 0                         |
| 50458      | 0                         |
| 50459      | 0                         |
| 50460      | 0                         |
| 50461      | 0                         |
| 50462      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Species : Rat |              |     |      |                  |      |            |           |            |
|------------|---|-----------------|------------------|---------------|--------------|-----|------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone   | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50151      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50152      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50153      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50154      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50155      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50156      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50157      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50158      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50159      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50160      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50161      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50162      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12            | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50151      | 0                         |
| 50152      | 0                         |
| 50153      | 0                         |
| 50154      | 0                         |
| 50155      | 0                         |
| 50156      | 0                         |
| 50157      | 0                         |
| 50158      | 0                         |
| 50159      | 0                         |
| 50160      | 0                         |
| 50161      | 0                         |
| 50162      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female              | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|---------------------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|                           | Stage : Day 21<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50251                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50252                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50253                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50254                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50255                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50256                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50257                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50258                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50259                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50260                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50261                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50262                     | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n                         | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |
| <hr/>                     |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Secretions/<br>Excretions |  |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.                |  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50251                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50252                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50253                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50254                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50255                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50256                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50257                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50258                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50259                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50260                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50261                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| 50262                     | 0  |                  |             |              |     |      |                  |      |            |           |            |               |
| n                         | 12   |                  |             |              |     |      |                  |      |            |           |            |               |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 21<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50351        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50352        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50353        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50354        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50355        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50356        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50357        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50358        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50359        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50360        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50361        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50362        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50351      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50352      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50353      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50354      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50355      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50356      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50357      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50358      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50359      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50360      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50361      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50362      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female              | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           | Species : Rat |
|---------------------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|---------------|
|                           | Stage : Day 21<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |               |
| Animal No.                | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation    |
| 50451                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50452                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50453                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50454                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50455                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50456                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50457                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50458                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50459                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50460                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50461                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 50462                     | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12            |
| <hr/>                     |   |                  |             |              |     |      |                  |      |            |           |               |
| Secretions/<br>Excretions |   |                  |             |              |     |      |                  |      |            |           |               |
| Animal No.                | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50451                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50452                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50453                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50454                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50455                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50456                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50457                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50458                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50459                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50460                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50461                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| 50462                     | 0   | 0                | 0           | 0            | 0   | 0    | 0                | 0    | 0          | 0         | 0             |
| n                         | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12            |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)       |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 28<br>Dose : PTSA Monohydrate 0 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50151        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50152        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50153        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50154        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50155        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50156        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50157        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50158        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50159        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50160        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50161        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50162        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |  |  |  |  |  |  |  |  |  |  |  |
|------------|---------------------------|--|--|--|--|--|--|--|--|--|--|--|
|            |                           |  |  |  |  |  |  |  |  |  |  |  |
| 50151      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50152      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50153      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50154      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50155      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50156      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50157      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50158      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50159      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50160      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50161      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| 50162      | 0                         |  |  |  |  |  |  |  |  |  |  |  |
| n          | 12                        |  |  |  |  |  |  |  |  |  |  |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 28<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50251        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50252        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50253        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50254        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50255        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50256        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50257        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50258        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50259        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50260        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50261        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50262        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50251      | 0                         |
| 50252      | 0                         |
| 50253      | 0                         |
| 50254      | 0                         |
| 50255      | 0                         |
| 50256      | 0                         |
| 50257      | 0                         |
| 50258      | 0                         |
| 50259      | 0                         |
| 50260      | 0                         |
| 50261      | 0                         |
| 50262      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Species : Rat |              |     |      |                  |      |            |           |            |
|------------|---|-----------------|------------------|---------------|--------------|-----|------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone   | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50351      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50352      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50353      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50354      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50355      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50356      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50357      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50358      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50359      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50360      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50361      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 50362      |   | 1               | 1                | 2             | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12            | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50351      | 0                         |
| 50352      | 0                         |
| 50353      | 0                         |
| 50354      | 0                         |
| 50355      | 0                         |
| 50356      | 0                         |
| 50357      | 0                         |
| 50358      | 0                         |
| 50359      | 0                         |
| 50360      | 0                         |
| 50361      | 0                         |
| 50362      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 28<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50451        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50452        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50453        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50454        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50455        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50456        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50457        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50458        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50459        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50460        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50461        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50462        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50451      | 0                         |
| 50452      | 0                         |
| 50453      | 0                         |
| 50454      | 0                         |
| 50455      | 0                         |
| 50456      | 0                         |
| 50457      | 0                         |
| 50458      | 0                         |
| 50459      | 0                         |
| 50460      | 0                         |
| 50461      | 0                         |
| 50462      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 35 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50151      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50152      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50153      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50154      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50155      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50156      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50157      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50158      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50159      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50160      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50161      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50162      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12             | 12           | 12  | 12            | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50151      | 0                         |
| 50152      | 0                         |
| 50153      | 0                         |
| 50154      | 0                         |
| 50155      | 0                         |
| 50156      | 0                         |
| 50157      | 0                         |
| 50158      | 0                         |
| 50159      | 0                         |
| 50160      | 0                         |
| 50161      | 0                         |
| 50162      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)        |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 35<br>Dose : PTSA Monohydrate 50 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                    | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50251        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50252        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50253        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50254        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50255        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50256        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50257        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50258        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50259        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50260        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50261        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50262        | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12   | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         | 12            |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50251      | 0                         |
| 50252      | 0                         |
| 50253      | 0                         |
| 50254      | 0                         |
| 50255      | 0                         |
| 50256      | 0                         |
| 50257      | 0                         |
| 50258      | 0                         |
| 50259      | 0                         |
| 50260      | 0                         |
| 50261      | 0                         |
| 50262      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Female | Detailed clinical observation (on the hand)         |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|--------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|              | Stage : Day 35<br>Dose : PTSA Monohydrate 200 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No.   | Ease of Removal                                     | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 50351        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50352        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50353        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50354        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50355        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50356        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50357        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50358        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50359        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50360        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50361        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 50362        | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n            | 12  | 12               | 12          | 12           | 12  | 12   | 12               | 12   | 12         | 12        | 12         |               |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50351      | 0                         |
| 50352      | 0                         |
| 50353      | 0                         |
| 50354      | 0                         |
| 50355      | 0                         |
| 50356      | 0                         |
| 50357      | 0                         |
| 50358      | 0                         |
| 50359      | 0                         |
| 50360      | 0                         |
| 50361      | 0                         |
| 50362      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 35 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50451      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50452      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50453      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50454      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50455      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50456      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50457      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50458      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50459      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50460      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50461      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50462      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 12              | 12               | 12             | 12           | 12  | 12            | 12               | 12   | 12         | 12        | 12         |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50451      | 0                         |
| 50452      | 0                         |
| 50453      | 0                         |
| 50454      | 0                         |
| 50455      | 0                         |
| 50456      | 0                         |
| 50457      | 0                         |
| 50458      | 0                         |
| 50459      | 0                         |
| 50460      | 0                         |
| 50461      | 0                         |
| 50462      | 0                         |
| n          | 12                        |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Sex : Female    |                  | Detailed clinical observation (on the hand) |              |     |      |                  |      |            |           |            |   | Species : Rat |
|------------|-----------------|------------------|---|--------------|-----|------|------------------|------|------------|-----------|------------|---|---------------|
|            | Ease of Removal | Ease of Handling | Muscle tone                                 | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |   |               |
| 50153      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50154      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50156      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50157      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50158      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50159      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50160      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| 50162      | 1               | 1                | 2   | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1 |               |
| n          | 8               | 8                | 8   | 8            | 8   | 8    | 8                | 8    | 8          | 8         | 8          | 8 |               |

| Animal No. | Secretions/<br>Excretions |   |   |   |   |   |   |   |   |   |   |   |
|------------|---------------------------|---|---|---|---|---|---|---|---|---|---|---|
|            | 50153                     | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50154      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50156      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50157      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50158      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50159      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50160      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 50162      | 0                         | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| n          | 8                         | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No.                | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 42 |              |     | Species : Rat |                  |      |            |           |            |
|---------------------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|                           | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50251                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50252                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50253                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50254                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50255                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50257                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50259                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50260                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50261                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50262                     |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n                         |   | 10              | 10               | 10             | 10           | 10  | 10            | 10               | 10   | 10         | 10        | 10         |
| <hr/>                     |   |                 |                  |                |              |     |               |                  |      |            |           |            |
| Secretions/<br>Excretions |   |                 |                  |                |              |     |               |                  |      |            |           |            |
| Animal No.                |   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50251                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50252                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50253                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50254                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50255                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50257                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50259                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50260                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50261                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| 50262                     | 0   |                 |                  |                |              |     |               |                  |      |            |           |            |
| n                         | 10  |                 |                  |                |              |     |               |                  |      |            |           |            |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 42 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female                                | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50351      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50352      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50353      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50356      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50357      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50358      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50359      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50361      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 8               | 8                | 8              | 8            | 8   | 8             | 8                | 8    | 8          | 8         | 8          |


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| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50351      | 0                         |  |
| 50352      | 0                         |  |
| 50353      | 0                         |  |
| 50356      | 0                         |  |
| 50357      | 0                         |  |
| 50358      | 0                         |  |
| 50359      | 0                         |  |
| 50361      | 0                         |  |
| n          | 8                         |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Detailed clinical observation (on the hand) |                 |                  |             | Stage : Day 42                    |     |      |                  | Species : Rat |            |           |            |
|---|-----------------|------------------|-------------|-----------------------------------|-----|------|------------------|---------------|------------|-----------|------------|
| Sex : Female                                |                 |                  |             | Dose : PTSA Monohydrate 800 mg/kg |     |      |                  |               |            |           |            |
| Animal No.                                  | Ease of Removal | Ease of Handling | Muscle tone | Piloerection                      | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50451                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50452                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50453                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50454                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50459                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50460                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50462                                       | 1               | 1                | 2           | 1                                 | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n   | 7               | 7                | 7           | 7                                 | 7   | 7    | 7                | 7             | 7          | 7         | 7          |
| <hr/>                                       |                 |                  |             |                                   |     |      |                  |               |            |           |            |
| Secretions/<br>Excretions                   |                 |                  |             |                                   |     |      |                  |               |            |           |            |
| Animal No.                                  |                 |                  |             |                                   |     |      |                  |               |            |           |            |
| 50451                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| 50452                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| 50453                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| 50454                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| 50459                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| 50460                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| 50462                                       | 0               |                  |             |                                   |     |      |                  |               |            |           |            |
| n   | 7               |                  |             |                                   |     |      |                  |               |            |           |            |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Pre administration |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone                | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50551      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50552      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50553      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50554      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50555      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50556      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50557      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50558      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50559      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50560      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 10              | 10               | 10                         | 10           | 10  | 10            | 10               | 10   | 10         | 10        | 10         |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50551      | 0                         |  |
| 50552      | 0                         |  |
| 50553      | 0                         |  |
| 50554      | 0                         |  |
| 50555      | 0                         |  |
| 50556      | 0                         |  |
| 50557      | 0                         |  |
| 50558      | 0                         |  |
| 50559      | 0                         |  |
| 50560      | 0                         |  |
| n          | 10                        |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Pre administration |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone                | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50651      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50652      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50653      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50654      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50655      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50656      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50660      |   | 1               | 1                | 2                          | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 10              | 10               | 10                         | 10           | 10  | 10            | 10               | 10   | 10         | 10        | 10         |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50651      | 0                         |  |
| 50652      | 0                         |  |
| 50653      | 0                         |  |
| 50654      | 0                         |  |
| 50655      | 0                         |  |
| 50656      | 0                         |  |
| 50657      | 0                         |  |
| 50658      | 0                         |  |
| 50659      | 0                         |  |
| 50660      | 0                         |  |
| n          | 10                        |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 7 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|---------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone   | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50551      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50552      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50553      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50554      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50555      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50556      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50557      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50558      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50559      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50560      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 10              | 10               | 10            | 10           | 10  | 10            | 10               | 10   | 10         | 10        | 10         |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50551      | 0                         |  |
| 50552      | 0                         |  |
| 50553      | 0                         |  |
| 50554      | 0                         |  |
| 50555      | 0                         |  |
| 50556      | 0                         |  |
| 50557      | 0                         |  |
| 50558      | 0                         |  |
| 50559      | 0                         |  |
| 50560      | 0                         |  |
| n          | 10                        |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 7 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|---------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone   | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50651      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50652      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50653      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50654      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50655      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50656      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2             | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 9               | 9                | 9             | 9            | 9   | 9             | 9                | 9    | 9          | 9         | 9          |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50651      | 0                         |  |
| 50652      | 0                         |  |
| 50653      | 0                         |  |
| 50654      | 0                         |  |
| 50655      | 0                         |  |
| 50656      | 0                         |  |
| 50657      | 0                         |  |
| 50658      | 0                         |  |
| 50659      | 0                         |  |
| n          | 9                         |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 14 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50551      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50552      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50553      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50554      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50555      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50556      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50557      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50558      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50559      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50560      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 10              | 10               | 10             | 10           | 10  | 10            | 10               | 10   | 10         | 10        | 10         |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50551      | 0                         |  |
| 50552      | 0                         |  |
| 50553      | 0                         |  |
| 50554      | 0                         |  |
| 50555      | 0                         |  |
| 50556      | 0                         |  |
| 50557      | 0                         |  |
| 50558      | 0                         |  |
| 50559      | 0                         |  |
| 50560      | 0                         |  |
| n          | 10                        |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 14 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50651      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50652      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50653      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50654      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50655      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50656      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 9               | 9                | 9              | 9            | 9   | 9             | 9                | 9    | 9          | 9         | 9          |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50651      | 0                         |  |
| 50652      | 0                         |  |
| 50653      | 0                         |  |
| 50654      | 0                         |  |
| 50655      | 0                         |  |
| 50656      | 0                         |  |
| 50657      | 0                         |  |
| 50658      | 0                         |  |
| 50659      | 0                         |  |
| n          | 9                         |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No.                | Detailed clinical observation (on the hand) |                  | Species : Rat  |              |     |                                 |                  |      |            |           |            |    |
|---------------------------|---|------------------|----------------|--------------|-----|---------------------------------|------------------|------|------------|-----------|------------|----|
|                           | Sex : Female (satellite)                    |                  | Stage : Day 21 |              |     | Dose : PTSA Monohydrate 0 mg/kg |                  |      |            |           |            |    |
|                           | Ease of Removal                             | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes                            | Mucous membranes | Skin | Pupil size | Lacration | Salivation |    |
| 50551                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50552                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50553                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50554                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50555                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50556                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50557                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50558                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50559                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| 50560                     | 1   | 1                | 2              | 1            | 1   | 1                               | 0                | 1    | 1          | 1         | 1          | 1  |
| n                         | 10  | 10               | 10             | 10           | 10  | 10                              | 10               | 10   | 10         | 10        | 10         | 10 |
| <hr/>                     |   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| Secretions/<br>Excretions |   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| Animal No.                |   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50551                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50552                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50553                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50554                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50555                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50556                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50557                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50558                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50559                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| 50560                     | 0   |                  |                |              |     |                                 |                  |      |            |           |            |    |
| n                         | 10  |                  |                |              |     |                                 |                  |      |            |           |            |    |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 21 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50651      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50652      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50653      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50654      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50655      |   | 1               | 1                | 2              | 1            | 2   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50656      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 9               | 9                | 9              | 9            | 9   | 9             | 9                | 9    | 9          | 9         | 9          |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50651      | 0                         |  |
| 50652      | 0                         |  |
| 50653      | 0                         |  |
| 50654      | 0                         |  |
| 50655      | 0                         |  |
| 50656      | 0                         |  |
| 50657      | 0                         |  |
| 50658      | 0                         |  |
| 50659      | 0                         |  |
| n          | 9                         |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 28 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50551      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50552      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50553      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50554      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50555      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50556      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50557      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50558      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50559      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50560      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 10              | 10               | 10             | 10           | 10  | 10            | 10               | 10   | 10         | 10        | 10         |

| Animal No. | Secretions/<br>Excretions |  |
|------------|---------------------------|--|
|            |                           |  |
| 50551      | 0                         |  |
| 50552      | 0                         |  |
| 50553      | 0                         |  |
| 50554      | 0                         |  |
| 50555      | 0                         |  |
| 50556      | 0                         |  |
| 50557      | 0                         |  |
| 50558      | 0                         |  |
| 50559      | 0                         |  |
| 50560      | 0                         |  |
| n          | 10                        |  |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Day 28 |              |     | Species : Rat |                  |      |            |           |            |
|------------|---|-----------------|------------------|----------------|--------------|-----|---------------|------------------|------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone    | Piloerection | Fur | Eyes          | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 50651      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50652      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50653      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50654      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50655      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50656      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2              | 1            | 1   | 1             | 0                | 1    | 1          | 1         | 1          |
| n          |   | 9               | 9                | 9              | 9            | 9   | 9             | 9                | 9    | 9          | 9         | 9          |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50651      | 0                         |
| 50652      | 0                         |
| 50653      | 0                         |
| 50654      | 0                         |
| 50655      | 0                         |
| 50656      | 0                         |
| 50657      | 0                         |
| 50658      | 0                         |
| 50659      | 0                         |
| n          | 9                         |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Detailed clinical observation (on the hand) |  |                                 |                  | Stage : Recovery Day 7 |              |     |      | Species : Rat    |      |            |           |            |
|---|--|---------------------------------|------------------|------------------------|--------------|-----|------|------------------|------|------------|-----------|------------|
| Sex : Male                                  |  | Dose : PTSA Monohydrate 0 mg/kg |                  |                        |              |     |      |                  |      |            |           |            |
| Animal No.                                  |  | Ease of Removal                 | Ease of Handling | Muscle tone            | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |
| 10103                                       |  | 1                               | 1                | 2                      | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 10104                                       |  | 1                               | 1                | 2                      | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 10105                                       |  | 1                               | 1                | 2                      | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 10106                                       |  | 1                               | 1                | 2                      | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| 10111                                       |  | 1                               | 1                | 2                      | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          |
| n   |  | 5                               | 5                | 5                      | 5            | 5   | 5    | 5                | 5    | 5          | 5         | 5          |

| Secretions/<br>Excretions |   |
|---------------------------|---|
| Animal No.                |   |
| 10103                     | 0 |
| 10104                     | 0 |
| 10105                     | 0 |
| 10106                     | 0 |
| 10111                     | 0 |
| n                         | 5 |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)                 |                  |             |              |     |      |                  |      |            |           | Species : Rat |
|------------|---|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|---------------|
|            | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |               |
| Animal No. | Ease of Removal   | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation    |
| 10402      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 10403      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 10407      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 10409      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| 10411      | 1   | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1             |
| n          | 5   | 5                | 5           | 5            | 5   | 5    | 5                | 5    | 5          | 5         | 5             |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
| 10402      | 0                         |
| 10403      | 0                         |
| 10407      | 0                         |
| 10409      | 0                         |
| 10411      | 0                         |
| n          | 5                         |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Detailed clinical observation (on the hand) |                 |                                 |             | Stage : Recovery Day 14 |     |      |                  | Species : Rat |            |           |            |
|---|-----------------|---------------------------------|-------------|-------------------------|-----|------|------------------|---------------|------------|-----------|------------|
| Sex : Male                                  |                 | Dose : PTSA Monohydrate 0 mg/kg |             |                         |     |      |                  |               |            |           |            |
| Animal No.                                  | Ease of Removal | Ease of Handling                | Muscle tone | Piloerection            | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 10103                                       | 1               | 1                               | 2           | 1                       | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 10104                                       | 1               | 1                               | 2           | 1                       | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 10105                                       | 1               | 1                               | 2           | 1                       | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 10106                                       | 1               | 1                               | 2           | 1                       | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 10111                                       | 1               | 1                               | 2           | 1                       | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n   | 5               | 5                               | 5           | 5                       | 5   | 5    | 5                | 5             | 5          | 5         | 5          |

| Secretions/<br>Excretions |   |
|---------------------------|---|
| Animal No.                |   |
| 10103                     | 0 |
| 10104                     | 0 |
| 10105                     | 0 |
| 10106                     | 0 |
| 10111                     | 0 |
| n                         | 5 |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (on the hand)                  |                  |             |              |     |      |                  |      |            |           |            | Species : Rat |
|------------|--|------------------|-------------|--------------|-----|------|------------------|------|------------|-----------|------------|---------------|
|            | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |                  |             |              |     |      |                  |      |            |           |            |               |
| Animal No. | Ease of Removal  | Ease of Handling | Muscle tone | Piloerection | Fur | Eyes | Mucous membranes | Skin | Pupil size | Lacration | Salivation |               |
| 10402      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10403      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10407      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10409      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| 10411      | 1  | 1                | 2           | 1            | 1   | 1    | 0                | 1    | 1          | 1         | 1          | 1             |
| n          | 5  | 5                | 5           | 5            | 5   | 5    | 5                | 5    | 5          | 5         | 5          |               |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
| 10402      | 0                         |
| 10403      | 0                         |
| 10407      | 0                         |
| 10409      | 0                         |
| 10411      | 0                         |
| n          | 5                         |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Detailed clinical observation (on the hand) |                 |                                 |             | Stage : Recovery Day 7 |     |      |                  | Species : Rat |            |           |            |
|---|-----------------|---------------------------------|-------------|------------------------|-----|------|------------------|---------------|------------|-----------|------------|
| Sex : Female (satellite)                    |                 | Dose : PTSA Monohydrate 0 mg/kg |             |                        |     |      |                  |               |            |           |            |
| Animal No.                                  | Ease of Removal | Ease of Handling                | Muscle tone | Piloerection           | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50556                                       | 1               | 1                               | 2           | 1                      | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50557                                       | 1               | 1                               | 2           | 1                      | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50558                                       | 1               | 1                               | 2           | 1                      | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50559                                       | 1               | 1                               | 2           | 1                      | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50560                                       | 1               | 1                               | 2           | 1                      | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n   | 5               | 5                               | 5           | 5                      | 5   | 5    | 5                | 5             | 5          | 5         | 5          |

| Secretions/<br>Excretions |   |
|---------------------------|---|
| Animal No.                |   |
| 50556                     | 0 |
| 50557                     | 0 |
| 50558                     | 0 |
| 50559                     | 0 |
| 50560                     | 0 |
| n                         | 5 |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Recovery Day 7 |              |     |      |                  | Species : Rat |            |           |            |
|------------|---|-----------------|------------------|------------------------|--------------|-----|------|------------------|---------------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone            | Piloerection | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50656      |   | 1               | 1                | 2                      | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2                      | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2                      | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2                      | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n          |   | 4               | 4                | 4                      | 4            | 4   | 4    | 4                | 4             | 4          | 4         | 4          |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
| 50656      | 0                         |
| 50657      | 0                         |
| 50658      | 0                         |
| 50659      | 0                         |
| n          | 4                         |

(Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

(Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

(Muscle tone) 1;Low, 2;Normal, 3;High.

(Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

(Fur) 1;Normal, 2;Slightly stained, 3;Stained.

(Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

(Mucous membranes) 1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

(Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

(Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

(Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

(Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

(Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Recovery Day 14 |              |     |      |                  | Species : Rat |            |           |            |
|------------|---|-----------------|------------------|-------------------------|--------------|-----|------|------------------|---------------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone             | Piloerection | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50556      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50557      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50558      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50559      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50560      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n          |   | 5               | 5                | 5                       | 5            | 5   | 5    | 5                | 5             | 5          | 5         | 5          |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50556      | 0                         |
| 50557      | 0                         |
| 50558      | 0                         |
| 50559      | 0                         |
| 50560      | 0                         |
| n          | 5                         |

Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

Muscle tone) 1;Low, 2;Normal, 3;High.

Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

Fur) 1;Normal, 2;Slightly stained, 3;Stained.

Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

Secretions/Excretions) 0;Not present, 1;Present.

| Animal No. | Detailed clinical observation (on the hand) |                 |                  | Stage : Recovery Day 14 |              |     |      |                  | Species : Rat |            |           |            |
|------------|---|-----------------|------------------|-------------------------|--------------|-----|------|------------------|---------------|------------|-----------|------------|
|            | Sex : Female (satellite)                    | Ease of Removal | Ease of Handling | Muscle tone             | Piloerection | Fur | Eyes | Mucous membranes | Skin          | Pupil size | Lacration | Salivation |
| 50656      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50657      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50658      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| 50659      |   | 1               | 1                | 2                       | 1            | 1   | 1    | 0                | 1             | 1          | 1         | 1          |
| n          |   | 4               | 4                | 4                       | 4            | 4   | 4    | 4                | 4             | 4          | 4         | 4          |

| Animal No. | Secretions/<br>Excretions |
|------------|---------------------------|
|            |                           |
| 50656      | 0                         |
| 50657      | 0                         |
| 50658      | 0                         |
| 50659      | 0                         |
| n          | 4                         |

(Ease of Removal) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

(Ease of Handling) 1;Very easy, 2;Easy, 3;Slightly difficult, 4;Difficult, 5;Very difficult.

(Muscle tone) 1;Low, 2;Normal, 3;High.

(Piloerection) 1;Normal, 2;Slightly present, around head and back, 3;Slightly present, systemic, 4;Severely present, systemic.

(Fur) 1;Normal, 2;Slightly stained, 3;Stained.

(Eyes) 1;Not present, normal, 2;Slight ptosis, half closed, 3;Ptosis, 4;Closed.

(Mucous membranes) -1;Dark purplish appearance, cyanosis, 0;Normal, 1;Red appearance.

(Skin) 0;Pale appearance, cyanosis, 1;Normal, 2;Red appearance.

(Pupil size) 1;Normal, 2;Slightly mydriatic, 3;Mydriatic.

(Lacration) 1;Not present, 2;Wet around the eye, 3;Wet, 4;Severely wet.

(Salivation) 1;Not present, 2;Wet around the mouth, 3;Wet, 4;Severely wet.

(Secretions/Excretions) 0;Not present, 1;Present.

| Sex : Male | Detailed clinical observation (in the open-field)             |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Pre administration<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10101      | 1   | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10102      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10103      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10104      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10105      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10106      | 1   | 1                         | 1                     | 1         | 1         | 1          | 1                  | 0                     | 1                | 1            | 1             |
| 10107      | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10108      | 1   | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10109      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10110      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10111      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10112      | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)              |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Pre administration<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10201      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10202      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10203      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10204      | 1  | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10205      | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10206      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10207      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10208      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10209      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10210      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10211      | 1  | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10212      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)               |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Pre administration<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10301      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10302      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10303      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10304      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10305      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10306      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10307      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10308      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10309      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10310      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10311      | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10312      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)               |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Pre administration<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10401      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10402      | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10403      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10404      | 1   | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10405      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10406      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10407      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10408      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10409      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10410      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10411      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10412      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 0 mg/kg  |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10101      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10102      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10103      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10104      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10105      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10106      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10107      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10108      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10109      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10110      | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10111      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10112      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10201      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10202      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10203      | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 10204      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10205      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10206      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10207      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10208      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10209      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10210      | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10211      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10212      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10301      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10302      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10303      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10304      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10305      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10306      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10307      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10308      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10309      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10310      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10311      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10312      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10401      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10402      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10403      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10404      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10405      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10406      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10407      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10408      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10409      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10410      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10411      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10412      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10101      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10102      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10103      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10104      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10105      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10106      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10107      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10108      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10109      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10110      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10111      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10112      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10201      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10202      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10203      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10204      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10205      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10206      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10207      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10208      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10209      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10210      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10211      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10212      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10301      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10302      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10303      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10304      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10305      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10306      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10307      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10308      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10309      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10310      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10311      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10312      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10401      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10402      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10403      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10404      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10405      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10406      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10407      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10408      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10409      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10410      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10411      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10412      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10101      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10102      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10103      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10104      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10105      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10106      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10107      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10108      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10109      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10110      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10111      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10112      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10201      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10202      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10203      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10204      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10205      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10206      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10207      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10208      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10209      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10210      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10211      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10212      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10301      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10302      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10303      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10304      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10305      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10306      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10307      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10308      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10309      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10310      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10311      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10312      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 21<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10401      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10402      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10403      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10404      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10405      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10406      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10407      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10408      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10409      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10410      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10411      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10412      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 28<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10101      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10102      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10103      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10104      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10105      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10106      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10107      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10108      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10109      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10110      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10111      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10112      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 28<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10201      | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10202      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10203      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10204      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10205      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10206      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10207      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10208      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10209      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10210      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10211      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10212      | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 28<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10301      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10302      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10303      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10304      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10305      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10306      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10307      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10308      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10309      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10310      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10311      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10312      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Male | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|            | Stage : Day 28<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No. | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 10401      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10402      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10403      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10404      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10405      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10406      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10407      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10408      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10409      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10410      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10411      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 10412      | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n          | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)             |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Pre administration<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50151        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50152        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50153        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50154        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50155        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50156        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50157        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50158        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50159        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50160        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50161        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50162        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)              |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Pre administration<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1  | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50256        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1  | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 50258        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)               |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Pre administration<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50351        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50352        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50353        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50354        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50355        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50356        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50357        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50358        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50359        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50360        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50361        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50362        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)               |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Pre administration<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50451        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50452        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50453        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50454        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50455        | 1   | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 50456        | 1   | 1                         | 1                     | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 50457        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50458        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50459        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50460        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50461        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50462        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |                           |                       | Stage : Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |           |            |                    |                       | Species : Rat    |              |            |
|------------|---|---------------------------|-----------------------|--|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching  | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50151      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50152      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50153      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50154      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50155      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50156      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50157      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50158      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50159      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50160      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50161      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50162      | 1   | 1                         | 1                     | 1  | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          | 12  | 12                        | 12                    | 12   | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2;Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 7<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1   | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50256        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50258        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1   | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Day 7<br>Dose : PTSA Monohydrate 200 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|------------|---|------|---------------------------|--|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli                              | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50351      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50352      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50353      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50354      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50355      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50356      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50357      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50358      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50359      |   | 1    | 1                         | 1  | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50360      |   | 1    | 1                         | 1  | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50361      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50362      |   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n          |   | 12   | 12                        | 12   | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field) |      |                           | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|--|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli                              | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| Animal No.  |      |                           |  |           |           |            |                    |                       |                  |              |               |  |
| 50451   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50452   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50453   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50454   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50455   | 1    | 1                         | 1  | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50456   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50457   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50458   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50459   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50460   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50461   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50462   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 12   | 12                        | 12   | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |                           |                       | Stage : Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |           |            |                    |                       | Species : Rat    |              |            |
|------------|---|---------------------------|-----------------------|---|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching   | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50151      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50152      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50153      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50154      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50155      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50156      | 1   | 1                         | 1                     | 1   | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50157      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50158      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50159      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50160      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50161      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50162      | 1   | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          | 12  | 12                        | 12                    | 12  | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2;Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 14<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50256        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50258        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50351      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50352      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50353      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50354      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50355      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50356      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50357      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50358      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50359      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50360      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50361      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50362      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50451      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50452      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50453      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50454      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50455      |   | 1    | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1          |
| 50456      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50457      |   | 1    | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50458      |   | 1    | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50459      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50460      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50461      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50462      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50151      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50152      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50153      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50154      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50155      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50156      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50157      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50158      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50159      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50160      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50161      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50162      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 21<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50256        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50258        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)   |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 21<br>Dose : PTSA Monohydrate 200 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50351        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50352        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50353        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50354        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50355        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50356        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50357        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50358        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50359        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50360        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50361        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50362        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field) |       |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|---|-------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
| Sex : Female                                      |       |                           | Stage : Day 21        |           |           |            |                    |                       |                  |              |            |
| Animal No.  | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
|   | 50451 | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50452   | 1     | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1          |
| 50453   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50454   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50455   | 1     | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50456   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50457   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50458   | 1     | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1          |
| 50459   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50460   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50461   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50462   | 1     | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n   | 12    | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 28<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50151        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50152        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50153        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50154        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50155        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50156        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50157        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50158        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50159        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50160        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50161        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50162        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12  | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 28<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50256        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50258        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50351      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50352      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50353      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50354      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50355      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50356      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50357      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50358      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50359      |   | 1    | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50360      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50361      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50362      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50451      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50452      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50453      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50454      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50455      |   | 1    | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50456      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50457      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50458      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50459      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50460      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50461      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50462      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50151      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50152      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50153      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50154      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50155      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50156      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50157      |   | 1    | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50158      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50159      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50160      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50161      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50162      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 35<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50256        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50258        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50351      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50352      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50353      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50354      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50355      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50356      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50357      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50358      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50359      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50360      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50361      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50362      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Species : Rat         |           |           |            |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female                                      | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50451      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50452      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50453      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50454      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50455      |   | 1    | 1                         | 1                     | 1         | 1         | 1          | 0                  | 0                     | 1                | 1            | 1          |
| 50456      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50457      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50458      |   | 1    | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50459      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50460      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50461      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50462      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 12   | 12                        | 12                    | 12        | 12        | 12         | 12                 | 12                    | 12               | 12           | 12         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field) |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 42<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50153        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50154        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50156        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50157        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50158        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50159        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50160        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50162        | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 8   | 8                         | 8                     | 8         | 8         | 8          | 8                  | 8                     | 8                | 8            | 8             |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Sex : Female | Detailed clinical observation (in the open-field)  |                           |                       |           |           |            |                    |                       |                  |              | Species : Rat |
|--------------|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|
|              | Stage : Day 42<br>Dose : PTSA Monohydrate 50 mg/kg |                           |                       |           |           |            |                    |                       |                  |              |               |
| Animal No.   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |
| 50251        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50252        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50253        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50254        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50255        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50257        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50259        | 1  | 1                         | 1                     | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50260        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50261        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| 50262        | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |
| n            | 10   | 10                        | 10                    | 10        | 10        | 10         | 10                 | 10                    | 10               | 10           | 10            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female |      |                           |                       | Stage : Day 42<br>Dose : PTSA Monohydrate 200 mg/kg |           |            |                    |                       | Species : Rat    |              |            |
|---|------|---------------------------|-----------------------|---|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli | Searching   | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50351   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50352   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50353   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50356   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50357   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50358   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50359   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50361   | 1    | 1                         | 1                     | 1   | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n   | 8    | 8                         | 8                     | 8   | 8         | 8          | 8                  | 8                     | 8                | 8            | 8          |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female |      |                           | Stage : Day 42<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|---|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                               | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50451   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50452   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50453   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50454   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50459   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50460   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50462   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 7    | 7                         | 7   | 7         | 7         | 7          | 7                  | 7                     | 7                | 7            | 7             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Pre administration |           |           |            |                    | Species : Rat         |                  |              |            |
|------------|---|------|---------------------------|----------------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female (satellite)                          | Gait | Co-ordination of movement | Reactivity to stimuli      | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50551      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50552      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50553      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50554      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50555      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50556      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50557      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50558      |   | 1    | 1                         | 1                          | 1         | 0         | 1          | 0                  | 0                     | 1                | 1            | 1          |
| 50559      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50560      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 10   | 10                        | 10                         | 10        | 10        | 10         | 10                 | 10                    | 10               | 10           | 10         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Pre administration |           |           |            |                    | Species : Rat         |                  |              |            |
|------------|---|------|---------------------------|----------------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female (satellite)                          | Gait | Co-ordination of movement | Reactivity to stimuli      | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50651      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50652      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50653      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50654      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50655      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50656      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50657      |   | 1    | 1                         | 1                          | 1         | 1         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50658      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50659      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50660      |   | 1    | 1                         | 1                          | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 10   | 10                        | 10                         | 10        | 10        | 10         | 10                 | 10                    | 10               | 10           | 10         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Day 7         |           |           |            |                    | Species : Rat         |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female (satellite)                          | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50551      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50552      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50553      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50554      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50555      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50556      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50557      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50558      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50559      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 50560      |   | 1    | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 10   | 10                        | 10                    | 10        | 10        | 10         | 10                 | 10                    | 10               | 10           | 10         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|--|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                              | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50651   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50652   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50653   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50654   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50655   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50656   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50657   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50658   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50659   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 9    | 9                         | 9  | 9         | 9         | 9          | 9                  | 9                     | 9                | 9            | 9             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Day 14        |           |           | Species : Rat |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|---------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female (satellite)                          | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation    | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50551      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50552      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50553      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50554      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50555      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50556      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50557      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50558      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50559      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50560      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 10   | 10                        | 10                    | 10        | 10        | 10            | 10                 | 10                    | 10               | 10           | 10         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|---|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                               | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50651   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50652   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50653   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50654   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50655   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50656   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50657   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50658   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50659   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 9    | 9                         | 9   | 9         | 9         | 9          | 9                  | 9                     | 9                | 9            | 9             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Day 21        |           |           | Species : Rat |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|---------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female (satellite)                          | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation    | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50551      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50552      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50553      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50554      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50555      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50556      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50557      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50558      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50559      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50560      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 10   | 10                        | 10                    | 10        | 10        | 10            | 10                 | 10                    | 10               | 10           | 10         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Day 21<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|---|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                               | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50651   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50652   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50653   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50654   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50655   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50656   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50657   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50658   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50659   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 9    | 9                         | 9   | 9         | 9         | 9          | 9                  | 9                     | 9                | 9            | 9             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Animal No. | Detailed clinical observation (in the open-field) |      |                           | Stage : Day 28        |           |           | Species : Rat |                    |                       |                  |              |            |
|------------|---|------|---------------------------|-----------------------|-----------|-----------|---------------|--------------------|-----------------------|------------------|--------------|------------|
|            | Sex : Female (satellite)                          | Gait | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation    | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| 50551      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50552      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50553      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50554      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50555      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50556      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50557      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50558      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50559      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| 50560      |   | 1    | 1                         | 1                     | 1         | 0         | 0             | 0                  | 0                     | 1                | 1            | 1          |
| n          |   | 10   | 10                        | 10                    | 10        | 10        | 10            | 10                 | 10                    | 10               | 10           | 10         |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Day 28<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|---|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                               | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50651   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50652   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50653   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50654   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50655   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50656   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50657   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50658   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50659   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 9    | 9                         | 9   | 9         | 9         | 9          | 9                  | 9                     | 9                | 9            | 9             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field) |   |   | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       | Species : Rat    |              |            |
|---|---|---|---|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
| Sex : Male  |   |   | Gait  | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| Animal No.  |   |   |   |                           |                       |           |           |            |                    |                       |                  |              |            |
| 10103   | 1 | 1 | 1   | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10104   | 1 | 1 | 1   | 1                         | 1                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10105   | 1 | 1 | 1   | 1                         | 0                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10106   | 1 | 1 | 1   | 1                         | 0                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10111   | 1 | 1 | 1   | 1                         | 0                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n   |   | 5 |   | 5                         |                       | 5         |           | 5          |                    | 5                     |                  | 5            |            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field) |      |                           | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |           |            |                    |                       |                  |              |            | Species : Rat |   |
|---|------|---------------------------|---|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|---------------|---|
| Sex : Male  |      |                           | Searching   | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |               |   |
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                                       |           |            |                    |                       |                  |              |            |               |   |
| 10402   | 1    | 1                         | 1   | 1         | 0          | 0                  | 0                     | 0                | 1            | 1          | 1             | 1 |
| 10403   | 1    | 1                         | 1   | 1         | 0          | 0                  | 0                     | 0                | 1            | 1          | 1             | 1 |
| 10407   | 1    | 1                         | 1   | 1         | 1          | 0                  | 0                     | 0                | 1            | 1          | 1             | 1 |
| 10409   | 1    | 1                         | 1   | 1         | 0          | 0                  | 0                     | 0                | 1            | 1          | 1             | 1 |
| 10411   | 1    | 1                         | 1   | 1         | 0          | 0                  | 0                     | 0                | 1            | 1          | 1             | 1 |
| n   | 5    | 5                         | 5   | 5         | 5          | 5                  | 5                     | 5                | 5            | 5          | 5             | 5 |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field) |   |   | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |                           |                       |           |           |            |                    |                       | Species : Rat    |              |            |
|---|---|---|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
| Sex : Male  |   |   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| Animal No.  |   |   |  |                           |                       |           |           |            |                    |                       |                  |              |            |
| 10103   | 1 | 1 | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10104   | 1 | 1 | 1  | 1                         | 1                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10105   | 1 | 1 | 1  | 1                         | 0                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10106   | 1 | 1 | 1  | 1                         | 0                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10111   | 1 | 1 | 1  | 1                         | 0                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n   | 5 | 5 | 5  | 5                         | 5                     | 5         | 5         | 5          | 5                  | 5                     | 5                | 5            | 5          |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field) |   |   | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |                           |                       |           |           |            |                    |                       | Species : Rat    |              |            |
|---|---|---|--|---------------------------|-----------------------|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|------------|
| Sex : Male  |   |   | Gait   | Co-ordination of movement | Reactivity to stimuli | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression |
| Animal No.  |   |   |  |                           |                       |           |           |            |                    |                       |                  |              |            |
| 10402   | 1 | 1 | 1  | 1                         | 1                     | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10403   | 1 | 1 | 1  | 1                         | 1                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10407   | 1 | 1 | 1  | 1                         | 1                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10409   | 1 | 1 | 1  | 1                         | 1                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| 10411   | 1 | 1 | 1  | 1                         | 1                     | 0         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1          |
| n   |   | 5 |  | 5                         |                       | 5         |           | 5          |                    | 5                     |                  | 5            |            |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 0 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|---|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                                     | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50556   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50557   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50558   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50559   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50560   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 5    | 5                         | 5   | 5         | 5         | 5          | 5                  | 5                     | 5                | 5            | 5             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Recovery Day 7<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|---|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                                       | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50656   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50657   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50658   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50659   | 1    | 1                         | 1   | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 4    | 4                         | 4   | 4         | 4         | 4          | 4                  | 4                     | 4                | 4            | 4             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 0 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|--|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli                                      | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50556   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50557   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50558   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50559   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50560   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 5    | 5                         | 5  | 5         | 5         | 5          | 5                  | 5                     | 5                | 5            | 5             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Detailed clinical observation (in the open-field)<br>Sex : Female (satellite) |      |                           | Stage : Recovery Day 14<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |            |                    |                       |                  |              | Species : Rat |  |
|---|------|---------------------------|--|-----------|-----------|------------|--------------------|-----------------------|------------------|--------------|---------------|--|
| Animal No.  | Gait | Co-ordination of movement | Reactivity to stimuli  | Searching | Urination | Defecation | Excessive grooming | Unusual head movement | Walking backward | Vocalization | Aggression    |  |
| 50656   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50657   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50658   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| 50659   | 1    | 1                         | 1  | 1         | 0         | 0          | 0                  | 0                     | 1                | 1            | 1             |  |
| n   | 4    | 4                         | 4  | 4         | 4         | 4          | 4                  | 4                     | 4                | 4            | 4             |  |

Gait) 0;Not moved, 1;Normal, 2; Difficult to walk, 3;Unable to walk, paralytic.

Co-ordination of movement) 0;Staggering (ataxic), 1;Normal.

Reactivity to stimuli) 0;Not present, 1;Present (to noise, etc.).

Searching) 0;Not present, 1;Present (sniffing, standing, etc.).

Urination) 0;Not present, 1;Present.

Defecation) 0;Not present, 1;Present.

Stereotype/Excessive grooming) 0;Not present, 1;Sometimes, 2;Frequently.

Stereotype/Unusual head movement) 0;Not present, 1;Sometimes, 2;Frequently.

Bizarre behavior/Walking backward) 1;Not present, 2;Present.

Bizarre behavior/Vocalization) 1;Not present, sometimes, 2;Present, frequently.

Aggression) 1;Not present, 2;Present.

| Functional observations (on the desk) |  | Stage : Week 4<br>Dose : PTSA Monohydrate 0 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|---|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Male                            |  | Visual reactivity                                 | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |   |                  |                     |                 |                           |                 |
| 10103                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10104                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10105                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10106                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10111                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5   | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Week 4<br>Dose : PTSA Monohydrate 50 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|--|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Male                            |  | Visual reactivity                                  | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |  |                  |                     |                 |                           |                 |
| 10202                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 10204                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 10207                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 10209                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 10210                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5  | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Week 4<br>Dose : PTSA Monohydrate 200 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|---|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Male                            |  | Visual reactivity                                   | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |   |                  |                     |                 |                           |                 |
| 10302                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10303                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10305                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10307                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10308                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5   | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Week 4<br>Dose : PTSA Monohydrate 800 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|---|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Male                            |  | Visual reactivity                                   | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |   |                  |                     |                 |                           |                 |
| 10402                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10403                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10407                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10409                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 10411                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5   | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |              | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 0 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--------------|--|------------------|---------------------|-----------------|---------------------------|-----------------|
|                                       | Sex : Female | Visual reactivity  | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |              |  |                  |                     |                 |                           |                 |
| 50151                                 |              | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50152                                 |              | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50153                                 |              | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50155                                 |              | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50161                                 |              | 4  | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |              | 5  | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 50 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|---|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Female                          |  | Visual reactivity   | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |   |                  |                     |                 |                           |                 |
| 50251                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 50252                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 50253                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 50256                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| 50258                                 |  | 4   | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5   | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 200 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|--|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Female                          |  | Visual reactivity  | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |  |                  |                     |                 |                           |                 |
| 50353                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50354                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50355                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50360                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50362                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5  | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 800 mg/kg |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|--|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Female                          |  | Visual reactivity  | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| Animal No.                            |  |  |                  |                     |                 |                           |                 |
| 50451                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50452                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50454                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50457                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| 50461                                 |  | 4  | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5  | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |                   |                  | Stage : Week 4                  |                 |                           | Species : Rat   |
|---------------------------------------|-------------------|------------------|---------------------------------|-----------------|---------------------------|-----------------|
| Sex : Female (satellite)              |                   |                  | Dose : PTSA Monohydrate 0 mg/kg |                 |                           |                 |
| Animal No.                            | Visual reactivity | Touch reactivity | Auditory reactivity             | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| 50556                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50557                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50558                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50559                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50560                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| n                                     | 5                 | 5                | 5                               | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |                   |                  | Stage : Week 4                    |                 |                           | Species : Rat   |
|---------------------------------------|-------------------|------------------|-----------------------------------|-----------------|---------------------------|-----------------|
| Sex : Female (satellite)              |                   |                  | Dose : PTSA Monohydrate 800 mg/kg |                 |                           |                 |
| Animal No.                            | Visual reactivity | Touch reactivity | Auditory reactivity               | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| 50656                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| 50657                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| 50658                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| 50659                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| n                                     | 4                 | 4                | 4                                 | 4               | 4                         | 4               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |  | Stage : Recovery Week 2         |                  |                     |                 |                           | Species : Rat   |
|---------------------------------------|--|---------------------------------|------------------|---------------------|-----------------|---------------------------|-----------------|
| Sex : Male                            |  | Dose : PTSA Monohydrate 0 mg/kg |                  |                     |                 |                           |                 |
| Animal No.                            |  | Visual reactivity               | Touch reactivity | Auditory reactivity | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| 10103                                 |  | 4                               | 2                | 1                   | 2               | 1                         | 1               |
| 10104                                 |  | 4                               | 2                | 1                   | 2               | 1                         | 1               |
| 10105                                 |  | 4                               | 2                | 1                   | 2               | 1                         | 1               |
| 10106                                 |  | 4                               | 2                | 1                   | 2               | 1                         | 1               |
| 10111                                 |  | 4                               | 2                | 1                   | 2               | 1                         | 1               |
| n                                     |  | 5                               | 5                | 5                   | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |                                   |                  | Stage : Recovery Week 2 |                 |                           | Species : Rat   |
|---------------------------------------|-----------------------------------|------------------|-------------------------|-----------------|---------------------------|-----------------|
| Sex : Male                            | Dose : PTSA Monohydrate 800 mg/kg |                  |                         |                 |                           |                 |
| Animal No.                            | Visual reactivity                 | Touch reactivity | Auditory reactivity     | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| 10402                                 | 4                                 | 2                | 1                       | 2               | 1                         | 1               |
| 10403                                 | 4                                 | 2                | 1                       | 2               | 1                         | 1               |
| 10407                                 | 4                                 | 2                | 1                       | 2               | 1                         | 1               |
| 10409                                 | 4                                 | 2                | 1                       | 2               | 1                         | 1               |
| 10411                                 | 4                                 | 2                | 1                       | 2               | 1                         | 1               |
| n                                     | 5                                 | 5                | 5                       | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |                   |                  | Stage : Recovery Week 2         |                 |                           | Species : Rat   |
|---------------------------------------|-------------------|------------------|---------------------------------|-----------------|---------------------------|-----------------|
| Sex : Female (satellite)              |                   |                  | Dose : PTSA Monohydrate 0 mg/kg |                 |                           |                 |
| Animal No.                            | Visual reactivity | Touch reactivity | Auditory reactivity             | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| 50556                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50557                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50558                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50559                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| 50560                                 | 4                 | 2                | 1                               | 2               | 1                         | 1               |
| n                                     | 5                 | 5                | 5                               | 5               | 5                         | 5               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Functional observations (on the desk) |                   |                  | Stage : Recovery Week 2           |                 |                           | Species : Rat   |
|---------------------------------------|-------------------|------------------|-----------------------------------|-----------------|---------------------------|-----------------|
| Sex : Female (satellite)              |                   |                  | Dose : PTSA Monohydrate 800 mg/kg |                 |                           |                 |
| Animal No.                            | Visual reactivity | Touch reactivity | Auditory reactivity               | Pain reactivity | Proprioceptive reactivity | Righting reflex |
| 50656                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| 50657                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| 50658                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| 50659                                 | 4                 | 2                | 1                                 | 2               | 1                         | 1               |
| n                                     | 4                 | 4                | 4                                 | 4               | 4                         | 4               |

Visual reactivity) 1;Jumping, 2;Turning away, 3;No reaction, 4;Approach, 5;Attack.

Touch reactivity) 1;Hyposensitive, 2;Turning away, 3;Hypersensitive.

Auditory reactivity) 0;No reaction, 1;Normal, moving the auricle, 2;Sensitive, moving the body, 3;Hypersensitive, surprising and jumping.

Pain reactivity) 0;No reaction, 1;Dull, vocalizing, 2;Normal, vocalizing and turning back, 3;Hypersensitive, attacking or jumping.

Proprioceptive reactivity) 0;No returning, 1;Returning.

Righting reflex) 1;Normal, landing by foot, 2;Abnormal, landing by body.

| Animal No. | Grip strength |               | Stage : Week 4                  |          |               |               | Species : Rat |        |
|------------|---------------|---------------|---------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Male    |               | Dose : PTSA Monohydrate 0 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                   | Forelimb |               |               |               |        |
| 10103      | g             | g             | g                               | g        | g             | g             | g             | g      |
| 10103      | 1756          | 1856          | 1262                            | 1624.7   | 850           | 813           | 768           | 810.3  |
| 10104      | 1663          | 1813          | 1790                            | 1755.3   | 779           | 620           | 587           | 662.0  |
| 10105      | 1588          | 1560          | 1621                            | 1589.7   | 761           | 764           | 705           | 743.3  |
| 10106      | 1622          | 1660          | 1368                            | 1550.0   | 570           | 711           | 641           | 640.7  |
| 10111      | 1403          | 1291          | 1639                            | 1444.3   | 749           | 839           | 859           | 815.7  |
| n          | 5             | 5             | 5                               | 5        | 5             | 5             | 5             | 5      |
| Mean       | 1606.4        | 1636.0        | 1536.0                          | 1592.80  | 741.8         | 749.4         | 712.0         | 734.40 |
| S.D.       | 129.9         | 226.4         | 215.4                           | 113.27   | 103.7         | 87.3          | 106.6         | 81.35  |

| Grip strength |        | Stage : Week 4                   |               |               |          |               |               | Species : Rat |          |
|---------------|--------|----------------------------------|---------------|---------------|----------|---------------|---------------|---------------|----------|
| Sex : Male    |        | Dose : PTSA Monohydrate 50 mg/kg |               |               |          |               |               |               |          |
|               |        | Forelimb, 1st                    | Forelimb, 2nd | Forelimb, 3rd | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd | Hindlimb |
| Animal No.    | g      | g                                | g             | g             | g        | g             | g             | g             | g        |
| 10202         | 1846   | 1567                             | 1732          | 1715.0        | 754      | 706           | 591           | 683.7         |          |
| 10204         | 1616   | 1568                             | 1667          | 1617.0        | 576      | 659           | 520           | 585.0         |          |
| 10207         | 1121   | 1065                             | 1026          | 1070.7        | 412      | 420           | 619           | 483.7         |          |
| 10209         | 1396   | 1570                             | 1450          | 1472.0        | 557      | 518           | 571           | 548.7         |          |
| 10210         | 1523   | 1712                             | 1644          | 1626.3        | 764      | 778           | 718           | 753.3         |          |
| n             | 5      | 5                                | 5             | 5             | 5        | 5             | 5             | 5             |          |
| Mean          | 1500.4 | 1496.4                           | 1503.8        | 1500.20       | 612.6    | 616.2         | 603.8         | 610.88        |          |
| S.D.          | 268.4  | 249.1                            | 287.0         | 255.42        | 148.0    | 145.1         | 73.4          | 107.58        |          |

| Animal No. | Grip strength |               | Stage : Week 4                    |          |               |               | Species : Rat |        |
|------------|---------------|---------------|-----------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Male    |               | Dose : PTSA Monohydrate 200 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                     | Forelimb |               |               |               |        |
| 10302      | g             | g             | g                                 | g        | g             | g             | g             | g      |
| 10302      | 1976          | 1973          | 1722                              | 1890.3   | 753           | 838           | 757           | 782.7  |
| 10303      | 1441          | 1244          | 1315                              | 1333.3   | 542           | 568           | 599           | 569.7  |
| 10305      | 1306          | 1531          | 1626                              | 1487.7   | 503           | 634           | 432           | 523.0  |
| 10307      | 1380          | 1437          | 1350                              | 1389.0   | 553           | 668           | 631           | 617.3  |
| 10308      | 1412          | 1215          | 1613                              | 1413.3   | 525           | 440           | 483           | 482.7  |
| n          | 5             | 5             | 5                                 | 5        | 5             | 5             | 5             | 5      |
| Mean       | 1503.0        | 1480.0        | 1525.2                            | 1502.72  | 575.2         | 629.6         | 580.4         | 595.08 |
| S.D.       | 269.2         | 305.5         | 181.3                             | 223.65   | 101.2         | 145.5         | 128.1         | 116.37 |

| Animal No. | Grip strength |               | Stage : Week 4 |          | Dose : PTSA Monohydrate 800 mg/kg |               | Species : Rat |          |
|------------|---------------|---------------|----------------|----------|-----------------------------------|---------------|---------------|----------|
|            | Sex : Male    |               | Forelimb       | Hindlimb | Hindlimb                          | Hindlimb      |               |          |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd  | Forelimb | Hindlimb, 1st                     | Hindlimb, 2nd | Hindlimb, 3rd | Hindlimb |
| 10402      | 1499          | 1444          | 1383           | 1442.0   | 571                               | 608           | 750           | 643.0    |
| 10403      | 1335          | 1390          | 1377           | 1367.3   | 458                               | 419           | 473           | 450.0    |
| 10407      | 1169          | 1251          | 1370           | 1263.3   | 548                               | 596           | 597           | 580.3    |
| 10409      | 1519          | 1609          | 1512           | 1546.7   | 681                               | 530           | 666           | 625.7    |
| 10411      | 1236          | 1339          | 1373           | 1316.0   | 485                               | 404           | 444           | 444.3    |
| n          | 5             | 5             | 5              | 5        | 5                                 | 5             | 5             | 5        |
| Mean       | 1351.6        | 1406.6        | 1403.0         | 1387.06  | 548.6                             | 511.4         | 586.0         | 548.66   |
| S.D.       | 155.5         | 133.6         | 61.1           | 110.97   | 87.0                              | 96.1          | 128.8         | 95.47    |

| Animal No. | Grip strength |        | Stage : Lactation Day 4 |          |          |          | Species : Rat |
|------------|---------------|--------|-------------------------|----------|----------|----------|---------------|
|            | Sex : Female  |        | Forelimb                | Forelimb | Hindlimb | Hindlimb |               |
|            | g             | g      | g                       | g        | g        | g        | g             |
| 50151      | 1161          | 1069   | 1116                    | 1115.3   | 533      | 535      | 534           |
| 50152      | 1090          | 1275   | 1053                    | 1139.3   | 385      | 394      | 398           |
| 50153      | 1396          | 1471   | 1082                    | 1316.3   | 502      | 582      | 506           |
| 50155      | 1183          | 993    | 1153                    | 1109.7   | 400      | 353      | 420           |
| 50161      | 1084          | 1104   | 937                     | 1041.7   | 564      | 502      | 542           |
| n          | 5             | 5      | 5                       | 5        | 5        | 5        | 5             |
| Mean       | 1182.8        | 1182.4 | 1068.2                  | 1144.46  | 476.8    | 473.2    | 480.0         |
| S.D.       | 126.8         | 191.5  | 82.3                    | 102.68   | 80.2     | 96.4     | 66.6          |
|            |               |        |                         |          |          |          | 77.63         |

| Animal No. | Grip strength |               | Stage : Lactation Day 4          |          |               |               | Species : Rat |        |
|------------|---------------|---------------|----------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Female  |               | Dose : PTSA Monohydrate 50 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                    | Forelimb |               |               |               |        |
| 50251      | g             | g             | g                                | g        | g             | g             | g             | g      |
| 50251      | 1401          | 1466          | 1532                             | 1466.3   | 572           | 420           | 588           | 526.7  |
| 50252      | 1365          | 1312          | 1402                             | 1359.7   | 676           | 631           | 668           | 658.3  |
| 50253      | 1453          | 1191          | 1400                             | 1348.0   | 431           | 587           | 493           | 503.7  |
| 50256      | 1038          | 1239          | 1116                             | 1131.0   | 467           | 590           | 458           | 505.0  |
| 50258      | 1420          | 1312          | 1306                             | 1346.0   | 449           | 435           | 450           | 444.7  |
| n          | 5             | 5             | 5                                | 5        | 5             | 5             | 5             | 5      |
| Mean       | 1335.4        | 1304.0        | 1351.2                           | 1330.20  | 519.0         | 532.6         | 531.4         | 527.68 |
| S.D.       | 169.3         | 104.1         | 154.1                            | 122.11   | 103.4         | 97.6          | 94.0          | 79.12  |

| Animal No. | Grip strength |               | Stage : Lactation Day 4           |          |               |               | Species : Rat |        |
|------------|---------------|---------------|-----------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Female  |               | Dose : PTSA Monohydrate 200 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                     | Forelimb |               |               |               |        |
| 50353      | 1247          | 1337          | 1217                              | 1267.0   | 444           | 423           | 409           | 425.3  |
| 50354      | 1118          | 966           | 1088                              | 1057.3   | 454           | 496           | 352           | 434.0  |
| 50355      | 997           | 985           | 1071                              | 1017.7   | 344           | 461           | 431           | 412.0  |
| 50360      | 816           | 915           | 969                               | 900.0    | 287           | 263           | 338           | 296.0  |
| 50362      | 1157          | 1228          | 1393                              | 1259.3   | 418           | 394           | 338           | 383.3  |
| n          | 5             | 5             | 5                                 | 5        | 5             | 5             | 5             | 5      |
| Mean       | 1067.0        | 1086.2        | 1147.6                            | 1100.26  | 389.4         | 407.4         | 373.6         | 390.12 |
| S.D.       | 166.6         | 185.1         | 163.1                             | 159.58   | 71.6          | 89.4          | 43.4          | 56.01  |

| Animal No. | Grip strength |               | Stage : Lactation Day 4           |          |               |               | Species : Rat |        |
|------------|---------------|---------------|-----------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Female  |               | Dose : PTSA Monohydrate 800 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                     | Forelimb |               |               |               |        |
| 50451      | 1363          | 1407          | 1465                              | 1411.7   | 394           | 360           | 564           | 439.3  |
| 50452      | 1246          | 1258          | 1410                              | 1304.7   | 441           | 388           | 455           | 428.0  |
| 50454      | 1251          | 1011          | 1028                              | 1096.7   | 558           | 504           | 507           | 523.0  |
| 50457      | 999           | 1314          | 1433                              | 1248.7   | 400           | 407           | 526           | 444.3  |
| 50461      | 1214          | 1288          | 1026                              | 1176.0   | 572           | 458           | 543           | 524.3  |
| n          | 5             | 5             | 5                                 | 5        | 5             | 5             | 5             | 5      |
| Mean       | 1214.6        | 1255.6        | 1272.4                            | 1247.56  | 473.0         | 423.4         | 519.0         | 471.78 |
| S.D.       | 133.1         | 147.7         | 224.9                             | 120.51   | 86.1          | 57.5          | 41.5          | 47.72  |

| Animal No. | Grip strength            |        | Stage : Week 4 |               | Dose : PTSA Monohydrate 0 mg/kg |          | Species : Rat |               |               |
|------------|--------------------------|--------|----------------|---------------|---------------------------------|----------|---------------|---------------|---------------|
|            | Sex : Female (satellite) |        | Forelimb, 1st  | Forelimb, 2nd | Forelimb, 3rd                   | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |
|            | g                        | g      | g              | g             | g                               | g        | g             | g             | g             |
| 50556      | 959                      | 864    | 1056           | 959.7         | 516                             | 440      | 393           | 449.7         |               |
| 50557      | 1142                     | 1075   | 780            | 999.0         | 485                             | 393      | 435           | 437.7         |               |
| 50558      | 1103                     | 940    | 1306           | 1116.3        | 455                             | 401      | 394           | 416.7         |               |
| 50559      | 1047                     | 1187   | 1311           | 1181.7        | 347                             | 492      | 469           | 436.0         |               |
| 50560      | 1012                     | 1135   | 1037           | 1061.3        | 541                             | 402      | 393           | 445.3         |               |
| n          | 5                        | 5      | 5              | 5             | 5                               | 5        | 5             | 5             | 5             |
| Mean       | 1052.6                   | 1040.2 | 1098.0         | 1063.60       | 468.8                           | 425.6    | 416.8         | 437.08        |               |
| S.D.       | 72.4                     | 134.9  | 220.9          | 89.02         | 75.4                            | 41.4     | 34.3          | 12.69         |               |

| Grip strength            |  | Stage : Week 4 |               |               |          |               |               | Species : Rat |          |  |
|--------------------------|--|----------------|---------------|---------------|----------|---------------|---------------|---------------|----------|--|
| Sex : Female (satellite) |  | Forelimb, 1st  | Forelimb, 2nd | Forelimb, 3rd | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd | Hindlimb |  |
| Animal No.               |  | g              | g             | g             | g        | g             | g             | g             | g        |  |
| 50656                    |  | 1134           | 1107          | 1396          | 1212.3   | 467           | 489           | 578           | 511.3    |  |
| 50657                    |  | 990            | 1009          | 1137          | 1045.3   | 420           | 465           | 619           | 501.3    |  |
| 50658                    |  | 984            | 1134          | 1015          | 1044.3   | 397           | 319           | 369           | 361.7    |  |
| 50659                    |  | 1047           | 954           | 1140          | 1047.0   | 416           | 441           | 402           | 419.7    |  |
| n                        |  | 4              | 4             | 4             | 4        | 4             | 4             | 4             | 4        |  |
| Mean                     |  | 1038.8         | 1051.0        | 1172.0        | 1087.23  | 425.0         | 428.5         | 492.0         | 448.50   |  |
| S.D.                     |  | 69.6           | 84.1          | 160.3         | 83.39    | 29.7          | 75.6          | 124.8         | 70.94    |  |

| Animal No. | Grip strength |               | Stage : Recovery Week 2         |          |               |               | Species : Rat |          |
|------------|---------------|---------------|---------------------------------|----------|---------------|---------------|---------------|----------|
|            | Sex : Male    |               | Dose : PTSA Monohydrate 0 mg/kg |          |               |               |               |          |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                   | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd | Hindlimb |
| 10103      | g             | g             | g                               | g        | g             | g             | g             | g        |
| 10103      | 1603          | 1491          | 1587                            | 1560.3   | 601           | 693           | 653           | 649.0    |
| 10104      | 1883          | 1974          | 1657                            | 1838.0   | 627           | 507           | 651           | 595.0    |
| 10105      | 1600          | 1633          | 1769                            | 1667.3   | 635           | 569           | 734           | 646.0    |
| 10106      | 2054          | 1900          | 1783                            | 1912.3   | 719           | 708           | 709           | 712.0    |
| 10111      | 1730          | 1610          | 1240                            | 1526.7   | 790           | 675           | 898           | 787.7    |
| n          | 5             | 5             | 5                               | 5        | 5             | 5             | 5             | 5        |
| Mean       | 1774.0        | 1721.6        | 1607.2                          | 1700.92  | 674.4         | 630.4         | 729.0         | 677.94   |
| S.D.       | 194.8         | 205.6         | 220.7                           | 169.36   | 78.3          | 87.9          | 101.1         | 74.07    |

| Animal No. | Grip strength |               | Stage : Recovery Week 2           |          |               |               | Species : Rat |        |
|------------|---------------|---------------|-----------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Male    |               | Dose : PTSA Monohydrate 800 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd                     | Forelimb |               |               |               |        |
| 10402      | g             | g             | g                                 | g        | g             | g             | g             | g      |
| 10402      | 1755          | 1883          | 1922                              | 1853.3   | 506           | 549           | 523           | 526.0  |
| 10403      | 1383          | 1519          | 1733                              | 1545.0   | 563           | 572           | 478           | 537.7  |
| 10407      | 1494          | 1465          | 1664                              | 1541.0   | 453           | 567           | 539           | 519.7  |
| 10409      | 1793          | 1896          | 1862                              | 1850.3   | 787           | 892           | 810           | 829.7  |
| 10411      | 1522          | 1384          | 1325                              | 1410.3   | 306           | 324           | 397           | 342.3  |
| n          | 5             | 5             | 5                                 | 5        | 5             | 5             | 5             | 5      |
| Mean       | 1589.4        | 1629.4        | 1701.2                            | 1639.98  | 523.0         | 580.8         | 549.4         | 551.08 |
| S.D.       | 176.9         | 242.3         | 233.7                             | 200.82   | 175.8         | 202.5         | 155.8         | 175.36 |

| Animal No. | Grip strength |               | Stage : Recovery Week 2 |          |               |               | Species : Rat |          |
|------------|---------------|---------------|-------------------------|----------|---------------|---------------|---------------|----------|
|            | Forelimb, 1st | Forelimb, 2nd | Forelimb, 3rd           | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd | Hindlimb |
| 50556      | 1115          | 1031          | 1218                    | 1121.3   | 400           | 479           | 521           | 466.7    |
| 50557      | 965           | 1147          | 1065                    | 1059.0   | 592           | 448           | 547           | 529.0    |
| 50558      | 1462          | 1328          | 1431                    | 1407.0   | 452           | 453           | 481           | 462.0    |
| 50559      | 1148          | 1199          | 1106                    | 1151.0   | 455           | 325           | 529           | 436.3    |
| 50560      | 911           | 1106          | 1118                    | 1045.0   | 414           | 434           | 430           | 426.0    |
| n          | 5             | 5             | 5                       | 5        | 5             | 5             | 5             | 5        |
| Mean       | 1120.2        | 1162.2        | 1187.6                  | 1156.66  | 462.6         | 427.8         | 501.6         | 464.00   |
| S.D.       | 215.3         | 111.2         | 147.2                   | 146.59   | 76.1          | 59.7          | 46.7          | 40.15    |

| Animal No. | Grip strength            |               | Stage : Recovery Week 2           |          |               |               | Species : Rat |        |
|------------|--------------------------|---------------|-----------------------------------|----------|---------------|---------------|---------------|--------|
|            | Sex : Female (satellite) |               | Dose : PTSA Monohydrate 800 mg/kg | Forelimb | Hindlimb, 1st | Hindlimb, 2nd | Hindlimb, 3rd |        |
|            | Forelimb, 1st            | Forelimb, 2nd | Forelimb, 3rd                     | Forelimb |               |               |               |        |
| 50656      | g                        | g             | g                                 | g        | g             | g             | g             | g      |
| 50656      | 1624                     | 1645          | 1381                              | 1550.0   | 524           | 580           | 608           | 570.7  |
| 50657      | 1326                     | 1324          | 1365                              | 1338.3   | 479           | 493           | 565           | 512.3  |
| 50658      | 1425                     | 1250          | 1299                              | 1324.7   | 383           | 443           | 442           | 422.7  |
| 50659      | 1357                     | 1324          | 1314                              | 1331.7   | 423           | 345           | 449           | 405.7  |
| n          | 4                        | 4             | 4                                 | 4        | 4             | 4             | 4             | 4      |
| Mean       | 1433.0                   | 1385.8        | 1339.8                            | 1386.18  | 452.3         | 465.3         | 516.0         | 477.85 |
| S.D.       | 133.9                    | 176.3         | 39.4                              | 109.36   | 62.0          | 98.1          | 83.3          | 77.58  |

| Motor activity measurements |       | Stage : Week 4                  |           |           |           |           |           | Species : Rat |  |
|-----------------------------|-------|---------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Male                  |       | Dose : PTSA Monohydrate 0 mg/kg |           |           |           |           |           |               |  |
|                             |       | 0' - 10'                        | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.   | No.                             | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 10103                       | 568   | 360                             | 90        | 23        | 115       | 61        | 1217      |               |  |
| 10104                       | 557   | 464                             | 284       | 343       | 192       | 119       | 1959      |               |  |
| 10105                       | 517   | 449                             | 310       | 151       | 228       | 208       | 1863      |               |  |
| 10106                       | 696   | 510                             | 323       | 406       | 338       | 152       | 2425      |               |  |
| 10111                       | 177   | 291                             | 147       | 156       | 106       | 109       | 986       |               |  |
| n                           | 5     | 5                               | 5         | 5         | 5         | 5         | 5         |               |  |
| Mean                        | 503.0 | 414.8                           | 230.8     | 215.8     | 195.8     | 129.8     | 1690.0    |               |  |
| S.D.                        | 194.2 | 88.0                            | 105.4     | 156.0     | 94.7      | 54.5      | 583.5     |               |  |

| Motor activity measurements |       | Stage : Week 4<br>Dose : PTSA Monohydrate 50 mg/kg |           |           |           |           |           | Species : Rat |
|-----------------------------|-------|--|-----------|-----------|-----------|-----------|-----------|---------------|
| Sex : Male                  |       | 0' - 10'   | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |
| Animal No.                  | No.   | No.  | No.       | No.       | No.       | No.       | No.       |               |
| 10202                       | 461   | 304  | 197       | 330       | 436       | 304       | 2032      |               |
| 10204                       | 347   | 312  | 263       | 277       | 199       | 121       | 1519      |               |
| 10207                       | 578   | 424  | 227       | 136       | 82        | 220       | 1667      |               |
| 10209                       | 1005  | 1122   | 452       | 153       | 0         | 0         | 2732      |               |
| 10210                       | 987   | 726  | 650       | 404       | 351       | 234       | 3352      |               |
| n                           | 5     | 5  | 5         | 5         | 5         | 5         | 5         |               |
| Mean                        | 675.6 | 577.6  | 357.8     | 260.0     | 213.6     | 175.8     | 2260.4    |               |
| S.D.                        | 303.7 | 349.1  | 191.2     | 114.8     | 181.3     | 118.0     | 769.4     |               |

| Motor activity measurements |       | Stage : Week 4                    |           |           |           |           |           | Species : Rat |  |
|-----------------------------|-------|-----------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Male                  |       | Dose : PTSA Monohydrate 200 mg/kg |           |           |           |           |           |               |  |
|                             |       | 0' - 10'                          | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.   | No.                               | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 10302                       | 751   | 530                               | 226       | 209       | 208       | 249       | 2173      |               |  |
| 10303                       | 748   | 405                               | 261       | 178       | 88        | 78        | 1758      |               |  |
| 10305                       | 315   | 141                               | 104       | 70        | 54        | 9         | 693       |               |  |
| 10307                       | 658   | 543                               | 442       | 455       | 438       | 239       | 2775      |               |  |
| 10308                       | 627   | 500                               | 406       | 167       | 51        | 3         | 1754      |               |  |
| n                           | 5     | 5                                 | 5         | 5         | 5         | 5         | 5         |               |  |
| Mean                        | 619.8 | 423.8                             | 287.8     | 215.8     | 167.8     | 115.6     | 1830.6    |               |  |
| S.D.                        | 178.9 | 167.0                             | 137.9     | 143.5     | 164.0     | 120.9     | 760.7     |               |  |

| Motor activity measurements |       | Stage : Week 4                    |           |           |           |           |           | Species : Rat |  |
|-----------------------------|-------|-----------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Male                  |       | Dose : PTSA Monohydrate 800 mg/kg |           |           |           |           |           |               |  |
|                             |       | 0' - 10'                          | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.   | No.                               | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 10402                       | 1078  | 572                               | 464       | 264       | 208       | 250       | 2836      |               |  |
| 10403                       | 684   | 583                               | 332       | 430       | 537       | 292       | 2858      |               |  |
| 10407                       | 560   | 531                               | 581       | 401       | 457       | 192       | 2722      |               |  |
| 10409                       | 116   | 0                                 | 0         | 0         | 0         | 0         | 116       |               |  |
| 10411                       | 363   | 319                               | 240       | 131       | 110       | 198       | 1361      |               |  |
| n                           | 5     | 5                                 | 5         | 5         | 5         | 5         | 5         |               |  |
| Mean                        | 560.2 | 401.0                             | 323.4     | 245.2     | 262.4     | 186.4     | 1978.6    |               |  |
| S.D.                        | 360.4 | 248.4                             | 222.3     | 181.6     | 228.2     | 111.9     | 1215.7    |               |  |

| Motor activity measurements |       | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 0 mg/kg |           |           |           |           |           | Species : Rat |
|-----------------------------|-------|--|-----------|-----------|-----------|-----------|-----------|---------------|
| Sex : Female                |       | 0' - 10'   | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |
| Animal No.                  | No.   | No.  | No.       | No.       | No.       | No.       | No.       |               |
| 50151                       | 877   | 747  | 219       | 653       | 640       | 831       | 3967      |               |
| 50152                       | 714   | 226  | 2         | 0         | 0         | 0         | 942       |               |
| 50153                       | 456   | 115  | 43        | 3         | 0         | 0         | 617       |               |
| 50155                       | 69    | 0  | 124       | 6         | 0         | 0         | 199       |               |
| 50161                       | 582   | 165  | 387       | 302       | 72        | 9         | 1517      |               |
| n                           | 5     | 5  | 5         | 5         | 5         | 5         | 5         |               |
| Mean                        | 539.6 | 250.6  | 155.0     | 192.8     | 142.4     | 168.0     | 1448.4    |               |
| S.D.                        | 306.0 | 289.6  | 154.0     | 288.0     | 279.9     | 370.6     | 1488.0    |               |

| Motor activity measurements |       | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 50 mg/kg |           |           |           |           |           | Species : Rat |
|-----------------------------|-------|---|-----------|-----------|-----------|-----------|-----------|---------------|
| Sex : Female                |       | 0' - 10'  | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |
| Animal No.                  | No.   | No.   | No.       | No.       | No.       | No.       | No.       |               |
| 50251                       | 868   | 352   | 0         | 217       | 6         | 0         | 1443      |               |
| 50252                       | 353   | 162   | 4         | 155       | 342       | 8         | 1024      |               |
| 50253                       | 703   | 664   | 424       | 9         | 192       | 501       | 2493      |               |
| 50256                       | 980   | 441   | 55        | 0         | 0         | 0         | 1476      |               |
| 50258                       | 884   | 401   | 86        | 5         | 0         | 0         | 1376      |               |
| n                           | 5     | 5   | 5         | 5         | 5         | 5         | 5         |               |
| Mean                        | 757.6 | 404.0   | 113.8     | 77.2      | 108.0     | 101.8     | 1562.4    |               |
| S.D.                        | 247.1 | 180.4   | 177.1     | 101.8     | 154.6     | 223.2     | 550.5     |               |

| Motor activity measurements |       | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 200 mg/kg |           |           |           |           |           | Species : Rat |
|-----------------------------|-------|--|-----------|-----------|-----------|-----------|-----------|---------------|
| Sex : Female                |       | 0' - 10'   | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |
| Animal No.                  | No.   | No.  | No.       | No.       | No.       | No.       | No.       |               |
| 50353                       | 689   | 643  | 124       | 54        | 0         | 27        | 1537      |               |
| 50354                       | 408   | 145  | 157       | 288       | 288       | 371       | 1657      |               |
| 50355                       | 876   | 386  | 296       | 0         | 0         | 1         | 1559      |               |
| 50360                       | 444   | 76   | 121       | 4         | 0         | 0         | 645       |               |
| 50362                       | 396   | 206  | 40        | 7         | 0         | 0         | 649       |               |
| n                           | 5     | 5  | 5         | 5         | 5         | 5         | 5         |               |
| Mean                        | 562.6 | 291.2  | 147.6     | 70.6      | 57.6      | 79.8      | 1209.4    |               |
| S.D.                        | 212.1 | 227.9  | 93.5      | 123.5     | 128.8     | 163.2     | 515.4     |               |

| Motor activity measurements |       | Stage : Lactation Day 4<br>Dose : PTSA Monohydrate 800 mg/kg |           |           |           |           |           | Species : Rat |
|-----------------------------|-------|--|-----------|-----------|-----------|-----------|-----------|---------------|
| Sex : Female                |       | 0' - 10'   | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |
| Animal No.                  | No.   | No.  | No.       | No.       | No.       | No.       | No.       |               |
| 50451                       | 1008  | 639  | 939       | 804       | 215       | 559       | 4164      |               |
| 50452                       | 323   | 0  | 0         | 45        | 2         | 0         | 370       |               |
| 50454                       | 405   | 109  | 138       | 54        | 0         | 12        | 718       |               |
| 50457                       | 587   | 279  | 248       | 630       | 20        | 0         | 1764      |               |
| 50461                       | 1140  | 117  | 0         | 0         | 214       | 208       | 1679      |               |
| n                           | 5     | 5  | 5         | 5         | 5         | 5         | 5         |               |
| Mean                        | 692.6 | 228.8  | 265.0     | 306.6     | 90.2      | 155.8     | 1739.0    |               |
| S.D.                        | 364.0 | 250.0  | 390.9     | 380.2     | 113.7     | 242.1     | 1483.4    |               |

| Motor activity measurements |          |           |           |           |           |           |          | Species : Rat |  |
|-----------------------------|----------|-----------|-----------|-----------|-----------|-----------|----------|---------------|--|
| Sex : Female (satellite)    |          |           |           |           |           |           |          |               |  |
|                             | 0' - 10' | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60' |               |  |
| Animal No.                  | No.      | No.       | No.       | No.       | No.       | No.       | No.      |               |  |
| 50556                       | 1301     | 1012      | 786       | 226       | 505       | 494       | 4324     |               |  |
| 50557                       | 1022     | 848       | 825       | 324       | 165       | 482       | 3666     |               |  |
| 50558                       | 1049     | 719       | 528       | 368       | 101       | 32        | 2797     |               |  |
| 50559                       | 1388     | 1042      | 613       | 363       | 215       | 0         | 3621     |               |  |
| 50560                       | 561      | 387       | 364       | 65        | 130       | 101       | 1608     |               |  |
| n                           | 5        | 5         | 5         | 5         | 5         | 5         | 5        |               |  |
| Mean                        | 1064.2   | 801.6     | 623.2     | 269.2     | 223.2     | 221.8     | 3203.2   |               |  |
| S.D.                        | 322.5    | 266.0     | 189.5     | 127.6     | 163.2     | 245.8     | 1043.4   |               |  |

| Motor activity measurements |        | Stage : Week 4                    |           |           |           |           |           | Species : Rat |  |
|-----------------------------|--------|-----------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Female (satellite)    |        | Dose : PTSA Monohydrate 800 mg/kg |           |           |           |           |           |               |  |
|                             |        | 0' - 10'                          | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.    | No.                               | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 50656                       | 589    | 432                               | 770       | 750       | 549       | 289       | 3379      |               |  |
| 50657                       | 1258   | 1004                              | 1059      | 1141      | 519       | 827       | 5808      |               |  |
| 50658                       | 1335   | 889                               | 1011      | 740       | 1090      | 626       | 5691      |               |  |
| 50659                       | 1376   | 891                               | 869       | 823       | 994       | 604       | 5557      |               |  |
| n                           | 4      | 4                                 | 4         | 4         | 4         | 4         | 4         |               |  |
| Mean                        | 1139.5 | 804.0                             | 927.3     | 863.5     | 788.0     | 586.5     | 5108.8    |               |  |
| S.D.                        | 370.2  | 253.8                             | 132.3     | 188.7     | 296.2     | 222.3     | 1157.7    |               |  |

| Motor activity measurements |       | Stage : Recovery Week 2         |           |           |           |           |           | Species : Rat |  |
|-----------------------------|-------|---------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Male                  |       | Dose : PTSA Monohydrate 0 mg/kg |           |           |           |           |           |               |  |
|                             |       | 0' - 10'                        | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.   | No.                             | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 10103                       | 589   | 293                             | 168       | 15        | 205       | 181       | 1451      |               |  |
| 10104                       | 1218  | 489                             | 574       | 403       | 345       | 164       | 3193      |               |  |
| 10105                       | 665   | 435                             | 317       | 123       | 116       | 251       | 1907      |               |  |
| 10106                       | 698   | 546                             | 511       | 309       | 255       | 169       | 2488      |               |  |
| 10111                       | 476   | 425                             | 407       | 296       | 380       | 162       | 2146      |               |  |
| n                           | 5     | 5                               | 5         | 5         | 5         | 5         | 5         |               |  |
| Mean                        | 729.2 | 437.6                           | 395.4     | 229.2     | 260.2     | 185.4     | 2237.0    |               |  |
| S.D.                        | 286.3 | 94.2                            | 160.7     | 156.7     | 106.5     | 37.4      | 654.2     |               |  |

| Motor activity measurements |       | Stage : Recovery Week 2           |           |           |           |           |           | Species : Rat |  |
|-----------------------------|-------|-----------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Male                  |       | Dose : PTSA Monohydrate 800 mg/kg |           |           |           |           |           |               |  |
|                             |       | 0' - 10'                          | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.   | No.                               | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 10402                       | 834   | 384                               | 349       | 191       | 291       | 186       | 2235      |               |  |
| 10403                       | 970   | 665                               | 420       | 608       | 437       | 76        | 3176      |               |  |
| 10407                       | 1132  | 861                               | 698       | 684       | 490       | 406       | 4271      |               |  |
| 10409                       | 1109  | 707                               | 596       | 163       | 395       | 43        | 3013      |               |  |
| 10411                       | 344   | 193                               | 163       | 241       | 85        | 165       | 1191      |               |  |
| n                           | 5     | 5                                 | 5         | 5         | 5         | 5         | 5         |               |  |
| Mean                        | 877.8 | 562.0                             | 445.2     | 377.4     | 339.6     | 175.2     | 2777.2    |               |  |
| S.D.                        | 321.5 | 268.7                             | 209.9     | 248.2     | 160.0     | 142.1     | 1146.3    |               |  |

| Motor activity measurements |       | Stage : Recovery Week 2         |           |           |           |           |           | Species : Rat |  |
|-----------------------------|-------|---------------------------------|-----------|-----------|-----------|-----------|-----------|---------------|--|
| Sex : Female (satellite)    |       | Dose : PTSA Monohydrate 0 mg/kg |           |           |           |           |           |               |  |
|                             |       | 0' - 10'                        | 10' - 20' | 20' - 30' | 30' - 40' | 40' - 50' | 50' - 60' | 0' - 60'      |  |
| Animal No.                  | No.   | No.                             | No.       | No.       | No.       | No.       | No.       | No.           |  |
| 50556                       | 780   | 797                             | 559       | 498       | 373       | 65        | 3072      |               |  |
| 50557                       | 580   | 709                             | 652       | 416       | 357       | 0         | 2714      |               |  |
| 50558                       | 806   | 445                             | 302       | 121       | 204       | 266       | 2144      |               |  |
| 50559                       | 1444  | 1138                            | 787       | 224       | 30        | 130       | 3753      |               |  |
| 50560                       | 510   | 368                             | 218       | 221       | 100       | 101       | 1518      |               |  |
| n                           | 5     | 5                               | 5         | 5         | 5         | 5         | 5         |               |  |
| Mean                        | 824.0 | 691.4                           | 503.6     | 296.0     | 212.8     | 112.4     | 2640.2    |               |  |
| S.D.                        | 369.1 | 306.7                           | 238.5     | 155.4     | 152.2     | 98.6      | 856.7     |               |  |

| Motor activity measurements       |       |           |       |           |       |           |        | Species : Rat           |
|-----------------------------------|-------|-----------|-------|-----------|-------|-----------|--------|-------------------------|
| Sex : Female (satellite)          |       |           |       |           |       |           |        |                         |
| 0' - 10'                          |       | 10' - 20' |       | 20' - 30' |       | 30' - 40' |        | Stage : Recovery Week 2 |
| Dose : PTSA Monohydrate 800 mg/kg |       | 40' - 50' |       | 50' - 60' |       | 0' - 60'  |        |                         |
| Animal No.                        | No.   | No.       | No.   | No.       | No.   | No.       | No.    |                         |
| 50656                             | 652   | 655       | 178   | 399       | 4     | 0         | 1888   |                         |
| 50657                             | 1054  | 955       | 411   | 305       | 308   | 230       | 3263   |                         |
| 50658                             | 563   | 551       | 457   | 253       | 203   | 321       | 2348   |                         |
| 50659                             | 729   | 556       | 457   | 226       | 257   | 93        | 2318   |                         |
| n                                 | 4     | 4         | 4     | 4         | 4     | 4         | 4      |                         |
| Mean                              | 749.5 | 679.3     | 375.8 | 295.8     | 193.0 | 161.0     | 2454.3 |                         |
| S.D.                              | 214.0 | 190.0     | 133.6 | 76.2      | 133.1 | 142.5     | 578.7  |                         |

| Animal No. | Body weight<br>Sex : Male<br>/Day |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 0 mg/kg |       |       |       |                     | Unit : g | Species : Rat |
|------------|-----------------------------------|-------|---|-------|-------|-------|---------------------|----------|---------------|
|            | 1                                 | 4     | 7   | 14    | 21    | 28    | Body weight<br>gain |          |               |
| 10101      | 388                               | 392   | 398   | 408   | 426   | 446   | 58                  |          |               |
| 10102      | 392                               | 410   | 427   | 453   | 485   | 521   | 129                 |          |               |
| 10103      | 405                               | 420   | 434   | 453   | 480   | 500   | 95                  |          |               |
| 10104      | 378                               | 383   | 392   | 412   | 436   | 447   | 69                  |          |               |
| 10105      | 388                               | 407   | 421   | 449   | 483   | 508   | 120                 |          |               |
| 10106      | 372                               | 388   | 411   | 444   | 471   | 496   | 124                 |          |               |
| 10107      | 425                               | 444   | 462   | 485   | 507   | 551   | 126                 |          |               |
| 10108      | 363                               | 375   | 379   | 395   | 403   | 424   | 61                  |          |               |
| 10109      | 420                               | 440   | 458   | 499   | 524   | 561   | 141                 |          |               |
| 10110      | 379                               | 386   | 390   | 411   | 440   | 450   | 71                  |          |               |
| 10111      | 396                               | 416   | 427   | 448   | 468   | 481   | 85                  |          |               |
| 10112      | 400                               | 414   | 425   | 457   | 489   | 519   | 119                 |          |               |
| n          | 12                                | 12    | 12  | 12    | 12    | 12    | 12                  |          |               |
| Mean       | 392.2                             | 406.3 | 418.7   | 442.8 | 467.7 | 492.0 | 99.8                |          |               |
| S.D.       | 18.5                              | 22.1  | 26.0  | 31.4  | 35.1  | 43.5  | 30.0                |          |               |

| Animal No. | Body weight<br>Sex : Male<br>/Day |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 50 mg/kg |       |       |       |                     | Unit : g | Species : Rat |
|------------|-----------------------------------|-------|--|-------|-------|-------|---------------------|----------|---------------|
|            | 1                                 | 4     | 7  | 14    | 21    | 28    | Body weight<br>gain |          |               |
| 10201      | 373                               | 371   | 379  | 396   | 423   | 445   | 72                  |          |               |
| 10202      | 385                               | 399   | 410  | 440   | 466   | 485   | 100                 |          |               |
| 10203      | 370                               | 379   | 392  | 416   | 437   | 460   | 90                  |          |               |
| 10204      | 408                               | 422   | 434  | 450   | 476   | 483   | 75                  |          |               |
| 10205      | 415                               | 429   | 442  | 466   | 489   | 497   | 82                  |          |               |
| 10206      | 385                               | 392   | 406  | 419   | 442   | 459   | 74                  |          |               |
| 10207      | 411                               | 428   | 444  | 462   | 482   | 492   | 81                  |          |               |
| 10208      | 396                               | 407   | 418  | 432   | 443   | 454   | 58                  |          |               |
| 10209      | 383                               | 401   | 413  | 441   | 462   | 488   | 105                 |          |               |
| 10210      | 397                               | 406   | 418  | 436   | 465   | 477   | 80                  |          |               |
| 10211      | 430                               | 442   | 458  | 477   | 519   | 544   | 114                 |          |               |
| 10212      | 396                               | 403   | 414  | 429   | 460   | 481   | 85                  |          |               |
| n          | 12                                | 12    | 12   | 12    | 12    | 12    | 12                  |          |               |
| Mean       | 395.8                             | 406.6 | 419.0  | 438.7 | 463.7 | 480.4 | 84.7                |          |               |
| S.D.       | 17.8                              | 20.9  | 22.4   | 22.9  | 26.1  | 25.9  | 15.5                |          |               |

| Animal No. | Body weight<br>Sex : Male<br>/Day |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 200 mg/kg |       |       |       |                     | Unit : g | Species : Rat |
|------------|-----------------------------------|-------|---|-------|-------|-------|---------------------|----------|---------------|
|            | 1                                 | 4     | 7   | 14    | 21    | 28    | Body weight<br>gain |          |               |
| 10301      | 398                               | 417   | 431   | 467   | 486   | 507   | 109                 |          |               |
| 10302      | 372                               | 382   | 400   | 426   | 442   | 454   | 82                  |          |               |
| 10303      | 402                               | 408   | 422   | 442   | 467   | 487   | 85                  |          |               |
| 10304      | 367                               | 380   | 393   | 409   | 437   | 455   | 88                  |          |               |
| 10305      | 398                               | 415   | 428   | 450   | 482   | 500   | 102                 |          |               |
| 10306      | 429                               | 443   | 455   | 485   | 508   | 540   | 111                 |          |               |
| 10307      | 404                               | 419   | 438   | 462   | 488   | 502   | 98                  |          |               |
| 10308      | 381                               | 386   | 401   | 421   | 444   | 464   | 83                  |          |               |
| 10309      | 422                               | 440   | 462   | 496   | 521   | 548   | 126                 |          |               |
| 10310      | 375                               | 384   | 393   | 419   | 436   | 459   | 84                  |          |               |
| 10311      | 415                               | 425   | 440   | 468   | 495   | 524   | 109                 |          |               |
| 10312      | 411                               | 430   | 445   | 476   | 516   | 539   | 128                 |          |               |
| n          | 12                                | 12    | 12  | 12    | 12    | 12    | 12                  |          |               |
| Mean       | 397.8                             | 410.8 | 425.7   | 451.8 | 476.8 | 498.3 | 100.4               |          |               |
| S.D.       | 20.2                              | 22.8  | 24.0  | 28.4  | 31.1  | 34.8  | 16.5                |          |               |

| Animal No. | Body weight<br>Sex : Male<br>/Day |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 800 mg/kg |       |       |       |                     | Unit : g | Species : Rat |
|------------|-----------------------------------|-------|---|-------|-------|-------|---------------------|----------|---------------|
|            | 1                                 | 4     | 7   | 14    | 21    | 28    | Body weight<br>gain |          |               |
| 10401      | 395                               | 398   | 405   | 421   | 439   | 466   | 71                  |          |               |
| 10402      | 400                               | 409   | 421   | 455   | 475   | 487   | 87                  |          |               |
| 10403      | 409                               | 418   | 428   | 445   | 461   | 469   | 60                  |          |               |
| 10404      | 367                               | 375   | 391   | 405   | 423   | 449   | 82                  |          |               |
| 10405      | 383                               | 398   | 407   | 419   | 441   | 463   | 80                  |          |               |
| 10406      | 428                               | 442   | 458   | 486   | 487   | 517   | 89                  |          |               |
| 10407      | 390                               | 410   | 425   | 456   | 474   | 483   | 93                  |          |               |
| 10408      | 379                               | 391   | 403   | 422   | 435   | 443   | 64                  |          |               |
| 10409      | 376                               | 390   | 410   | 431   | 449   | 446   | 70                  |          |               |
| 10410      | 356                               | 345   | 370   | 398   | 412   | 434   | 78                  |          |               |
| 10411      | 410                               | 425   | 444   | 465   | 478   | 506   | 96                  |          |               |
| 10412      | 424                               | 438   | 443   | 478   | 495   | 524   | 100                 |          |               |
| n          | 12                                | 12    | 12  | 12    | 12    | 12    | 12                  |          |               |
| Mean       | 393.1                             | 403.3 | 417.1   | 440.1 | 455.8 | 473.9 | 80.8                |          |               |
| S.D.       | 22.2                              | 27.1  | 24.6  | 28.4  | 26.5  | 29.9  | 12.8                |          |               |

| Animal No. | Body weight<br>Sex : Female<br>/Day |       |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|-------------------------------------|-------|-------|-------|---|----------|---------------|
|            | 1                                   | 4     | 7     | 14    |   |          |               |
| 50151      | 234                                 | 237   | 243   | 249   | 15  |          |               |
| 50152      | 247                                 | 246   | 245   | 256   | 9   |          |               |
| 50153      | 244                                 | 241   | 255   | 266   | 22  |          |               |
| 50154      | 238                                 | 239   | 244   | 243   | 5   |          |               |
| 50155      | 253                                 | 256   | 261   | 276   | 23  |          |               |
| 50156      | 227                                 | 230   | 233   | 232   | 5   |          |               |
| 50157      | 270                                 | 270   | 277   | 289   | 19  |          |               |
| 50158      | 255                                 | 266   | 272   | 285   | 30  |          |               |
| 50159      | 254                                 | 265   | 267   | 281   | 27  |          |               |
| 50160      | 279                                 | 285   | 304   | 329   | 50  |          |               |
| 50161      | 232                                 | 231   | 229   | 243   | 11  |          |               |
| 50162      | 252                                 | 256   | 258   | 260   | 8   |          |               |
| n          | 12                                  | 12    | 12    | 12    | 12  |          |               |
| Mean       | 248.8                               | 251.8 | 257.3 | 267.4 | 18.7  |          |               |
| S.D.       | 15.3                                | 17.3  | 20.9  | 26.6  | 13.0  |          |               |

Body weight of Animal No. 50160 on Day 21 was 361 g

| Animal No. | Body weight<br>Sex : Female<br>/Day |        | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 0 mg/kg |        |                     | Unit : g | Species : Rat |
|------------|-------------------------------------|--------|---|--------|---------------------|----------|---------------|
|            | 0                                   | 7      | 14  | 20     | Body weight<br>gain |          |               |
| 50151      | 258                                 | 299    | 335   | 412    | 154                 |          |               |
| 50152      | 260                                 | 290    | 327   | 419    | 159                 |          |               |
| 50153      | 268                                 | 309    | 348   | 422    | 154                 |          |               |
| 50154      | 262                                 | 302    | 336   | 412    | 150                 |          |               |
| 50155      | 283                                 | 324    | 366   | 444    | 161                 |          |               |
| 50156      | 242                                 | 274    | 312   | 377    | 135                 |          |               |
| 50157      | 323                                 | 378    | 420   | 481    | 158                 |          |               |
| 50158      | 306                                 | 336    | 387   | 471    | 165                 |          |               |
| 50159      | 300                                 | 320    | 351   | 444    | 144                 |          |               |
| 50160      | 358 \$                              | 399 \$ | 443 \$  | 461 \$ | 103 \$              |          |               |
| 50161      | 240                                 | 282    | 315   | 410    | 170                 |          |               |
| 50162      | 282                                 | 321    | 358   | 459    | 177                 |          |               |
| n          | 11                                  | 11     | 11  | 11     | 11                  |          |               |
| Mean       | 274.9                               | 312.3  | 350.5   | 431.9  | 157.0               |          |               |
| S.D.       | 26.5                                | 28.9   | 32.0  | 30.8   | 11.7                |          |               |

Animal No. 50160 : Non-pregnancy

\$ : Excepted data from calculation

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 0 mg/kg |                     | Unit : g | Species : Rat |
|------------|-----------------------------|-------|--|---------------------|----------|---------------|
|            | /Day                        | 0     | 4  | Body weight<br>gain |          |               |
| 50151      |                             | 301   | 301  | 0                   |          |               |
| 50152      |                             | 314   | 332  | 18                  |          |               |
| 50153      |                             | 327   | 353  | 26                  |          |               |
| 50154      |                             | 331   | 336  | 5                   |          |               |
| 50155      |                             | 359   | 367  | 8                   |          |               |
| 50156      |                             | 288   | 315  | 27                  |          |               |
| 50157      |                             | 416   | 436  | 20                  |          |               |
| 50158      |                             | 346   | 366  | 20                  |          |               |
| 50159      |                             | 318   | 345  | 27                  |          |               |
| 50161      |                             | 292   | 324  | 32                  |          |               |
| 50162      |                             | 347   | 374  | 27                  |          |               |
| n          |                             | 11    | 11   | 11                  |          |               |
| Mean       |                             | 330.8 | 349.9  | 19.1                |          |               |
| S.D.       |                             | 36.4  | 36.6   | 10.4                |          |               |

| Animal No. | Body weight<br>Sex : Female<br>/Day |       |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 50 mg/kg | Unit : g | Species : Rat |
|------------|-------------------------------------|-------|-------|-------|--|----------|---------------|
|            | 1                                   | 4     | 7     | 14    |  |          |               |
| 50251      | 234                                 | 240   | 240   | 242   | 8  |          |               |
| 50252      | 233                                 | 238   | 240   | 245   | 12   |          |               |
| 50253      | 252                                 | 254   | 267   | 276   | 24   |          |               |
| 50254      | 245                                 | 250   | 255   | 264   | 19   |          |               |
| 50255      | 231                                 | 240   | 241   | 251   | 20   |          |               |
| 50256      | 272                                 | 275   | 276   | 292   | 20   |          |               |
| 50257      | 227                                 | 232   | 235   | 238   | 11   |          |               |
| 50258      | 229                                 | 232   | 237   | 245   | 16   |          |               |
| 50259      | 266                                 | 268   | 270   | 278   | 12   |          |               |
| 50260      | 228                                 | 231   | 230   | 231   | 3  |          |               |
| 50261      | 250                                 | 262   | 262   | 271   | 21   |          |               |
| 50262      | 256                                 | 261   | 269   | 278   | 22   |          |               |
| n          | 12                                  | 12    | 12    | 12    | 12   |          |               |
| Mean       | 243.6                               | 248.6 | 251.8 | 259.3 | 15.7   |          |               |
| S.D.       | 15.6                                | 15.3  | 16.3  | 19.6  | 6.4  |          |               |

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 50 mg/kg |       |       | Unit : g            | Species : Rat |
|------------|-----------------------------|-------|--|-------|-------|---------------------|---------------|
|            | /Day                        | 0     | 7  | 14    | 20    | Body weight<br>gain |               |
| 50251      |                             | 256   | 285  | 325   | 413   | 157                 |               |
| 50252      |                             | 263   | 306  | 337   | 418   | 155                 |               |
| 50253      |                             | 281   | 309  | 342   | 436   | 155                 |               |
| 50254      |                             | 293   | 330  | 364   | 449   | 156                 |               |
| 50255      |                             | 259   | 286  | 316   | 386   | 127                 |               |
| 50256      |                             | 297   | 340  | 373   | 449   | 152                 |               |
| 50257      |                             | 252   | 289  | 327   | 405   | 153                 |               |
| 50258      |                             | 248   | 282  | 312   | 394   | 146                 |               |
| 50259      |                             | 307   | 339  | 382   | 453   | 146                 |               |
| 50260      |                             | 246   | 269  | 308   | 391   | 145                 |               |
| 50261      |                             | 273   | 313  | 360   | 454   | 181                 |               |
| 50262      |                             | 301   | 339  | 375   | 470   | 169                 |               |
| n          |                             | 12    | 12   | 12    | 12    | 12                  |               |
| Mean       |                             | 273.0 | 307.3  | 343.4 | 426.5 | 153.5               |               |
| S.D.       |                             | 22.1  | 25.3   | 26.5  | 28.8  | 13.2                |               |

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 50 mg/kg | Unit : g            | Species : Rat |
|------------|-----------------------------|-------|---|---------------------|---------------|
|            | /Day                        | 0     | 4   | Body weight<br>gain |               |
| 50251      |                             | 297   | 320   | 23                  |               |
| 50252      |                             | 312   | 335   | 23                  |               |
| 50253      |                             | 323   | 346   | 23                  |               |
| 50254      |                             | 354   | 365   | 11                  |               |
| 50255      |                             | 307   | 311   | 4                   |               |
| 50256      |                             | 348   | 368   | 20                  |               |
| 50257      |                             | 315   | 341   | 26                  |               |
| 50258      |                             | 296   | 323   | 27                  |               |
| 50259      |                             | 357   | 403   | 46                  |               |
| 50260      |                             | 290   | 330   | 40                  |               |
| 50261      |                             | 341   | 359   | 18                  |               |
| 50262      |                             | 363   | 373   | 10                  |               |
| n          |                             | 12    | 12  | 12                  |               |
| Mean       |                             | 325.3 | 347.8   | 22.6                |               |
| S.D.       |                             | 26.2  | 26.6  | 11.9                |               |

| Animal No. | Body weight<br>Sex : Female<br>/Day |       |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 200 mg/kg | Unit : g | Species : Rat |
|------------|-------------------------------------|-------|-------|-------|---|----------|---------------|
|            | 1                                   | 4     | 7     | 14    |   |          |               |
| 50351      | 244                                 | 251   | 254   | 267   | 23  |          |               |
| 50352      | 223                                 | 236   | 239   | 246   | 23  |          |               |
| 50353      | 244                                 | 244   | 257   | 259   | 15  |          |               |
| 50354      | 250                                 | 251   | 256   | 277   | 27  |          |               |
| 50355      | 239                                 | 244   | 247   | 269   | 30  |          |               |
| 50356      | 235                                 | 237   | 248   | 260   | 25  |          |               |
| 50357      | 274                                 | 285   | 289   | 288   | 14  |          |               |
| 50358      | 222                                 | 227   | 237   | 246   | 24  |          |               |
| 50359      | 259                                 | 267   | 281   | 295   | 36  |          |               |
| 50360      | 231                                 | 234   | 236   | 251   | 20  |          |               |
| 50361      | 271                                 | 274   | 284   | 302   | 31  |          |               |
| 50362      | 252                                 | 260   | 263   | 280   | 28  |          |               |
| n          | 12                                  | 12    | 12    | 12    | 12  |          |               |
| Mean       | 245.3                               | 250.8 | 257.6 | 270.0 | 24.7  |          |               |
| S.D.       | 16.9                                | 17.6  | 18.4  | 18.7  | 6.4   |          |               |

Body weight of Animal No. 50351 on Day 21 was 316 g

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 200 mg/kg |       |       | Unit : g | Species : Rat       |  |
|------------|-----------------------------|-------|---|-------|-------|----------|---------------------|--|
|            | /Day                        |       | 0   | 7     | 14    | 20       | Body weight<br>gain |  |
| 50351      |                             | 325   | 360   | 406   | 491   | 166      |                     |  |
| 50352      |                             | 255   | 286   | 324   | 400   | 145      |                     |  |
| 50353      |                             | 260   | 298   | 346   | 429   | 169      |                     |  |
| 50354      |                             | 278   | 312   | 348   | 424   | 146      |                     |  |
| 50355      |                             | 271   | 312   | 357   | 456   | 185      |                     |  |
| 50356      |                             | 262   | 302   | 344   | 431   | 169      |                     |  |
| 50357      |                             | 307   | 338   | 371   | 449   | 142      |                     |  |
| 50358      |                             | 252   | 286   | 318   | 410   | 158      |                     |  |
| 50359      |                             | 305   | 346   | 387   | 497   | 192      |                     |  |
| 50360      |                             | 249   | 289   | 329   | 419   | 170      |                     |  |
| 50361      |                             | 309   | 352   | 397   | 485   | 176      |                     |  |
| 50362      |                             | 271   | 314   | 351   | 418   | 147      |                     |  |
| n          |                             | 12    | 12  | 12    | 12    | 12       |                     |  |
| Mean       |                             | 278.7 | 316.3   | 356.5 | 442.4 | 163.8    |                     |  |
| S.D.       |                             | 26.0  | 26.5  | 28.4  | 33.1  | 16.4     |                     |  |

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 200 mg/kg | Unit : g            | Species : Rat |
|------------|-----------------------------|-------|--|---------------------|---------------|
|            | /Day                        | 0     | 4  | Body weight<br>gain |               |
| 50351      |                             | 379   | 396  | 17                  |               |
| 50352      |                             | 302   | 315  | 13                  |               |
| 50353      |                             | 327   | 342  | 15                  |               |
| 50354      |                             | 321   | 339  | 18                  |               |
| 50355      |                             | 323   | 330  | 7                   |               |
| 50356      |                             | 325   | 347  | 22                  |               |
| 50357      |                             | 343   | 371  | 28                  |               |
| 50358      |                             | 308   | 346  | 38                  |               |
| 50359      |                             | 370   | 401  | 31                  |               |
| 50360      |                             | 310   | 335  | 25                  |               |
| 50361      |                             | 384   | 405  | 21                  |               |
| 50362      |                             | 343   | 359  | 16                  |               |
| n          |                             | 12    | 12   | 12                  |               |
| Mean       |                             | 336.3 | 357.2  | 20.9                |               |
| S.D.       |                             | 28.0  | 29.7   | 8.5                 |               |

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 800 mg/kg |       |       | Unit : g | Species : Rat       |  |
|------------|-----------------------------|-------|---|-------|-------|----------|---------------------|--|
|            | /Day                        |       | 1   | 4     | 7     | 14       | Body weight<br>gain |  |
| 50451      |                             | 235   | 229   | 241   | 257   | 22       |                     |  |
| 50452      |                             | 225   | 226   | 233   | 243   | 18       |                     |  |
| 50453      |                             | 236   | 240   | 243   | 245   | 9        |                     |  |
| 50454      |                             | 246   | 237   | 255   | 267   | 21       |                     |  |
| 50455      |                             | 253   | 255   | 253   | 261   | 8        |                     |  |
| 50456      |                             | 257   | 256   | 266   | 271   | 14       |                     |  |
| 50457      |                             | 258   | 263   | 265   | 283   | 25       |                     |  |
| 50458      |                             | 235   | 221   | 234   | 247   | 12       |                     |  |
| 50459      |                             | 255   | 251   | 259   | 255   | 0        |                     |  |
| 50460      |                             | 274   | 287   | 299   | 324   | 50       |                     |  |
| 50461      |                             | 260   | 269   | 274   | 301   | 41       |                     |  |
| 50462      |                             | 215   | 220   | 215   | 226   | 11       |                     |  |
| n          |                             | 12    | 12  | 12    | 12    | 12       |                     |  |
| Mean       |                             | 245.8 | 246.2   | 253.1 | 265.0 | 19.3     |                     |  |
| S.D.       |                             | 16.8  | 20.9  | 22.1  | 27.1  | 14.2     |                     |  |

| Animal No. | Body weight<br>Sex : Female<br>/Day |        | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 800 mg/kg |        |                     | Unit : g | Species : Rat |
|------------|-------------------------------------|--------|---|--------|---------------------|----------|---------------|
|            | 0                                   | 7      | 14  | 20     | Body weight<br>gain |          |               |
| 50451      | 266                                 | 302    | 349   | 443    | 177                 |          |               |
| 50452      | 258                                 | 269    | 330   | 416    | 158                 |          |               |
| 50453      | 260                                 | 300    | 333   | 389    | 129                 |          |               |
| 50454      | 270                                 | 296    | 335   | 404    | 134                 |          |               |
| 50455      | 259                                 | 331    | 390   | 474    | 215                 |          |               |
| 50456      | 265 \$                              | 307 \$ | 320 \$  | 318 \$ | 53 \$               |          |               |
| 50457      | 291                                 | 332    | 391   | 460    | 169                 |          |               |
| 50458      | 258                                 | 286    | 324   | 402    | 144                 |          |               |
| 50459      | 276                                 | 300    | 338   | 407    | 131                 |          |               |
| 50460      | 340                                 | 384    | 438   | 524    | 184                 |          |               |
| 50461      | 303                                 | 346    | 396   | 495    | 192                 |          |               |
| 50462      | 235                                 | 275    | 320   | 392    | 157                 |          |               |
| n          | 11                                  | 11     | 11  | 11     | 11                  |          |               |
| Mean       | 274.2                               | 311.0  | 358.5   | 436.9  | 162.7               |          |               |
| S.D.       | 28.3                                | 34.1   | 38.7  | 45.7   | 27.7                |          |               |

Animal No. 50456 : Non-pregnancy

\$ : Excepted data from calculation

| Animal No. | Body weight<br>Sex : Female |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g            | Species : Rat |
|------------|-----------------------------|-------|--|---------------------|---------------|
|            | /Day                        | 0     | 4  | Body weight<br>gain |               |
| 50451      |                             | 332   | 350  | 18                  |               |
| 50452      |                             | 299   | 332  | 33                  |               |
| 50453      |                             | 315   | 339  | 24                  |               |
| 50454      |                             | 316   | 328  | 12                  |               |
| 50455      |                             | 357   | 369 \$   | 12 \$               |               |
| 50457      |                             | 353   | 371  | 18                  |               |
| 50458      |                             | 288   | ...  | ...                 |               |
| 50459      |                             | 319   | 352  | 33                  |               |
| 50460      |                             | 422   | 446  | 24                  |               |
| 50461      |                             | 379   | 392  | 13                  |               |
| 50462      |                             | 297   | 323  | 26                  |               |
| n          |                             | 11    | 9  | 9                   |               |
| Mean       |                             | 334.3 | 359.2  | 22.3                |               |
| S.D.       |                             | 40.4  | 39.2   | 7.7                 |               |

Animal No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

Animal No. 50458 : Died on lactation day 0 after the parturition

\$ : Excepted data from calculation

... : Not applicable

| Animal No. | Body weight<br>Sex : Female (satellite) |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 0 mg/kg |       |       |       |       | Unit : g | Species : Rat       |  |
|------------|---|-------|---|-------|-------|-------|-------|----------|---------------------|--|
|            | /Day                                    |       | 1   | 4     | 7     | 14    | 21    | 28       | Body weight<br>gain |  |
| 50551      |   | 236   | 239   | 238   | 256   | 261   | 264   | 28       |                     |  |
| 50552      |   | 235   | 240   | 249   | 245   | 261   | 272   | 37       |                     |  |
| 50553      |   | 235   | 243   | 250   | 251   | 272   | 285   | 50       |                     |  |
| 50554      |   | 244   | 245   | 251   | 255   | 279   | 293   | 49       |                     |  |
| 50555      |   | 248   | 251   | 269   | 265   | 292   | 299   | 51       |                     |  |
| 50556      |   | 242   | 248   | 251   | 266   | 279   | 280   | 38       |                     |  |
| 50557      |   | 247   | 250   | 247   | 254   | 264   | 267   | 20       |                     |  |
| 50558      |   | 233   | 233   | 233   | 238   | 252   | 294   | 61       |                     |  |
| 50559      |   | 245   | 253   | 265   | 275   | 275   | 294   | 49       |                     |  |
| 50560      |   | 251   | 260   | 258   | 269   | 282   | 282   | 31       |                     |  |
| n          |   | 10    | 10  | 10    | 10    | 10    | 10    | 10       |                     |  |
| Mean       |   | 241.6 | 246.2   | 251.1 | 257.4 | 271.7 | 283.0 | 41.4     |                     |  |
| S.D.       |   | 6.4   | 7.8   | 11.0  | 11.4  | 12.1  | 12.2  | 12.7     |                     |  |

| Animal No. | Body weight<br>Sex : Female (satellite) |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 800 mg/kg |       |       |       | Unit : g | Species : Rat |
|------------|---|-------|---|-------|-------|-------|----------|---------------|
|            | /Day                                    | 1     | 4   | 7     | 14    | 21    | 28       |               |
| 50651      |   | 241   | 215   | 248   | 286   | 280   | 283      | 42            |
| 50652      |   | 236   | 233   | 247   | 255   | 260   | 281      | 45            |
| 50653      |   | 230   | 244   | 254   | 266   | 260   | 287      | 57            |
| 50654      |   | 232   | 229   | 224   | 270   | 249   | 263      | 31            |
| 50655      |   | 255   | 240   | 227   | 293   | 258   | 281      | 26            |
| 50656      |   | 224   | 235   | 238   | 237   | 237   | 238      | 14            |
| 50657      |   | 257   | 251   | 267   | 274   | 295   | 304      | 47            |
| 50658      |   | 243   | 246   | 246   | 256   | 257   | 265      | 22            |
| 50659      |   | 244   | 239   | 249   | 256   | 270   | 293      | 49            |
| 50660      |   | 227   | ...   | ...   | ...   | ...   | ...      | ...           |
| n          |   | 10    | 9   | 9     | 9     | 9     | 9        | 9             |
| Mean       |   | 238.9 | 236.9   | 244.4 | 265.9 | 262.9 | 277.2    | 37.0          |
| S.D.       |   | 11.2  | 10.6  | 13.3  | 17.2  | 17.0  | 19.4     | 14.3          |

Animal No. 50660 : Died on administration day 3

... : Not applicable

| Animal No. | Body weight /Day |       |       | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|------------------|-------|-------|---|----------|---------------|
|            | 1                | 7     | 14    |   |          |               |
| 10103      | 497              | 523   | 538   | 41  |          |               |
| 10104      | 450              | 472   | 485   | 35  |          |               |
| 10105      | 512              | 538   | 549   | 37  |          |               |
| 10106      | 489              | 505   | 530   | 41  |          |               |
| 10111      | 471              | 490   | 504   | 33  |          |               |
| n          | 5                | 5     | 5     | 5   |          |               |
| Mean       | 483.8            | 505.6 | 521.2 | 37.4  |          |               |
| S.D.       | 24.0             | 26.1  | 26.2  | 3.6   |          |               |

| Animal No. | Body weight /Day |       |       | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|------------|------------------|-------|-------|---|----------|---------------|
|            | 1                | 7     | 14    |   |          |               |
| 10402      | 480              | 520   | 531   | 51  |          |               |
| 10403      | 466              | 494   | 510   | 44  |          |               |
| 10407      | 485              | 508   | 522   | 37  |          |               |
| 10409      | 447              | 484   | 498   | 51  |          |               |
| 10411      | 504              | 535   | 552   | 48  |          |               |
| n          | 5                | 5     | 5     | 5   |          |               |
| Mean       | 476.4            | 508.2 | 522.6 | 46.2  |          |               |
| S.D.       | 21.3             | 20.3  | 20.6  | 5.9   |          |               |

| Animal No. | Body weight<br>Sex : Female (satellite) |       |       | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|---|-------|-------|---|----------|---------------|
|            | /Day                                    | 1     | 7     |   |          |               |
| 50556      |   | 282   | 290   | 312   | 30       |               |
| 50557      |   | 271   | 272   | 282   | 11       |               |
| 50558      |   | 299   | 329   | 322   | 23       |               |
| 50559      |   | 293   | 303   | 302   | 9        |               |
| 50560      |   | 281   | 287   | 300   | 19       |               |
| n          |   | 5     | 5     | 5   | 5        |               |
| Mean       |   | 285.2 | 296.2 | 303.6   | 18.4     |               |
| S.D.       |   | 11.0  | 21.4  | 14.9  | 8.6      |               |

| Animal No. | Body weight<br>Sex : Female (satellite) |       |       | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|------------|---|-------|-------|---|----------|---------------|
|            | /Day                                    | 1     | 7     |   |          |               |
| 50656      |   | 229   | 246   | 254   | 25       |               |
| 50657      |   | 296   | 318   | 333   | 37       |               |
| 50658      |   | 264   | 276   | 281   | 17       |               |
| 50659      |   | 284   | 307   | 321   | 37       |               |
| n          |   | 4     | 4     | 4   | 4        |               |
| Mean       |   | 268.3 | 286.8 | 297.3   | 29.0     |               |
| S.D.       |   | 29.3  | 32.5  | 36.4  | 9.8      |               |

| Animal No. | Food consumption<br>Sex : Male<br>/Day |       |       |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|-------|---|----------|---------------|
|            | 4                                      | 7     | 14    | 28    |   |          |               |
| 10101      | 23.7                                   | 22.9  | 22.7  | 24.8  |   |          |               |
| 10102      | 26.0                                   | 28.4  | 29.7  | 31.0  |   |          |               |
| 10103      | 28.2                                   | 28.6  | 28.4  | 28.3  |   |          |               |
| 10104      | 25.4                                   | 24.9  | 26.0  | 25.9  |   |          |               |
| 10105      | 27.4                                   | 27.4  | 28.3  | 28.8  |   |          |               |
| 10106      | 26.7                                   | 27.7  | 27.9  | 28.2  |   |          |               |
| 10107      | 27.5                                   | 27.6  | 27.7  | 31.9  |   |          |               |
| 10108      | 24.3                                   | 24.3  | 24.3  | 23.8  |   |          |               |
| 10109      | 28.8                                   | 29.3  | 30.2  | 31.4  |   |          |               |
| 10110      | 24.2                                   | 22.7  | 24.5  | ...   |   |          |               |
| 10111      | 29.6                                   | 30.9  | 29.5  | 27.8  |   |          |               |
| 10112      | 27.4                                   | 27.8  | 28.9  | 31.3  |   |          |               |
| n          | 12                                     | 12    | 12    | 11    |   |          |               |
| Mean       | 26.60                                  | 26.88 | 27.34 | 28.47 |   |          |               |
| S.D.       | 1.90                                   | 2.58  | 2.41  | 2.78  |   |          |               |

... : During mating

| Animal No. | Food consumption<br>Sex : Male<br>/Day |       |       |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 50 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|-------|--|----------|---------------|
|            | 4                                      | 7     | 14    | 28    |  |          |               |
| 10201      | 24.1                                   | 24.1  | 24.8  | 26.3  |  |          |               |
| 10202      | 26.5                                   | 25.2  | 27.1  | 26.9  |  |          |               |
| 10203      | 24.2                                   | 24.3  | 25.9  | 26.0  |  |          |               |
| 10204      | 28.6                                   | 29.8  | 28.9  | 27.4  |  |          |               |
| 10205      | 28.3                                   | 28.9  | 28.5  | 28.0  |  |          |               |
| 10206      | 24.5                                   | 24.0  | 24.5  | 25.4  |  |          |               |
| 10207      | 32.9                                   | 30.3  | 30.4  | 29.7  |  |          |               |
| 10208      | 27.9                                   | 27.5  | 27.1  | 26.7  |  |          |               |
| 10209      | 27.1                                   | 26.7  | 27.7  | 26.4  |  |          |               |
| 10210      | 27.2                                   | 25.8  | 25.6  | 25.7  |  |          |               |
| 10211      | 28.9                                   | 28.4  | 27.7  | 29.8  |  |          |               |
| 10212      | 28.2                                   | 28.5  | 28.2  | 31.4  |  |          |               |
| n          | 12                                     | 12    | 12    | 12    |  |          |               |
| Mean       | 27.37                                  | 26.96 | 27.20 | 27.48 |  |          |               |
| S.D.       | 2.45                                   | 2.26  | 1.75  | 1.89  |  |          |               |

| Animal No. | Food consumption<br>Sex : Male<br>/Day |       |       |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 200 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|-------|---|----------|---------------|
|            | 4                                      | 7     | 14    | 28    |   |          |               |
| 10301      | 28.7                                   | 28.6  | 28.8  | ...   |   |          |               |
| 10302      | 24.4                                   | 25.8  | 25.0  | 22.9  |   |          |               |
| 10303      | 28.2                                   | 28.7  | 28.8  | 29.8  |   |          |               |
| 10304      | 26.8                                   | 25.9  | 25.9  | 26.9  |   |          |               |
| 10305      | 25.8                                   | 24.7  | 24.6  | 25.2  |   |          |               |
| 10306      | 29.1                                   | 29.4  | 28.8  | 31.4  |   |          |               |
| 10307      | 29.2                                   | 29.2  | 29.0  | 27.8  |   |          |               |
| 10308      | 26.1                                   | 27.3  | 27.4  | 27.3  |   |          |               |
| 10309      | 31.2                                   | 32.1  | 31.9  | 30.4  |   |          |               |
| 10310      | 24.2                                   | 24.3  | 24.9  | 25.6  |   |          |               |
| 10311      | 28.8                                   | 28.4  | 29.7  | 31.7  |   |          |               |
| 10312      | 29.0                                   | 29.3  | 29.7  | 30.9  |   |          |               |
| n          | 12                                     | 12    | 12    | 11    |   |          |               |
| Mean       | 27.63                                  | 27.81 | 27.88 | 28.17 |   |          |               |
| S.D.       | 2.15                                   | 2.27  | 2.31  | 2.89  |   |          |               |

... : During mating

| Animal No. | Food consumption<br>Sex : Male<br>/Day |       |       |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|-------|---|----------|---------------|
|            | 4                                      | 7     | 14    | 28    |   |          |               |
| 10401      | 26.0                                   | 26.0  | 27.6  | 29.5  |   |          |               |
| 10402      | 26.0                                   | 28.9  | 30.1  | 27.4  |   |          |               |
| 10403      | 29.5                                   | 27.9  | 28.7  | 26.6  |   |          |               |
| 10404      | 24.7                                   | 25.4  | 24.8  | 27.8  |   |          |               |
| 10405      | 26.7                                   | 27.8  | 27.4  | 29.3  |   |          |               |
| 10406      | 29.3                                   | 30.5  | 31.1  | 29.9  |   |          |               |
| 10407      | 28.9                                   | 28.3  | 29.7  | 27.4  |   |          |               |
| 10408      | 26.4                                   | 24.8  | 26.3  | 25.1  |   |          |               |
| 10409      | 26.2                                   | 28.6  | 27.0  | 23.9  |   |          |               |
| 10410      | 16.3                                   | 22.4  | 27.1  | 25.8  |   |          |               |
| 10411      | 28.9                                   | 30.2  | 29.4  | 29.9  |   |          |               |
| 10412      | 29.1                                   | 28.6  | 30.2  | 29.3  |   |          |               |
| n          | 12                                     | 12    | 12    | 12    |   |          |               |
| Mean       | 26.50                                  | 27.45 | 28.28 | 27.66 |   |          |               |
| S.D.       | 3.61                                   | 2.36  | 1.88  | 2.01  |   |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|---|----------|---------------|
|            | 4  | 7     | 14    |   |          |               |
| 50151      | 19.5                                     | 21.9  | 20.9  |   |          |               |
| 50152      | 16.8                                     | 17.9  | 19.2  |   |          |               |
| 50153      | 18.0                                     | 19.2  | 18.9  |   |          |               |
| 50154      | 17.0                                     | 17.5  | 18.6  |   |          |               |
| 50155      | 17.6                                     | 19.5  | 21.3  |   |          |               |
| 50156      | 17.2                                     | 18.0  | 18.9  |   |          |               |
| 50157      | 21.0                                     | 20.4  | 22.8  |   |          |               |
| 50158      | 19.3                                     | 20.2  | 21.8  |   |          |               |
| 50159      | 20.3                                     | 20.6  | 22.0  |   |          |               |
| 50160      | 22.1                                     | 24.6  | 24.1  |   |          |               |
| 50161      | 16.9                                     | 17.0  | 18.4  |   |          |               |
| 50162      | 17.7                                     | 18.3  | 20.1  |   |          |               |
| n          | 12                                       | 12    | 12    |   |          |               |
| Mean       | 18.62                                    | 19.59 | 20.58 |   |          |               |
| S.D.       | 1.78                                     | 2.15  | 1.86  |   |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |         |         | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|--|---------|---------|---|----------|---------------|
|            | 7  | 14      | 20      |   |          |               |
| 50151      | 26.3                                     | 27.4    | 25.4    |   |          |               |
| 50152      | 21.9                                     | 24.0    | 25.2    |   |          |               |
| 50153      | 24.2                                     | 26.4    | 28.3    |   |          |               |
| 50154      | 22.5                                     | 23.8    | 24.3    |   |          |               |
| 50155      | 25.2                                     | 28.5    | 27.1    |   |          |               |
| 50156      | 22.5                                     | 26.3    | 25.6    |   |          |               |
| 50157      | 30.5                                     | 33.8    | 30.6    |   |          |               |
| 50158      | 22.9                                     | 27.3    | 24.8    |   |          |               |
| 50159      | 21.9                                     | 21.8    | 24.1    |   |          |               |
| 50160      | 30.6 \$                                  | 33.6 \$ | 30.2 \$ |   |          |               |
| 50161      | 23.5                                     | 26.8    | 25.3    |   |          |               |
| 50162      | 26.8                                     | 26.9    | 26.3    |   |          |               |
| n          | 11                                       | 11      | 11      |   |          |               |
| Mean       | 24.38                                    | 26.64   | 26.09   |   |          |               |
| S.D.       | 2.65                                     | 3.07    | 1.93    |   |          |               |

Animal No. 50160 : Non-pregnancy

\$ : Excepted data from calculation

| Food consumption<br>Sex : Female<br><u>/Day</u> |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|---|-------|--|----------|---------------|
| Animal No.                                      | 4     |  |          |               |
| 50151   | 26.7  |  |          |               |
| 50152   | 34.0  |  |          |               |
| 50153   | 38.5  |  |          |               |
| 50154   | 33.1  |  |          |               |
| 50155   | 31.2  |  |          |               |
| 50156   | 33.9  |  |          |               |
| 50157   | 39.7  |  |          |               |
| 50158   | 35.2  |  |          |               |
| 50159   | 34.6  |  |          |               |
| 50161   | 40.3  |  |          |               |
| 50162   | 34.9  |  |          |               |
| n   | 11    |  |          |               |
| Mean  | 34.74 |  |          |               |
| S.D.  | 3.89  |  |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 50 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|--|----------|---------------|
|            | 4  | 7     | 14    |  |          |               |
| 50251      | 17.4                                     | 16.9  | 18.6  |  |          |               |
| 50252      | 16.4                                     | 15.7  | 17.8  |  |          |               |
| 50253      | 18.1                                     | 19.9  | 18.5  |  |          |               |
| 50254      | 15.8                                     | 16.8  | 19.1  |  |          |               |
| 50255      | 18.8                                     | 16.2  | 18.8  |  |          |               |
| 50256      | 20.1                                     | 18.9  | 21.7  |  |          |               |
| 50257      | 15.7                                     | 15.8  | 17.3  |  |          |               |
| 50258      | 16.2                                     | 18.1  | 18.9  |  |          |               |
| 50259      | 18.0                                     | 18.2  | 20.4  |  |          |               |
| 50260      | 16.1                                     | 15.8  | 17.4  |  |          |               |
| 50261      | 20.3                                     | 18.6  | 19.6  |  |          |               |
| 50262      | 18.2                                     | 20.0  | 21.4  |  |          |               |
| n          | 12                                       | 12    | 12    |  |          |               |
| Mean       | 17.59                                    | 17.58 | 19.13 |  |          |               |
| S.D.       | 1.60                                     | 1.58  | 1.43  |  |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |       |       | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 50 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|--|----------|---------------|
|            | 7  | 14    | 20    |  |          |               |
| 50251      | 21.5                                     | 23.4  | 23.7  |  |          |               |
| 50252      | 23.8                                     | 23.9  | 21.9  |  |          |               |
| 50253      | 22.8                                     | 24.5  | 24.4  |  |          |               |
| 50254      | 24.9                                     | 26.5  | 26.8  |  |          |               |
| 50255      | 21.9                                     | 23.4  | 25.4  |  |          |               |
| 50256      | 24.6                                     | 25.5  | 26.3  |  |          |               |
| 50257      | 24.5                                     | 25.0  | 23.0  |  |          |               |
| 50258      | 21.9                                     | 22.6  | 23.2  |  |          |               |
| 50259      | 25.3                                     | 26.8  | 25.3  |  |          |               |
| 50260      | 21.5                                     | 22.8  | 23.1  |  |          |               |
| 50261      | 24.9                                     | 27.4  | 28.0  |  |          |               |
| 50262      | 25.3                                     | 27.7  | 29.2  |  |          |               |
| n          | 12                                       | 12    | 12    |  |          |               |
| Mean       | 23.58                                    | 24.96 | 25.03 |  |          |               |
| S.D.       | 1.54                                     | 1.81  | 2.22  |  |          |               |

| Food consumption<br>Sex : Female<br><u>/Day</u> |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 50 mg/kg | Unit : g | Species : Rat |
|---|-------|---|----------|---------------|
| Animal No.                                      | 4     |   |          |               |
| 50251   | 34.5  |   |          |               |
| 50252   | 36.7  |   |          |               |
| 50253   | 35.6  |   |          |               |
| 50254   | 34.9  |   |          |               |
| 50255   | 30.6  |   |          |               |
| 50256   | 31.6  |   |          |               |
| 50257   | 29.9  |   |          |               |
| 50258   | 34.3  |   |          |               |
| 50259   | 42.5  |   |          |               |
| 50260   | 38.0  |   |          |               |
| 50261   | 39.4  |   |          |               |
| 50262   | 35.0  |   |          |               |
| n   | 12    |   |          |               |
| Mean  | 35.25 |   |          |               |
| S.D.  | 3.63  |   |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 200 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|---|----------|---------------|
|            | 4  | 7     | 14    |   |          |               |
| 50351      | 16.9                                     | 17.1  | 19.5  |   |          |               |
| 50352      | 19.4                                     | 17.7  | 18.5  |   |          |               |
| 50353      | 17.6                                     | 20.4  | 18.4  |   |          |               |
| 50354      | 18.8                                     | 20.5  | 22.7  |   |          |               |
| 50355      | 19.4                                     | 20.9  | 22.3  |   |          |               |
| 50356      | 18.5                                     | 19.9  | 19.4  |   |          |               |
| 50357      | 21.7                                     | 21.7  | 22.9  |   |          |               |
| 50358      | 20.0                                     | 19.1  | 19.8  |   |          |               |
| 50359      | 21.6                                     | 22.9  | 22.9  |   |          |               |
| 50360      | 16.3                                     | 16.4  | 18.2  |   |          |               |
| 50361      | 22.4                                     | 24.3  | 23.9  |   |          |               |
| 50362      | 18.5                                     | 20.2  | 21.0  |   |          |               |
| n          | 12                                       | 12    | 12    |   |          |               |
| Mean       | 19.26                                    | 20.09 | 20.79 |   |          |               |
| S.D.       | 1.91                                     | 2.30  | 2.06  |   |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |       |       | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 200 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|---|----------|---------------|
|            | 7  | 14    | 20    |   |          |               |
| 50351      | 26.2                                     | 27.9  | 26.9  |   |          |               |
| 50352      | 23.2                                     | 25.3  | 25.1  |   |          |               |
| 50353      | 21.9                                     | 26.9  | 27.2  |   |          |               |
| 50354      | 24.5                                     | 26.7  | 23.2  |   |          |               |
| 50355      | 27.1                                     | 29.9  | 26.6  |   |          |               |
| 50356      | 23.8                                     | 26.4  | 26.4  |   |          |               |
| 50357      | 25.5                                     | 27.1  | 27.2  |   |          |               |
| 50358      | 22.4                                     | 25.1  | 27.1  |   |          |               |
| 50359      | 28.2                                     | 30.1  | 31.3  |   |          |               |
| 50360      | 22.5                                     | 25.6  | 24.9  |   |          |               |
| 50361      | 26.0                                     | 28.8  | 29.5  |   |          |               |
| 50362      | 24.4                                     | 27.1  | 27.4  |   |          |               |
| n          | 12                                       | 12    | 12    |   |          |               |
| Mean       | 24.64                                    | 27.24 | 26.90 |   |          |               |
| S.D.       | 1.99                                     | 1.66  | 2.09  |   |          |               |

| Food consumption<br>Sex : Female<br>/Day |       | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 200 mg/kg | Unit : g | Species : Rat |
|--|-------|--|----------|---------------|
| Animal No.                               | 4     |  |          |               |
| 50351                                    | 32.5  |  |          |               |
| 50352                                    | 36.3  |  |          |               |
| 50353                                    | 31.2  |  |          |               |
| 50354                                    | 31.5  |  |          |               |
| 50355                                    | 34.3  |  |          |               |
| 50356                                    | 34.0  |  |          |               |
| 50357                                    | 35.2  |  |          |               |
| 50358                                    | 35.7  |  |          |               |
| 50359                                    | 38.3  |  |          |               |
| 50360                                    | 36.3  |  |          |               |
| 50361                                    | 36.9  |  |          |               |
| 50362                                    | 32.3  |  |          |               |
| n  | 12    |  |          |               |
| Mean                                     | 34.54 |  |          |               |
| S.D.                                     | 2.29  |  |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |       |       | Period : F0 before mating Day 1-14<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|---|----------|---------------|
|            | 4  | 7     | 14    |   |          |               |
| 50451      | 11.6                                     | 22.4  | 22.3  |   |          |               |
| 50452      | 13.7                                     | 15.9  | 18.7  |   |          |               |
| 50453      | 16.1                                     | 16.6  | 17.3  |   |          |               |
| 50454      | 14.5                                     | 22.3  | 21.2  |   |          |               |
| 50455      | 18.0                                     | 18.6  | 19.3  |   |          |               |
| 50456      | 15.1                                     | 18.7  | 20.2  |   |          |               |
| 50457      | 20.2                                     | 20.9  | 22.0  |   |          |               |
| 50458      | 11.2                                     | 18.1  | 19.8  |   |          |               |
| 50459      | 15.3                                     | 17.2  | 17.5  |   |          |               |
| 50460      | 23.8                                     | 25.8  | 26.9  |   |          |               |
| 50461      | 23.2                                     | 25.3  | 24.7  |   |          |               |
| 50462      | 15.1                                     | 15.0  | 18.4  |   |          |               |
| n          | 12                                       | 12    | 12    |   |          |               |
| Mean       | 16.48                                    | 19.73 | 20.69 |   |          |               |
| S.D.       | 4.09                                     | 3.58  | 2.91  |   |          |               |

| Animal No. | Food consumption<br>Sex : Female<br>/Day |         |         | Period : F0 gestation Day 0-20<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|------------|--|---------|---------|---|----------|---------------|
|            | 7  | 14      | 20      |   |          |               |
| 50451      | 25.7                                     | 30.0    | 30.2    |   |          |               |
| 50452      | 15.6                                     | 27.2    | 26.6    |   |          |               |
| 50453      | 23.8                                     | 24.6    | 24.5    |   |          |               |
| 50454      | 24.1                                     | 26.9    | 24.2    |   |          |               |
| 50455      | 29.2                                     | 36.1    | 35.1    |   |          |               |
| 50456      | 24.3 \$                                  | 25.1 \$ | 20.8 \$ |   |          |               |
| 50457      | 25.0                                     | 33.3    | 24.3    |   |          |               |
| 50458      | 19.5                                     | 24.6    | 26.8    |   |          |               |
| 50459      | 19.8                                     | 24.7    | 22.4    |   |          |               |
| 50460      | 30.1                                     | 37.7    | 31.8    |   |          |               |
| 50461      | 29.0                                     | 32.6    | 32.9    |   |          |               |
| 50462      | 24.3                                     | 26.1    | 25.8    |   |          |               |
| n          | 11                                       | 11      | 11      |   |          |               |
| Mean       | 24.19                                    | 29.44   | 27.69   |   |          |               |
| S.D.       | 4.49                                     | 4.79    | 4.15    |   |          |               |

Animal No. 50456 : Non-pregnancy

\$ : Excepted data from calculation

| Food consumption<br>Sex : Female<br>/Day |         | Period : F0 lactation Day 0-4<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|--|---------|--|----------|---------------|
| Animal No.                               | 4       |  |          |               |
| 50451                                    | 38.3    |  |          |               |
| 50452                                    | 34.8    |  |          |               |
| 50453                                    | 34.8    |  |          |               |
| 50454                                    | 30.8    |  |          |               |
| 50455                                    | 32.7 \$ |  |          |               |
| 50457                                    | 37.2    |  |          |               |
| 50458                                    | ...     |  |          |               |
| 50459                                    | 36.5    |  |          |               |
| 50460                                    | 48.5    |  |          |               |
| 50461                                    | 38.3    |  |          |               |
| 50462                                    | 34.1    |  |          |               |
| n  | 9       |  |          |               |
| Mean                                     | 37.03   |  |          |               |
| S.D.                                     | 4.90    |  |          |               |

Animal No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

Animal No. 50458 : Died on lactation day 0 after the parturition

\$ : Excepted data from calculation

... : Not applicable

| Animal No. | Food consumption<br>Sex : Female (satellite)<br>/Day |       |       |       |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|-------|-------|-------|---|----------|---------------|
|            | 4  | 7     | 14    | 21    | 28    |   |          |               |
| 50551      | 16.2   | 16.1  | 18.9  | 17.0  | 17.6  |   |          |               |
| 50552      | 18.9   | 19.2  | 19.2  | 19.2  | 19.5  |   |          |               |
| 50553      | 18.0   | 18.6  | 19.4  | 20.0  | 20.5  |   |          |               |
| 50554      | 17.0   | 17.0  | 18.1  | 19.6  | 21.3  |   |          |               |
| 50555      | 19.5   | 22.5  | 20.4  | 21.3  | 22.0  |   |          |               |
| 50556      | 19.4   | 20.6  | 20.1  | 20.2  | 18.3  |   |          |               |
| 50557      | 17.6   | 18.6  | 19.0  | 17.5  | 18.7  |   |          |               |
| 50558      | 15.6   | 16.0  | 17.4  | 16.5  | 22.0  |   |          |               |
| 50559      | 20.2   | 21.0  | 23.7  | 21.2  | 23.6  |   |          |               |
| 50560      | 20.3   | 19.5  | 21.0  | 19.4  | 19.1  |   |          |               |
| n          | 10   | 10    | 10    | 10    | 10    |   |          |               |
| Mean       | 18.27  | 18.91 | 19.72 | 19.19 | 20.26 |   |          |               |
| S.D.       | 1.65   | 2.13  | 1.75  | 1.68  | 1.93  |   |          |               |

| Animal No. | Food consumption<br>Sex : Female (satellite) |       | Period : Administration Day 1-28<br>Dose : PTSA Monohydrate 800 mg/kg |       |       | Unit : g | Species : Rat |
|------------|--|-------|---|-------|-------|----------|---------------|
|            | /Day   |       | 4   | 7     | 14    | 21       | 28            |
| 50651      |  | 1.8   | 18.4  | 23.3  | 19.5  | 16.8     |               |
| 50652      |  | 11.9  | 19.6  | 18.5  | 18.8  | 20.2     |               |
| 50653      |  | 20.2  | 19.4  | 21.1  | 18.4  | 19.3     |               |
| 50654      |  | 15.6  | 7.7   | 23.1  | 18.5  | 19.0     |               |
| 50655      |  | 15.1  | 5.0   | 26.9  | 16.7  | 21.0     |               |
| 50656      |  | 15.6  | 14.4  | 15.5  | 14.9  | 13.2     |               |
| 50657      |  | 16.5  | 21.9  | 20.6  | 21.1  | 19.9     |               |
| 50658      |  | 16.9  | 17.2  | 19.1  | 17.3  | 17.5     |               |
| 50659      |  | 16.3  | 16.6  | 20.1  | 19.1  | 24.9     |               |
| 50660      |  | ...   | ...   | ...   | ...   | ...      |               |
| n          |  | 9     | 9   | 9     | 9     | 9        |               |
| Mean       |  | 14.43 | 15.58   | 20.91 | 18.26 | 19.09    |               |
| S.D.       |  | 5.20  | 5.68  | 3.27  | 1.78  | 3.20     |               |

Animal No. 50660 : Died on administration day 3

... : Not applicable

| Animal No. | Food consumption<br>Sex : Male<br>/Day |       | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|------------|--|-------|---|----------|---------------|
|            | 7                                      | 14    |   |          |               |
| 10103      | 28.7                                   | 29.1  |   |          |               |
| 10104      | 27.1                                   | 26.2  |   |          |               |
| 10105      | 30.7                                   | 27.0  |   |          |               |
| 10106      | 28.1                                   | 27.9  |   |          |               |
| 10111      | 26.2                                   | 28.0  |   |          |               |
| n          | 5                                      | 5     |   |          |               |
| Mean       | 28.16                                  | 27.64 |   |          |               |
| S.D.       | 1.71                                   | 1.10  |   |          |               |

| Food consumption<br>Sex : Male<br><u>/Day</u> |       | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|---|-------|---|----------|---------------|
| Animal No.                                    | 7     | 14  |          |               |
| 10402   | 29.9  | 27.0  |          |               |
| 10403   | 28.8  | 28.0  |          |               |
| 10407   | 28.5  | 27.7  |          |               |
| 10409   | 26.9  | 26.0  |          |               |
| 10411   | 29.9  | 29.3  |          |               |
| n   | 5     | 5   |          |               |
| Mean  | 28.80 | 27.60   |          |               |
| S.D.  | 1.24  | 1.22  |          |               |

| Food consumption<br>Sex : Female (satellite) |      | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|--|------|---|----------|---------------|
| Animal No.                                   | /Day | 7   | 14       |               |
| 50556  |      | 20.8  | 21.1     |               |
| 50557  |      | 19.0  | 19.0     |               |
| 50558  |      | 29.5  | 21.1     |               |
| 50559  |      | 20.6  | 21.6     |               |
| 50560  |      | 18.2  | 19.6     |               |
| n  |      | 5   | 5        |               |
| Mean   |      | 21.62   | 20.48    |               |
| S.D.   |      | 4.54  | 1.12     |               |

| Food consumption<br>Sex : Female (satellite) |      | Period : Recovery Day 1-14<br>Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|--|------|---|----------|---------------|
| Animal No.                                   | /Day | 7   | 14       |               |
| 50656  |      | 15.2  | 15.1     |               |
| 50657  |      | 22.1  | 21.7     |               |
| 50658  |      | 19.2  | 18.5     |               |
| 50659  |      | 23.9  | 22.5     |               |
| n  |      | 4   | 4        |               |
| Mean   |      | 20.10   | 19.45    |               |
| S.D.   |      | 3.80  | 3.38     |               |

| Sex : Male | Urinary findings |         |         |             |              |           |              | Species : Rat |
|------------|------------------|---------|---------|-------------|--------------|-----------|--------------|---------------|
|            | pH               | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood |               |
| Animal No. | EU/dL            |         |         |             |              |           |              |               |
| 10103      | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10104      | 8.5              | ±       | -       | -           | 0.1          | -         | ±            | A             |
| 10105      | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10106      | 8.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| 10111      | 8.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| n          | 5                | 5       | 5       | 5           | 5            | 5         | 5            | 5             |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings |  | Stage : Week 4                  | Species : Rat |
|------------------|--|---------------------------------|---------------|
| Sex : Male       |  | Dose : PTSA Monohydrate 0 mg/kg |               |
| Urine volume     |  |                                 |               |
| Animal No.       |  | mL/24hr                         |               |
| 10103            |  | 13.0                            |               |
| 10104            |  | 16.0                            |               |
| 10105            |  | 10.5                            |               |
| 10106            |  | 16.0                            |               |
| 10111            |  | 15.5                            |               |
| n                |  | 5                               |               |
| Mean             |  | 14.20                           |               |
| S.D.             |  | 2.41                            |               |

| Urinary findings<br>Sex : Male<br>Specific gravity | Stage : Week 4<br>Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
|--|---|---------------|
| <hr/>  |   |               |
| Animal No.   |   |               |
| 10103  | 4   |               |
| 10104  | 4   |               |
| 10105  | 4   |               |
| 10106  | 4   |               |
| 10111  | 4   |               |
| n  | 5   |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Male        | Urinary findings |     |          |       |             |      | Species : Rat |
|-------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                   | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b> |                  |     |          |       |             |      |               |
| 10103             | -                | -   | -        | -     | -           | -    |               |
| 10104             | -                | -   | ±        | -     | -           | -    |               |
| 10105             | -                | -   | -        | -     | -           | -    |               |
| 10106             | -                | -   | -        | -     | -           | -    |               |
| 10111             | -                | -   | -        | -     | -           | -    |               |
| n                 | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Sex : Male   | Urinary findings |         |         |             |              |           |              | Species : Rat |
|--|------------------|---------|---------|-------------|--------------|-----------|--------------|---------------|
|  | pH               | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood |               |
| Stage : Week 4<br>Dose : PTSA Monohydrate 50 mg/kg |                  |         |         |             |              |           |              |               |
| Animal No.   |                  |         |         |             | EU/dL        |           |              |               |
| 10202  | 8.0              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10204  | 8.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| 10207  | 8.5              | ±       | -       | -           | 0.1          | -         | ±            | A             |
| 10209  | 8.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| 10210  | 8.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| n  | 5                | 5       | 5       | 5           | 5            | 5         | 5            | 5             |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings |  | Stage : Week 4                   | Species : Rat |
|------------------|--|----------------------------------|---------------|
| Sex : Male       |  | Dose : PTSA Monohydrate 50 mg/kg |               |
| Urine volume     |  |                                  |               |
| Animal No.       |  | mL/24hr                          |               |
| 10202            |  | 12.0                             |               |
| 10204            |  | 19.5                             |               |
| 10207            |  | 15.0                             |               |
| 10209            |  | 12.0                             |               |
| 10210            |  | 14.5                             |               |
| n                |  | 5                                |               |
| Mean             |  | 14.60                            |               |
| S.D.             |  | 3.07                             |               |

| Urinary findings<br>Sex : Male<br>Specific gravity | Stage : Week 4<br>Dose : PTSA Monohydrate 50 mg/kg | Species : Rat |
|--|--|---------------|
| <hr/>  |  |               |
| Animal No.   |  |               |
| 10202  | 5  |               |
| 10204  | 3  |               |
| 10207  | 3  |               |
| 10209  | 4  |               |
| 10210  | 4  |               |
| n  | 5  |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Male        | Urinary findings |     |          |       |             |      | Species : Rat |
|-------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                   | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b> |                  |     |          |       |             |      |               |
| 10202             | -                | -   | -        | -     | -           | -    |               |
| 10204             | -                | -   | -        | -     | -           | -    |               |
| 10207             | -                | -   | -        | -     | -           | -    |               |
| 10209             | -                | -   | -        | -     | -           | -    |               |
| 10210             | -                | -   | -        | -     | -           | -    |               |
| n                 | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Urinary findings<br>Sex : Male |     | Stage : Week 4<br>Dose : PTSA Monohydrate 200 mg/kg |         |             |              |           |              | Species : Rat |
|--------------------------------|-----|---|---------|-------------|--------------|-----------|--------------|---------------|
| Animal No.                     | pH  | Protein   | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood | Color         |
| 10302                          | 8.5 | ±   | -       | -           | 0.1          | -         | -            | A             |
| 10303                          | 8.5 | ±   | -       | -           | 0.1          | -         | -            | A             |
| 10305                          | 8.5 | ±   | -       | -           | 0.1          | -         | -            | A             |
| 10307                          | 8.5 | -   | -       | -           | 0.1          | -         | -            | A             |
| 10308                          | 8.0 | ±   | -       | -           | 0.1          | -         | -            | A             |
| n                              | 5   | 5   | 5       | 5           | 5            | 5         | 5            | 5             |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings |  | Stage : Week 4                    | Species : Rat |
|------------------|--|-----------------------------------|---------------|
| Sex : Male       |  | Dose : PTSA Monohydrate 200 mg/kg |               |
| Urine volume     |  |                                   |               |
| Animal No.       |  | mL/24hr                           |               |
| 10302            |  | 11.0                              |               |
| 10303            |  | 20.0                              |               |
| 10305            |  | 16.5                              |               |
| 10307            |  | 31.0                              |               |
| 10308            |  | 14.5                              |               |
| n                |  | 5                                 |               |
| Mean             |  | 18.60                             |               |
| S.D.             |  | 7.66                              |               |

|                  |                                   |               |
|------------------|-----------------------------------|---------------|
| Urinary findings | Stage : Week 4                    |               |
| Sex : Male       | Dose : PTSA Monohydrate 200 mg/kg | Species : Rat |
| Specific gravity |                                   |               |
| <hr/>            |                                   |               |
| Animal No.       |                                   |               |
| 10302            | 4                                 |               |
| 10303            | 3                                 |               |
| 10305            | 3                                 |               |
| 10307            | 2                                 |               |
| 10308            | 4                                 |               |
| n                | 5                                 |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Male        | Urinary findings |     |          |       |             |      | Species : Rat |
|-------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                   | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b> |                  |     |          |       |             |      |               |
| 10302             | -                | -   | -        | -     | -           | -    |               |
| 10303             | -                | -   | -        | -     | -           | -    |               |
| 10305             | -                | -   | -        | -     | -           | -    |               |
| 10307             | -                | -   | -        | -     | -           | -    |               |
| 10308             | -                | -   | -        | -     | -           | -    |               |
| n                 | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Sex : Male  | Urinary findings |         |         |             |              |           |              | Species : Rat |
|---|------------------|---------|---------|-------------|--------------|-----------|--------------|---------------|
|   | pH               | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood |               |
| Stage : Week 4<br>Dose : PTSA Monohydrate 800 mg/kg |                  |         |         |             |              |           |              |               |
| Animal No.  |                  |         |         |             | EU/dL        |           |              |               |
| 10402   | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10403   | 7.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| 10407   | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10409   | 7.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10411   | 6.5              | +       | -       | -           | 0.1          | -         | 2+           | A             |
| n   | 5                | 5       | 5       | 5           | 5            | 5         | 5            | 5             |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings |  | Stage : Week 4                    | Species : Rat |
|------------------|--|-----------------------------------|---------------|
| Sex : Male       |  | Dose : PTSA Monohydrate 800 mg/kg |               |
| Urine volume     |  |                                   |               |
| Animal No.       |  | mL/21hr                           |               |
| 10402            |  | 27.0                              |               |
| 10403            |  | 17.0                              |               |
| 10407            |  | 13.0                              |               |
| 10409            |  | 14.0                              |               |
| 10411            |  | 12.5                              |               |
| n                |  | 5                                 |               |
| Mean             |  | 16.70                             |               |
| S.D.             |  | 6.02                              |               |

| Urinary findings<br>Sex : Male<br>Specific gravity | Stage : Week 4<br>Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
|--|---|---------------|
| <hr/>  |   |               |
| Animal No.   |   |               |
| 10402  | 2   |               |
| 10403  | 3   |               |
| 10407  | 5   |               |
| 10409  | 4   |               |
| 10411  | 5   |               |
| n  | 5   |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Male        | Urinary findings |     |          |       |             |      | Species : Rat |
|-------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                   | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b> |                  |     |          |       |             |      |               |
| 10402             | -                | -   | -        | -     | -           | -    |               |
| 10403             | -                | -   | ±        | -     | -           | -    |               |
| 10407             | -                | -   | -        | -     | -           | -    |               |
| 10409             | -                | -   | ±        | -     | -           | -    |               |
| 10411             | 2+               | -   | -        | -     | -           | -    |               |
| n                 | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Urinary findings<br>Sex : Female (satellite) |  | Stage : Week 4<br>Dose : PTSA Monohydrate 0 mg/kg |         |         |             |              |           | Species : Rat |       |
|--|--|---|---------|---------|-------------|--------------|-----------|---------------|-------|
| Animal No.                                   |  | pH  | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood  | Color |
| 50556  |  | 8.0   | -       | -       | -           | 0.1          | -         | -             | A     |
| 50557  |  | 8.5   | -       | -       | -           | 0.1          | -         | -             | A     |
| 50558  |  | 8.5   | -       | -       | -           | 0.1          | -         | -             | A     |
| 50559  |  | 8.5   | ±       | -       | -           | 0.1          | -         | -             | A     |
| 50560  |  | 8.0   | -       | -       | -           | 0.1          | -         | -             | A     |
| n  |  | 5   | 5       | 5       | 5           | 5            | 5         | 5             | 5     |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings<br>Sex : Female (satellite) |         | Stage : Week 4<br>Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
|--|---------|---|---------------|
| Urine volume                                 |         |   |               |
| Animal No.                                   | mL/21hr |   |               |
| 50556  | 7.0     |   |               |
| 50557  | 5.0     |   |               |
| 50558  | 8.0     |   |               |
| 50559  | 18.0    |   |               |
| 50560  | 18.0    |   |               |
| n  | 5       |   |               |
| Mean   | 11.20   |   |               |
| S.D.   | 6.30    |   |               |

| Urinary findings<br>Sex : Female (satellite)<br>Specific gravity | Stage : Week 4<br>Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
|--|---|---------------|
| Animal No.   |   |               |
| 50556  | 3   |               |
| 50557  | 5   |               |
| 50558  | 4   |               |
| 50559  | 3   |               |
| 50560  | 2   |               |
| n  | 5   |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Animal No. | Urinary findings |     |          | Stage : Week 4 |             |      | Species : Rat |
|------------|------------------|-----|----------|----------------|-------------|------|---------------|
|            | RBC              | WBC | Squamous | Round          | Small round | Cast |               |
| 50556      | -                | -   | ±        | -              | -           | -    |               |
| 50557      | -                | -   | -        | -              | -           | -    |               |
| 50558      | -                | -   | -        | -              | -           | -    |               |
| 50559      | -                | -   | -        | -              | -           | -    |               |
| 50560      | -                | -   | ±        | -              | -           | -    |               |
| n          | 5                | 5   | 5        | 5              | 5           | 5    |               |

| Urinary findings<br>Sex : Female (satellite) |  | Stage : Week 4<br>Dose : PTSA Monohydrate 800 mg/kg |         |         |             |              |           | Species : Rat |       |
|--|--|---|---------|---------|-------------|--------------|-----------|---------------|-------|
| Animal No.                                   |  | pH  | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood  | Color |
| 50656  |  | 6.0   | 3+      | 3+      | -           | 0.1          | -         | ±             | A     |
| 50657  |  | 6.0   | -       | -       | -           | 0.1          | -         | -             | A     |
| 50658  |  | 8.0   | 2+      | -       | -           | 0.1          | -         | +             | A     |
| 50659  |  | 8.5   | -       | -       | -           | 0.1          | -         | -             | A     |
| n  |  | 4   | 4       | 4       | 4           | 4            | 4         | 4             | 4     |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings<br>Sex : Female (satellite) |         | Stage : Week 4<br>Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
|--|---------|---|---------------|
| Urine volume                                 |         |   |               |
| Animal No.                                   | mL/21hr |   |               |
| 50656  | 17.0    |   |               |
| 50657  | 26.0    |   |               |
| 50658  | 13.5    |   |               |
| 50659  | 14.5    |   |               |
| n  | 4       |   |               |
| Mean   | 17.75   |   |               |
| S.D.   | 5.69    |   |               |

|  |   |               |
|--|---|---------------|
| Urinary findings<br>Sex : Female (satellite)<br>Specific gravity | Stage : Week 4<br>Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
| <hr/>  |   |               |
| Animal No.   |   |               |
| 50656  | 3   |               |
| 50657  | 1   |               |
| 50658  | 3   |               |
| 50659  | 3   |               |
| n  | 4   |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Female (satellite) | Urinary findings |     |          |       |             |      | Species : Rat |
|--------------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                          | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b>        |                  |     |          |       |             |      |               |
| 50656                    | -                | -   | ±        | -     | ±           | -    |               |
| 50657                    | -                | -   | -        | -     | -           | -    |               |
| 50658                    | -                | -   | ±        | -     | -           | -    |               |
| 50659                    | -                | -   | -        | -     | -           | -    |               |
| n                        | 4                | 4   | 4        | 4     | 4           | 4    |               |

| Sex : Male   | Urinary findings |         |         |             |              |           |              | Species : Rat |
|--|------------------|---------|---------|-------------|--------------|-----------|--------------|---------------|
|  | pH               | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood |               |
| Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 0 mg/kg |                  |         |         |             |              |           |              |               |
| Animal No.   |                  |         |         |             | EU/dL        |           |              |               |
| 10103  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10104  | 8.5              | ±       | -       | -           | 0.1          | -         | -            | A             |
| 10105  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10106  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10111  | 8.5              | +       | -       | -           | 0.1          | -         | ±            | A             |
| n  | 5                | 5       | 5       | 5           | 5            | 5         | 5            | 5             |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings |  | Stage : Recovery Week 2         | Species : Rat |
|------------------|--|---------------------------------|---------------|
| Sex : Male       |  | Dose : PTSA Monohydrate 0 mg/kg |               |
| Urine volume     |  |                                 |               |
| Animal No.       |  | mL/24hr                         |               |
| 10103            |  | 10.0                            |               |
| 10104            |  | 16.0                            |               |
| 10105            |  | 11.5                            |               |
| 10106            |  | 9.5                             |               |
| 10111            |  | 10.0                            |               |
| n                |  | 5                               |               |
| Mean             |  | 11.40                           |               |
| S.D.             |  | 2.68                            |               |

| Urinary findings<br>Sex : Male<br>Specific gravity | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
|--|--|---------------|
| Animal No.   |  |               |
| 10103  | 5  |               |
| 10104  | 4  |               |
| 10105  | 4  |               |
| 10106  | 5  |               |
| 10111  | 5  |               |
| n  | 5  |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Male        | Urinary findings |     |          |       |             |      | Species : Rat |
|-------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                   | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b> |                  |     |          |       |             |      |               |
| 10103             | -                | -   | ±        | -     | -           | -    |               |
| 10104             | -                | -   | ±        | -     | -           | -    |               |
| 10105             | -                | -   | ±        | -     | -           | -    |               |
| 10106             | -                | -   | -        | -     | -           | -    |               |
| 10111             | -                | -   | ±        | -     | -           | -    |               |
| n                 | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Sex : Male   | Urinary findings |         |         |             |              |           |              | Species : Rat |
|--|------------------|---------|---------|-------------|--------------|-----------|--------------|---------------|
|  | pH               | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood |               |
| Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 800 mg/kg |                  |         |         |             |              |           |              |               |
| Animal No.   |                  |         |         |             | EU/dL        |           |              |               |
| 10402  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10403  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10407  | 8.5              | 2+      | -       | -           | 0.1          | -         | -            | A             |
| 10409  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| 10411  | 8.5              | +       | -       | -           | 0.1          | -         | -            | A             |
| n  | 5                | 5       | 5       | 5           | 5            | 5         | 5            | 5             |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings |  | Stage : Recovery Week 2           | Species : Rat |
|------------------|--|-----------------------------------|---------------|
| Sex : Male       |  | Dose : PTSA Monohydrate 800 mg/kg |               |
| Urine volume     |  |                                   |               |
| Animal No.       |  | mL/24hr                           |               |
| 10402            |  | 20.0                              |               |
| 10403            |  | 13.0                              |               |
| 10407            |  | 11.5                              |               |
| 10409            |  | 13.0                              |               |
| 10411            |  | 15.0                              |               |
| n                |  | 5                                 |               |
| Mean             |  | 14.50                             |               |
| S.D.             |  | 3.32                              |               |

| Urinary findings<br>Sex : Male<br>Specific gravity | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
|--|--|---------------|
| Animal No.   |  |               |
| 10402  | 2  |               |
| 10403  | 4  |               |
| 10407  | 5  |               |
| 10409  | 4  |               |
| 10411  | 4  |               |
| n  | 5  |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Male        | Urinary findings |     |          |       |             |      | Species : Rat |
|-------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                   | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b> |                  |     |          |       |             |      |               |
| 10402             | -                | -   | -        | -     | -           | -    |               |
| 10403             | -                | -   | ±        | -     | -           | -    |               |
| 10407             | -                | -   | -        | -     | -           | -    |               |
| 10409             | -                | -   | -        | -     | -           | -    |               |
| 10411             | -                | -   | -        | -     | -           | -    |               |
| n                 | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Urinary findings<br>Sex : Female (satellite) |  | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 0 mg/kg |         |         |             |              |           | Species : Rat |       |
|--|--|--|---------|---------|-------------|--------------|-----------|---------------|-------|
| Animal No.                                   |  | pH   | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood  | Color |
| 50556  |  | 8.5  | +       | -       | -           | 0.1          | -         | ±             | A     |
| 50557  |  | 8.5  | -       | -       | -           | 0.1          | -         | -             | A     |
| 50558  |  | 6.5  | ±       | -       | -           | 0.1          | -         | -             | A     |
| 50559  |  | 7.5  | -       | -       | -           | 0.1          | -         | -             | A     |
| 50560  |  | 8.0  | +       | -       | -           | 0.1          | -         | -             | A     |
| n  |  | 5  | 5       | 5       | 5           | 5            | 5         | 5             | 5     |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings<br>Sex : Female (satellite) |         | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
|--|---------|--|---------------|
| Urine volume                                 |         |  |               |
| Animal No.                                   | mL/21hr |  |               |
| 50556  | 12.0    |  |               |
| 50557  | 14.0    |  |               |
| 50558  | 7.0     |  |               |
| 50559  | 13.0    |  |               |
| 50560  | 14.0    |  |               |
| n  | 5       |  |               |
| Mean   | 12.00   |  |               |
| S.D.   | 2.92    |  |               |

|  |  |               |
|--|--|---------------|
| Urinary findings<br>Sex : Female (satellite)<br>Specific gravity | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
| <hr/>  |  |               |
| Animal No.   |  |               |
| 50556  | 4  |               |
| 50557  | 4  |               |
| 50558  | 5  |               |
| 50559  | 4  |               |
| 50560  | 3  |               |
| n  | 5  |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Female (satellite) | Urinary findings |     |          |       |             |      | Species : Rat |
|--------------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                          | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b>        |                  |     |          |       |             |      |               |
| 50556                    | -                | -   | -        | -     | -           | -    |               |
| 50557                    | -                | -   | -        | -     | -           | -    |               |
| 50558                    | -                | -   | -        | -     | -           | -    |               |
| 50559                    | -                | -   | -        | -     | -           | -    |               |
| 50560                    | -                | -   | -        | -     | -           | -    |               |
| n                        | 5                | 5   | 5        | 5     | 5           | 5    |               |

| Urinary findings<br>Sex : Female (satellite) |  | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 800 mg/kg |         |         |             |              |           | Species : Rat |       |
|--|--|--|---------|---------|-------------|--------------|-----------|---------------|-------|
| Animal No.                                   |  | pH   | Protein | Glucose | Ketone body | Urobilinogen | Bilirubin | Occult blood  | Color |
| 50656  |  | 7.5  | +       | -       | -           | 0.1          | -         | -             | A     |
| 50657  |  | 8.5  | -       | -       | -           | 0.1          | -         | -             | A     |
| 50658  |  | 8.5  | +       | -       | -           | 0.1          | -         | -             | A     |
| 50659  |  | 8.5  | +       | -       | -           | 0.1          | -         | -             | A     |
| n  |  | 4  | 4       | 4       | 4           | 4            | 4         | 4             | 4     |

A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white

| Urinary findings<br>Sex : Female (satellite) |         | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
|--|---------|--|---------------|
| Urine volume                                 |         |  |               |
| Animal No.                                   | mL/21hr |  |               |
| 50656  | 4.5     |  |               |
| 50657  | 12.5    |  |               |
| 50658  | 9.5     |  |               |
| 50659  | 13.5    |  |               |
| n  | 4       |  |               |
| Mean   | 10.00   |  |               |
| S.D.   | 4.04    |  |               |

|  |  |               |
|--|--|---------------|
| Urinary findings<br>Sex : Female (satellite)<br>Specific gravity | Stage : Recovery Week 2<br>Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
| <hr/>  |  |               |
| Animal No.   |  |               |
| 50656  | 5  |               |
| 50657  | 4  |               |
| 50658  | 4  |               |
| 50659  | 3  |               |
| n  | 4  |               |

0;1.001~1.010,1;1.011~1.020,2;1.021~1.030,3;1.031~1.040,4;1.041~1.050,5;1.050<

| Sex : Female (satellite) | Urinary findings |     |          |       |             |      | Species : Rat |
|--------------------------|------------------|-----|----------|-------|-------------|------|---------------|
|                          | RBC              | WBC | Squamous | Round | Small round | Cast |               |
| <b>Animal No.</b>        |                  |     |          |       |             |      |               |
| 50656                    | -                | -   | -        | -     | -           | -    |               |
| 50657                    | -                | -   | -        | -     | -           | -    |               |
| 50658                    | -                | -   | -        | -     | -           | -    |               |
| 50659                    | -                | -   | ±        | -     | -           | -    |               |
| n                        | 4                | 4   | 4        | 4     | 4           | 4    |               |

| Hematological findings |  | Stage : Day 29      |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |  |  |
|------------------------|--|---------------------|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|--|
| Sex : Male             |  | RBC                 | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |  |
| Animal No.             |  | 10 <sup>4</sup> /µL | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |  |
| 10101                  |  | 921                 | 16.0                | 43.5                | 47.2  | 17.4  | 36.8  | 3.19         | 116.2               | 93.5                | 18.3                | 70.8                |  |  |
| 10102                  |  | 851                 | 15.4                | 44.1                | 51.8  | 18.1  | 34.9  | 3.02         | 100.2               | 52.6                | 15.8                | 32.6                |  |  |
| 10107                  |  | 834                 | 15.1                | 43.0                | 51.6  | 18.1  | 35.1  | 3.11         | 104.0               | 66.8                | 10.0                | 54.1                |  |  |
| 10108                  |  | 834                 | 14.7                | 41.2                | 49.4  | 17.6  | 35.7  | 2.48         | 119.4               | 40.7                | 9.0                 | 30.5                |  |  |
| 10109                  |  | 815                 | 14.9                | 42.6                | 52.3  | 18.3  | 35.0  | 3.75         | 90.5                | 86.0                | 11.6                | 71.5                |  |  |
| n                      |  | 5                   | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |  |
| Mean                   |  | 851.0               | 15.22               | 42.88               | 50.46 | 17.90 | 35.50 | 3.110        | 106.06              | 67.92               | 12.94               | 51.90               |  |  |
| S.D.                   |  | 41.2                | 0.51                | 1.09                | 2.13  | 0.38  | 0.79  | 0.453        | 11.85               | 22.13               | 3.96                | 19.85               |  |  |
|                        |  |                     |                     |                     |       |       |       |              |                     |                     |                     |                     |  |  |
| Monocyte               |  | Eosinophil          | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |  |
| Animal No.             |  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |  |
| 10101                  |  | 3.4                 | 1.0                 | 0.0                 | 26.3  | 25.7  |       |              |                     |                     |                     |                     |  |  |
| 10102                  |  | 3.3                 | 0.9                 | 0.0                 | 20.2  | 21.3  |       |              |                     |                     |                     |                     |  |  |
| 10107                  |  | 2.2                 | 0.5                 | 0.0                 | 19.5  | 19.2  |       |              |                     |                     |                     |                     |  |  |
| 10108                  |  | 0.5                 | 0.7                 | 0.0                 | 17.9  | 18.0  |       |              |                     |                     |                     |                     |  |  |
| 10109                  |  | 2.6                 | 0.3                 | 0.0                 | 19.2  | 23.6  |       |              |                     |                     |                     |                     |  |  |
| n                      |  | 5                   | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |  |
| Mean                   |  | 2.40                | 0.68                | 0.00                | 20.62 | 21.56 |       |              |                     |                     |                     |                     |  |  |
| S.D.                   |  | 1.17                | 0.29                | 0.00                | 3.28  | 3.15  |       |              |                     |                     |                     |                     |  |  |

| Hematological findings<br>Sex : Male |                                 |                                   |                                 | Stage : Day 29<br>Dose : PTSA Monohydrate 50 mg/kg |             |              |                   |                                 | Species : Rat              |                                   |                                   |
|--------------------------------------|---------------------------------|-----------------------------------|---------------------------------|--|-------------|--------------|-------------------|---------------------------------|----------------------------|-----------------------------------|-----------------------------------|
|                                      | RBC<br>10 <sup>4</sup> /µL      | HGB<br>g/dL                       | HCT<br>%                        | MCV<br>fL  | MCH<br>pg   | MCHC<br>g/dL | Reticulocyte<br>% | Platelet<br>10 <sup>4</sup> /µL | WBC<br>10 <sup>2</sup> /µL | Neutrophil<br>10 <sup>2</sup> /µL | Lymphocyte<br>10 <sup>2</sup> /µL |
| Animal No.                           |                                 |                                   |                                 |  |             |              |                   |                                 |                            |                                   |                                   |
| 10201                                | 881                             | 15.8                              | 43.1                            | 48.9   | 17.9        | 36.7         | 3.47              | 100.7                           | 62.5                       | 10.8                              | 48.8                              |
| 10203                                | 865                             | 15.9                              | 44.6                            | 51.6   | 18.4        | 35.7         | 2.81              | 118.1                           | 54.4                       | 8.0                               | 44.2                              |
| 10205                                | 866                             | 15.3                              | 43.0                            | 49.7   | 17.7        | 35.6         | 2.24              | 115.0                           | 79.6                       | 24.9                              | 50.3                              |
| 10206                                | 862                             | 16.2                              | 45.8                            | 53.1   | 18.8        | 35.4         | 2.96              | 99.3                            | 35.1                       | 5.8                               | 27.5                              |
| 10208                                | 867                             | 15.4                              | 43.3                            | 49.9   | 17.8        | 35.6         | 2.65              | 119.5                           | 54.1                       | 11.1                              | 40.7                              |
| n                                    | 5                               | 5                                 | 5                               | 5  | 5           | 5            | 5                 | 5                               | 5                          | 5                                 | 5                                 |
| Mean                                 | 868.2                           | 15.72                             | 43.96                           | 50.64  | 18.12       | 35.80        | 2.826             | 110.52                          | 57.14                      | 12.12                             | 42.30                             |
| S.D.                                 | 7.4                             | 0.37                              | 1.21                            | 1.69   | 0.47        | 0.51         | 0.449             | 9.75                            | 16.09                      | 7.47                              | 9.10                              |
| <hr/>                                |                                 |                                   |                                 |  |             |              |                   |                                 |                            |                                   |                                   |
|                                      | Monocyte<br>10 <sup>2</sup> /µL | Eosinophil<br>10 <sup>2</sup> /µL | Basophil<br>10 <sup>2</sup> /µL | PT<br>sec  | APTT<br>sec |              |                   |                                 |                            |                                   |                                   |
| Animal No.                           |                                 |                                   |                                 |  |             |              |                   |                                 |                            |                                   |                                   |
| 10201                                | 2.1                             | 0.8                               | 0.0                             | 32.8   | 24.5        |              |                   |                                 |                            |                                   |                                   |
| 10203                                | 1.5                             | 0.7                               | 0.0                             | 26.8   | 24.2        |              |                   |                                 |                            |                                   |                                   |
| 10205                                | 3.2                             | 1.1                               | 0.1                             | 19.3   | 21.2        |              |                   |                                 |                            |                                   |                                   |
| 10206                                | 0.8                             | 1.0                               | 0.0                             | 37.2   | 27.9        |              |                   |                                 |                            |                                   |                                   |
| 10208                                | 1.1                             | 1.2                               | 0.0                             | 35.1   | 27.2        |              |                   |                                 |                            |                                   |                                   |
| n                                    | 5                               | 5                                 | 5                               | 5  | 5           |              |                   |                                 |                            |                                   |                                   |
| Mean                                 | 1.74                            | 0.96                              | 0.02                            | 30.24  | 25.00       |              |                   |                                 |                            |                                   |                                   |
| S.D.                                 | 0.95                            | 0.21                              | 0.04                            | 7.25   | 2.67        |              |                   |                                 |                            |                                   |                                   |

| Hematological findings<br>Sex : Male |                                 |                                   |                                 | Stage : Day 29<br>Dose : PTSA Monohydrate 200 mg/kg |       |       |                   |                                 | Species : Rat              |                                   |                                   |
|--------------------------------------|---------------------------------|-----------------------------------|---------------------------------|---|-------|-------|-------------------|---------------------------------|----------------------------|-----------------------------------|-----------------------------------|
|                                      | RBC<br>10 <sup>4</sup> /µL      | HGB<br>g/dL                       | HCT<br>%                        | MCV   | MCH   | MCHC  | Reticulocyte<br>% | Platelet<br>10 <sup>4</sup> /µL | WBC<br>10 <sup>2</sup> /µL | Neutrophil<br>10 <sup>2</sup> /µL | Lymphocyte<br>10 <sup>2</sup> /µL |
| Animal No.                           |                                 |                                   |                                 |   |       |       |                   |                                 |                            |                                   |                                   |
| 10301                                | 885                             | 15.5                              | 42.6                            | 48.1  | 17.5  | 36.4  | 3.18              | 123.0                           | 86.7                       | 12.7                              | 69.9                              |
| 10304                                | 894                             | 15.9                              | 44.2                            | 49.4  | 17.8  | 36.0  | 2.93              | 90.7                            | 70.5                       | 8.2                               | 60.1                              |
| 10306                                | 841                             | 15.9                              | 45.0                            | 53.5  | 18.9  | 35.3  | 3.35              | 127.8                           | 95.1                       | 16.6                              | 74.3                              |
| 10309                                | 853                             | 15.6                              | 43.8                            | 51.3  | 18.3  | 35.6  | 3.04              | 103.6                           | 45.5                       | 7.8                               | 35.6                              |
| 10310                                | 904                             | 16.7                              | 46.5                            | 51.4  | 18.5  | 35.9  | 3.01              | 111.0                           | 41.8                       | 8.5                               | 31.2                              |
| n                                    | 5                               | 5                                 | 5                               | 5   | 5     | 5     | 5                 | 5                               | 5                          | 5                                 | 5                                 |
| Mean                                 | 875.4                           | 15.92                             | 44.42                           | 50.74   | 18.20 | 35.84 | 3.102             | 111.22                          | 67.92                      | 10.76                             | 54.22                             |
| S.D.                                 | 27.1                            | 0.47                              | 1.45                            | 2.07  | 0.56  | 0.42  | 0.165             | 14.94                           | 23.89                      | 3.82                              | 19.75                             |
| <hr/>                                |                                 |                                   |                                 |   |       |       |                   |                                 |                            |                                   |                                   |
|                                      | Monocyte<br>10 <sup>2</sup> /µL | Eosinophil<br>10 <sup>2</sup> /µL | Basophil<br>10 <sup>2</sup> /µL | PT<br>sec   | APTT  |       |                   |                                 |                            |                                   |                                   |
| Animal No.                           |                                 |                                   |                                 |   |       |       |                   |                                 |                            |                                   |                                   |
| 10301                                | 3.2                             | 0.9                               | 0.0                             | 29.7  | APTT  |       |                   |                                 |                            |                                   |                                   |
| 10304                                | 1.8                             | 0.4                               | 0.0                             | 21.7  | APTT  |       |                   |                                 |                            |                                   |                                   |
| 10306                                | 2.7                             | 1.5                               | 0.0                             | 22.5  | APTT  |       |                   |                                 |                            |                                   |                                   |
| 10309                                | 1.4                             | 0.7                               | 0.0                             | 35.2  | APTT  |       |                   |                                 |                            |                                   |                                   |
| 10310                                | 1.0                             | 1.1                               | 0.0                             | 28.0  | APTT  |       |                   |                                 |                            |                                   |                                   |
| n                                    | 5                               | 5                                 | 5                               | 5   | APTT  |       |                   |                                 |                            |                                   |                                   |
| Mean                                 | 2.02                            | 0.92                              | 0.00                            | 27.42   | APTT  |       |                   |                                 |                            |                                   |                                   |
| S.D.                                 | 0.91                            | 0.41                              | 0.00                            | 5.54  | APTT  |       |                   |                                 |                            |                                   |                                   |

| Hematological findings |  | Stage : Day 29      |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |  |  |
|------------------------|--|---------------------|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|--|
| Sex : Male             |  | RBC                 | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |  |
| Animal No.             |  | 10 <sup>4</sup> /µL | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |  |
| 10401                  |  | 849                 | 15.2                | 41.8                | 49.2  | 17.9  | 36.4  | 3.47         | 127.1               | 67.7                | 10.5                | 54.8                |  |  |
| 10404                  |  | 855                 | 15.3                | 44.0                | 51.5  | 17.9  | 34.8  | 2.93         | 143.4               | 53.4                | 10.1                | 40.8                |  |  |
| 10405                  |  | 867                 | 15.2                | 42.3                | 48.8  | 17.5  | 35.9  | 3.10         | 131.2               | 72.0                | 9.7                 | 58.6                |  |  |
| 10406                  |  | 856                 | 15.6                | 43.9                | 51.3  | 18.2  | 35.5  | 4.22         | 117.2               | 67.5                | 23.6                | 39.7                |  |  |
| 10408                  |  | 855                 | 14.8                | 41.4                | 48.4  | 17.3  | 35.7  | 2.49         | 115.7               | 46.7                | 6.8                 | 37.6                |  |  |
| n                      |  | 5                   | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |  |
| Mean                   |  | 856.4               | 15.22               | 42.68               | 49.84 | 17.76 | 35.66 | 3.242        | 126.92              | 61.46               | 12.14               | 46.30               |  |  |
| S.D.                   |  | 6.5                 | 0.29                | 1.20                | 1.45  | 0.36  | 0.59  | 0.650        | 11.29               | 10.83               | 6.57                | 9.66                |  |  |
|                        |  |                     |                     |                     |       |       |       |              |                     |                     |                     |                     |  |  |
| Monocyte               |  | Eosinophil          | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |  |
| Animal No.             |  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |  |
| 10401                  |  | 1.3                 | 1.1                 | 0.0                 | 16.1  | 22.1  |       |              |                     |                     |                     |                     |  |  |
| 10404                  |  | 1.8                 | 0.7                 | 0.0                 | 18.7  | 21.4  |       |              |                     |                     |                     |                     |  |  |
| 10405                  |  | 2.5                 | 1.2                 | 0.0                 | 23.8  | 23.1  |       |              |                     |                     |                     |                     |  |  |
| 10406                  |  | 1.7                 | 2.5                 | 0.0                 | 21.1  | 22.7  |       |              |                     |                     |                     |                     |  |  |
| 10408                  |  | 1.7                 | 0.6                 | 0.0                 | 16.8  | 22.1  |       |              |                     |                     |                     |                     |  |  |
| n                      |  | 5                   | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |  |
| Mean                   |  | 1.80                | 1.22                | 0.00                | 19.30 | 22.28 |       |              |                     |                     |                     |                     |  |  |
| S.D.                   |  | 0.44                | 0.76                | 0.00                | 3.18  | 0.65  |       |              |                     |                     |                     |                     |  |  |

| Hematological findings |  | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 0 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |
|------------------------|--|--|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|
| Sex : Female           |  | RBC  | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |
| Animal No.             |  | 10 <sup>4</sup> /µL  | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| 50151                  |  | 784  | 15.1                | 42.7                | 54.5  | 19.3  | 35.4  | 5.46         | 134.1               | 88.4                | 41.7                | 43.8                |
| 50152                  |  | 723  | 13.7                | 39.9                | 55.2  | 18.9  | 34.3  | 5.55         | 134.7               | 87.7                | 22.5                | 61.2                |
| 50153                  |  | 736  | 14.3                | 40.2                | 54.6  | 19.4  | 35.6  | 5.39         | 151.6               | 67.4                | 27.1                | 36.8                |
| 50155                  |  | 743  | 14.3                | 41.2                | 55.5  | 19.2  | 34.7  | 4.15         | 132.4               | 91.7                | 45.5                | 41.2                |
| 50161                  |  | 716  | 13.5                | 38.8                | 54.2  | 18.9  | 34.8  | 6.49         | 94.8                | 69.0                | 35.9                | 28.9                |
| n                      |  | 5  | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |
| Mean                   |  | 740.4  | 14.18               | 40.56               | 54.80 | 19.14 | 34.96 | 5.408        | 129.52              | 80.84               | 34.54               | 42.38               |
| S.D.                   |  | 26.6   | 0.63                | 1.47                | 0.53  | 0.23  | 0.53  | 0.833        | 20.91               | 11.65               | 9.66                | 11.94               |
|                        |  |  |                     |                     |       |       |       |              |                     |                     |                     |                     |
| Monocyte               |  | Eosinophil   | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |
| Animal No.             |  | 10 <sup>2</sup> /µL  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   | sec   | sec          | sec                 | sec                 | sec                 |                     |
| 50151                  |  | 2.4  | 0.5                 | 0.0                 | 16.5  | 16.6  |       |              |                     |                     |                     |                     |
| 50152                  |  | 3.3  | 0.7                 | 0.0                 | 17.5  | 17.5  |       |              |                     |                     |                     |                     |
| 50153                  |  | 2.7  | 0.8                 | 0.0                 | 16.9  | 15.9  |       |              |                     |                     |                     |                     |
| 50155                  |  | 3.4  | 1.6                 | 0.0                 | 16.8  | 16.0  |       |              |                     |                     |                     |                     |
| 50161                  |  | 3.1  | 1.1                 | 0.0                 | 17.3  | 16.3  |       |              |                     |                     |                     |                     |
| n                      |  | 5  | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |
| Mean                   |  | 2.98   | 0.94                | 0.00                | 17.00 | 16.46 |       |              |                     |                     |                     |                     |
| S.D.                   |  | 0.42   | 0.43                | 0.00                | 0.40  | 0.64  |       |              |                     |                     |                     |                     |

| Hematological findings<br>Sex : Female |  | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 50 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |
|--|--|---|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|
|  |  | RBC   | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |
| Animal No.                             |  | 10 <sup>4</sup> /µL   | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| 50251                                  |  | 745   | 13.6                | 39.5                | 53.0  | 18.3  | 34.4  | 8.24         | 157.8               | 84.1                | 22.7                | 58.3                |
| 50252                                  |  | 664   | 13.6                | 39.7                | 59.8  | 20.5  | 34.3  | 11.78        | 134.1               | 105.1               | 36.6                | 65.8                |
| 50253                                  |  | 698   | 13.5                | 39.1                | 56.0  | 19.3  | 34.5  | 9.22         | 122.4               | 85.7                | 34.6                | 49.1                |
| 50256                                  |  | 740   | 14.7                | 42.6                | 57.6  | 19.9  | 34.5  | 8.14         | 131.4               | 81.9                | 23.7                | 55.4                |
| 50258                                  |  | 780   | 14.2                | 40.4                | 51.8  | 18.2  | 35.1  | 5.56         | 119.4               | 93.4                | 31.9                | 57.8                |
| n                                      |  | 5   | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |
| Mean                                   |  | 725.4   | 13.92               | 40.26               | 55.64 | 19.24 | 34.56 | 8.588        | 133.02              | 90.04               | 29.90               | 57.28               |
| S.D.                                   |  | 45.0  | 0.52                | 1.39                | 3.28  | 1.00  | 0.31  | 2.240        | 15.13               | 9.47                | 6.35                | 6.01                |
|  |  |   |                     |                     |       |       |       |              |                     |                     |                     |                     |
| Monocyte                               |  | Eosinophil  | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |
| Animal No.                             |  | 10 <sup>2</sup> /µL   | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |
| 50251                                  |  | 2.6   | 0.5                 | 0.0                 | 17.9  | 16.3  |       |              |                     |                     |                     |                     |
| 50252                                  |  | 2.3   | 0.4                 | 0.0                 | 17.4  | 17.0  |       |              |                     |                     |                     |                     |
| 50253                                  |  | 1.4   | 0.6                 | 0.0                 | 17.9  | 17.9  |       |              |                     |                     |                     |                     |
| 50256                                  |  | 2.0   | 0.8                 | 0.0                 | 16.6  | 15.5  |       |              |                     |                     |                     |                     |
| 50258                                  |  | 3.1   | 0.6                 | 0.0                 | 18.6  | 17.2  |       |              |                     |                     |                     |                     |
| n                                      |  | 5   | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |
| Mean                                   |  | 2.28  | 0.58                | 0.00                | 17.68 | 16.78 |       |              |                     |                     |                     |                     |
| S.D.                                   |  | 0.64  | 0.15                | 0.00                | 0.74  | 0.91  |       |              |                     |                     |                     |                     |

| Hematological findings |  | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 200 mg/kg |                     |                     |       |       |       |              | Species : Rat       |                     |                     |                     |  |  |
|------------------------|--|--|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|--|
| Sex : Female           |  | RBC  | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |  |
| Animal No.             |  | 10 <sup>4</sup> /µL  | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |  |
| 50353                  |  | 764  | 14.1                | 39.7                | 52.0  | 18.5  | 35.5  | 5.34         | 119.7               | 61.7                | 27.0                | 32.5                |  |  |
| 50354                  |  | 644  | 13.3                | 38.9                | 60.4  | 20.7  | 34.2  | 12.46        | 129.9               | 103.5               | 31.8                | 67.4                |  |  |
| 50355                  |  | 613  | 12.4                | 37.4                | 61.0  | 20.2  | 33.2  | 12.96        | 113.9               | 82.4                | 29.8                | 51.6                |  |  |
| 50360                  |  | 710  | 13.8                | 40.6                | 57.2  | 19.4  | 34.0  | 7.24         | 103.7               | 42.1                | 17.6                | 22.5                |  |  |
| 50362                  |  | 567  | 11.6                | 35.4                | 62.4  | 20.5  | 32.8  | 13.08        | 117.0               | 96.3                | 43.7                | 48.8                |  |  |
| n                      |  | 5  | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |  |
| Mean                   |  | 659.6  | 13.04               | 38.40               | 58.60 | 19.86 | 33.94 | 10.216       | 116.84              | 77.20               | 29.98               | 44.56               |  |  |
| S.D.                   |  | 78.1   | 1.03                | 2.05                | 4.15  | 0.91  | 1.04  | 3.654        | 9.49                | 25.28               | 9.40                | 17.47               |  |  |
|                        |  |  |                     |                     |       |       |       |              |                     |                     |                     |                     |  |  |
| Monocyte               |  | Eosinophil   | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |  |
| Animal No.             |  | 10 <sup>2</sup> /µL  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |  |
| 50353                  |  | 1.9  | 0.3                 | 0.0                 | 17.6  | 18.5  |       |              |                     |                     |                     |                     |  |  |
| 50354                  |  | 3.2  | 1.1                 | 0.0                 | 15.7  | 15.2  |       |              |                     |                     |                     |                     |  |  |
| 50355                  |  | 0.8  | 0.2                 | 0.0                 | 18.0  | 16.9  |       |              |                     |                     |                     |                     |  |  |
| 50360                  |  | 1.7  | 0.3                 | 0.0                 | 17.8  | 17.6  |       |              |                     |                     |                     |                     |  |  |
| 50362                  |  | 2.9  | 0.9                 | 0.0                 | 15.8  | 17.4  |       |              |                     |                     |                     |                     |  |  |
| n                      |  | 5  | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |  |
| Mean                   |  | 2.10   | 0.56                | 0.00                | 16.98 | 17.12 |       |              |                     |                     |                     |                     |  |  |
| S.D.                   |  | 0.97   | 0.41                | 0.00                | 1.13  | 1.22  |       |              |                     |                     |                     |                     |  |  |

| Hematological findings<br>Sex : Female |  | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 800 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |
|--|--|--|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|
|  |  | RBC  | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |
| Animal No.                             |  | 10 <sup>4</sup> /µL  | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| 50451                                  |  | 683  | 12.5                | 36.3                | 53.1  | 18.3  | 34.4  | 7.25         | 118.2               | 80.7                | 25.9                | 53.5                |
| 50452                                  |  | 745  | 13.9                | 39.7                | 53.3  | 18.7  | 35.0  | 6.19         | 138.1               | 171.4               | 39.8                | 126.5               |
| 50454                                  |  | 749  | 13.4                | 38.1                | 50.9  | 17.9  | 35.2  | 6.03         | 117.6               | 64.1                | 27.5                | 34.6                |
| 50457                                  |  | 722  | 13.8                | 40.3                | 55.8  | 19.1  | 34.2  | 7.31         | 123.0               | 71.8                | 28.4                | 40.4                |
| 50461                                  |  | 688  | 12.9                | 38.0                | 55.2  | 18.8  | 33.9  | 7.22         | 108.7               | 98.2                | 45.9                | 48.9                |
| n                                      |  | 5  | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |
| Mean                                   |  | 717.4  | 13.30               | 38.48               | 53.66 | 18.56 | 34.54 | 6.800        | 121.12              | 97.24               | 33.50               | 60.78               |
| S.D.                                   |  | 30.9   | 0.60                | 1.58                | 1.94  | 0.47  | 0.55  | 0.633        | 10.81               | 43.36               | 8.85                | 37.46               |
|  |  |  |                     |                     |       |       |       |              |                     |                     |                     |                     |
| Monocyte                               |  | Eosinophil   | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |
| Animal No.                             |  | 10 <sup>2</sup> /µL  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |
| 50451                                  |  | 0.8  | 0.5                 | 0.0                 | 17.9  | 18.1  |       |              |                     |                     |                     |                     |
| 50452                                  |  | 3.4  | 1.6                 | 0.1                 | 17.3  | 17.3  |       |              |                     |                     |                     |                     |
| 50454                                  |  | 1.7  | 0.3                 | 0.0                 | 18.1  | 17.0  |       |              |                     |                     |                     |                     |
| 50457                                  |  | 2.2  | 0.8                 | 0.0                 | 17.6  | 14.5  |       |              |                     |                     |                     |                     |
| 50461                                  |  | 2.1  | 1.3                 | 0.0                 | 16.6  | 17.0  |       |              |                     |                     |                     |                     |
| n                                      |  | 5  | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |
| Mean                                   |  | 2.04   | 0.90                | 0.02                | 17.50 | 16.78 |       |              |                     |                     |                     |                     |
| S.D.                                   |  | 0.94   | 0.54                | 0.04                | 0.59  | 1.35  |       |              |                     |                     |                     |                     |

| Hematological findings<br>Sex : Female (satellite) |  | Stage : Day 29<br>Dose : PTSA Monohydrate 0 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |  |
|--|--|---|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|
|  |  | RBC   | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |
| Animal No.   |  | 10 <sup>4</sup> /µL                               | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |
| 50551  |  | 798   | 14.8                | 40.5                | 50.8  | 18.5  | 36.5  | 2.40         | 105.1               | 28.6                | 4.3                 | 23.2                |  |
| 50552  |  | 827   | 15.0                | 41.7                | 50.4  | 18.1  | 36.0  | 3.12         | 136.8               | 30.6                | 4.4                 | 25.3                |  |
| 50553  |  | 809   | 14.6                | 40.7                | 50.3  | 18.0  | 35.9  | 3.59         | 150.8               | 36.9                | 7.7                 | 27.0                |  |
| 50554  |  | 848   | 16.0                | 44.5                | 52.5  | 18.9  | 36.0  | 3.79         | 118.3               | 35.3                | 6.4                 | 26.4                |  |
| 50555  |  | 857   | 15.2                | 42.3                | 49.4  | 17.7  | 35.9  | 2.76         | 128.5               | 37.6                | 10.4                | 25.0                |  |
| n  |  | 5   | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |
| Mean   |  | 827.8   | 15.12               | 41.94               | 50.68 | 18.24 | 36.06 | 3.132        | 127.90              | 33.80               | 6.64                | 25.38               |  |
| S.D.   |  | 25.0  | 0.54                | 1.61                | 1.14  | 0.47  | 0.25  | 0.574        | 17.44               | 3.99                | 2.54                | 1.46                |  |
|  |  |   |                     |                     |       |       |       |              |                     |                     |                     |                     |  |
| Monocyte   |  | Eosinophil  | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |
| Animal No.   |  | 10 <sup>2</sup> /µL                               | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |
| 50551  |  | 0.7   | 0.4                 | 0.0                 | 17.1  | 15.1  |       |              |                     |                     |                     |                     |  |
| 50552  |  | 0.6   | 0.3                 | 0.0                 | 16.9  | 15.9  |       |              |                     |                     |                     |                     |  |
| 50553  |  | 1.6   | 0.6                 | 0.0                 | 17.9  | 15.5  |       |              |                     |                     |                     |                     |  |
| 50554  |  | 1.5   | 1.0                 | 0.0                 | 17.3  | 14.4  |       |              |                     |                     |                     |                     |  |
| 50555  |  | 1.4   | 0.8                 | 0.0                 | 15.2  | 13.4  |       |              |                     |                     |                     |                     |  |
| n  |  | 5   | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |
| Mean   |  | 1.16  | 0.62                | 0.00                | 16.88 | 14.86 |       |              |                     |                     |                     |                     |  |
| S.D.   |  | 0.47  | 0.29                | 0.00                | 1.01  | 0.99  |       |              |                     |                     |                     |                     |  |

| Hematological findings<br>Sex : Female (satellite) |  | Stage : Day 29<br>Dose : PTSA Monohydrate 800 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |  |
|--|--|---|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|
|  |  | RBC   | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |
| Animal No.   |  | 10 <sup>4</sup> /µL                                 | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |
| 50651  |  | 849   | 15.9                | 45.2                | 53.2  | 18.7  | 35.2  | 2.82         | 123.6               | 25.9                | 4.8                 | 19.8                |  |
| 50652  |  | 756   | 14.4                | 40.1                | 53.0  | 19.0  | 35.9  | 3.54         | 117.5               | 59.6                | 5.4                 | 52.6                |  |
| 50653  |  | 825   | 14.8                | 41.3                | 50.1  | 17.9  | 35.8  | 3.77         | 138.7               | 31.6                | 6.9                 | 22.4                |  |
| 50654  |  | 784   | 14.3                | 39.9                | 50.9  | 18.2  | 35.8  | 3.61         | 111.0               | 58.1                | 10.4                | 45.3                |  |
| 50655  |  | 705   | 13.5                | 38.1                | 54.0  | 19.1  | 35.4  | 4.24         | 152.4               | 55.5                | 14.6                | 36.9                |  |
| n  |  | 5   | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |
| Mean   |  | 783.8   | 14.58               | 40.92               | 52.24 | 18.58 | 35.62 | 3.596        | 128.64              | 46.14               | 8.42                | 35.40               |  |
| S.D.   |  | 56.9  | 0.88                | 2.65                | 1.66  | 0.52  | 0.30  | 0.512        | 16.78               | 16.07               | 4.08                | 14.22               |  |
|  |  |   |                     |                     |       |       |       |              |                     |                     |                     |                     |  |
| Monocyte   |  | Eosinophil  | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |
| Animal No.   |  | 10 <sup>2</sup> /µL                                 | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |
| 50651  |  | 0.9   | 0.4                 | 0.0                 | 16.5  | 15.3  |       |              |                     |                     |                     |                     |  |
| 50652  |  | 1.3   | 0.3                 | 0.0                 | 15.2  | 18.1  |       |              |                     |                     |                     |                     |  |
| 50653  |  | 1.6   | 0.7                 | 0.0                 | 15.6  | 14.4  |       |              |                     |                     |                     |                     |  |
| 50654  |  | 1.8   | 0.6                 | 0.0                 | 15.5  | 17.2  |       |              |                     |                     |                     |                     |  |
| 50655  |  | 2.3   | 1.7                 | 0.0                 | 15.0  | 17.7  |       |              |                     |                     |                     |                     |  |
| n  |  | 5   | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |
| Mean   |  | 1.58  | 0.74                | 0.00                | 15.56 | 16.54 |       |              |                     |                     |                     |                     |  |
| S.D.   |  | 0.53  | 0.56                | 0.00                | 0.58  | 1.61  |       |              |                     |                     |                     |                     |  |

| Hematological findings |  | Stage : Recovery Day 15 |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |  |  |
|------------------------|--|-------------------------|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|--|
| Sex : Male             |  | RBC                     | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |  |
| Animal No.             |  | 10 <sup>4</sup> /µL     | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |  |
| 10103                  |  | 966                     | 16.1                | 44.9                | 46.5  | 16.7  | 35.9  | 2.65         | 129.5               | 57.0                | 11.2                | 41.4                |  |  |
| 10104                  |  | 971                     | 17.3                | 48.8                | 50.3  | 17.8  | 35.5  | 2.21         | 108.7               | 67.3                | 21.6                | 41.2                |  |  |
| 10105                  |  | 885                     | 15.6                | 43.3                | 48.9  | 17.6  | 36.0  | 3.08         | 132.0               | 79.6                | 14.0                | 60.0                |  |  |
| 10106                  |  | 874                     | 15.1                | 43.0                | 49.2  | 17.3  | 35.1  | 3.57         | 110.8               | 82.5                | 15.4                | 62.4                |  |  |
| 10111                  |  | 922                     | 16.2                | 45.1                | 48.9  | 17.6  | 35.9  | 2.94         | 122.7               | 49.0                | 13.1                | 32.9                |  |  |
| n                      |  | 5                       | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |  |
| Mean                   |  | 923.6                   | 16.06               | 45.02               | 48.76 | 17.40 | 35.68 | 2.890        | 120.74              | 67.08               | 15.06               | 47.58               |  |  |
| S.D.                   |  | 44.7                    | 0.82                | 2.31                | 1.39  | 0.43  | 0.38  | 0.505        | 10.62               | 14.34               | 3.96                | 12.93               |  |  |
|                        |  |                         |                     |                     |       |       |       |              |                     |                     |                     |                     |  |  |
| Monocyte               |  | Eosinophil              | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |  |
| Animal No.             |  | 10 <sup>2</sup> /µL     | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |  |
| 10103                  |  | 3.1                     | 1.3                 | 0.0                 | 22.5  | 23.7  |       |              |                     |                     |                     |                     |  |  |
| 10104                  |  | 3.6                     | 0.9                 | 0.0                 | 22.3  | 20.9  |       |              |                     |                     |                     |                     |  |  |
| 10105                  |  | 3.9                     | 1.7                 | 0.0                 | 30.5  | 25.9  |       |              |                     |                     |                     |                     |  |  |
| 10106                  |  | 2.4                     | 2.3                 | 0.0                 | 21.7  | 25.4  |       |              |                     |                     |                     |                     |  |  |
| 10111                  |  | 1.9                     | 1.1                 | 0.0                 | 21.2  | 23.6  |       |              |                     |                     |                     |                     |  |  |
| n                      |  | 5                       | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |  |
| Mean                   |  | 2.98                    | 1.46                | 0.00                | 23.64 | 23.90 |       |              |                     |                     |                     |                     |  |  |
| S.D.                   |  | 0.83                    | 0.55                | 0.00                | 3.87  | 1.96  |       |              |                     |                     |                     |                     |  |  |

| Hematological findings<br>Sex : Male |                                 |                                   |                                 | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 800 mg/kg |       |       |                   |                                 |                            | Species : Rat                     |                                   |
|--------------------------------------|---------------------------------|-----------------------------------|---------------------------------|--|-------|-------|-------------------|---------------------------------|----------------------------|-----------------------------------|-----------------------------------|
|                                      | RBC<br>10 <sup>4</sup> /µL      | HGB<br>g/dL                       | HCT<br>%                        | MCV  | MCH   | MCHC  | Reticulocyte<br>% | Platelet<br>10 <sup>4</sup> /µL | WBC<br>10 <sup>2</sup> /µL | Neutrophil<br>10 <sup>2</sup> /µL | Lymphocyte<br>10 <sup>2</sup> /µL |
| Animal No.                           |                                 |                                   |                                 |  |       |       |                   |                                 |                            |                                   |                                   |
| 10402                                | 896                             | 15.6                              | 43.8                            | 48.9   | 17.4  | 35.6  | 3.02              | 115.3                           | 119.4                      | 24.0                              | 88.9                              |
| 10403                                | 898                             | 16.5                              | 46.5                            | 51.8   | 18.4  | 35.5  | 3.12              | 129.9                           | 69.5                       | 9.0                               | 55.5                              |
| 10407                                | 862                             | 15.6                              | 44.0                            | 51.0   | 18.1  | 35.5  | 2.92              | 118.2                           | 62.1                       | 14.6                              | 43.4                              |
| 10409                                | 862                             | 15.6                              | 44.2                            | 51.3   | 18.1  | 35.3  | 3.00              | 116.7                           | 58.3                       | 10.1                              | 44.7                              |
| 10411                                | 914                             | 15.7                              | 43.9                            | 48.0   | 17.2  | 35.8  | 3.21              | 143.3                           | 97.2                       | 27.0                              | 63.1                              |
| n                                    | 5                               | 5                                 | 5                               | 5  | 5     | 5     | 5                 | 5                               | 5                          | 5                                 | 5                                 |
| Mean                                 | 886.4                           | 15.80                             | 44.48                           | 50.20  | 17.84 | 35.54 | 3.054             | 124.68                          | 81.30                      | 16.94                             | 59.12                             |
| S.D.                                 | 23.3                            | 0.39                              | 1.14                            | 1.65   | 0.51  | 0.18  | 0.113             | 11.91                           | 26.18                      | 8.16                              | 18.51                             |
| <hr/>                                |                                 |                                   |                                 |  |       |       |                   |                                 |                            |                                   |                                   |
|                                      | Monocyte<br>10 <sup>2</sup> /µL | Eosinophil<br>10 <sup>2</sup> /µL | Basophil<br>10 <sup>2</sup> /µL | PT<br>sec  | APTT  |       |                   |                                 |                            |                                   |                                   |
| Animal No.                           |                                 |                                   |                                 |  |       |       |                   |                                 |                            |                                   |                                   |
| 10402                                | 4.5                             | 1.9                               | 0.1                             | 23.0   |       |       |                   |                                 |                            |                                   |                                   |
| 10403                                | 3.1                             | 1.9                               | 0.0                             | 29.3   |       |       |                   |                                 |                            |                                   |                                   |
| 10407                                | 2.4                             | 1.7                               | 0.0                             | 21.5   |       |       |                   |                                 |                            |                                   |                                   |
| 10409                                | 2.3                             | 1.2                               | 0.0                             | 22.3   |       |       |                   |                                 |                            |                                   |                                   |
| 10411                                | 4.8                             | 2.3                               | 0.0                             | 27.1   |       |       |                   |                                 |                            |                                   |                                   |
| n                                    | 5                               | 5                                 | 5                               | 5  |       |       |                   |                                 |                            |                                   |                                   |
| Mean                                 | 3.42                            | 1.80                              | 0.02                            | 24.64  |       |       |                   |                                 |                            |                                   |                                   |
| S.D.                                 | 1.17                            | 0.40                              | 0.04                            | 3.38   |       |       |                   |                                 |                            |                                   |                                   |

| Hematological findings<br>Sex : Female (satellite) |  | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 0 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |  |
|--|--|--|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|--|
|  |  | RBC  | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |  |
| Animal No.   |  | 10 <sup>4</sup> /µL  | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |  |
| 50556  |  | 902  | 16.4                | 45.9                | 50.9  | 18.2  | 35.7  | 2.88         | 116.9               | 73.5                | 7.6                 | 63.6                |  |
| 50557  |  | 864  | 15.7                | 44.9                | 52.0  | 18.2  | 35.0  | 3.20         | 119.1               | 53.2                | 3.1                 | 47.8                |  |
| 50558  |  | 829  | 15.9                | 46.1                | 55.6  | 19.2  | 34.5  | 1.50         | 120.1               | 60.9                | 11.6                | 44.9                |  |
| 50559  |  | 814  | 15.9                | 44.5                | 54.7  | 19.5  | 35.7  | 2.32         | 104.1               | 44.3                | 6.9                 | 35.4                |  |
| 50560  |  | 792  | 14.3                | 40.0                | 50.5  | 18.1  | 35.8  | 2.82         | 138.8               | 32.2                | 4.0                 | 25.7                |  |
| n  |  | 5  | 5                   | 5                   | 5     | 5     | 5     | 5            | 5                   | 5                   | 5                   | 5                   |  |
| Mean   |  | 840.2  | 15.64               | 44.28               | 52.74 | 18.64 | 35.34 | 2.544        | 119.80              | 52.82               | 6.64                | 43.48               |  |
| S.D.   |  | 43.4   | 0.79                | 2.48                | 2.29  | 0.66  | 0.57  | 0.663        | 12.41               | 15.74               | 3.36                | 14.20               |  |
|  |  |  |                     |                     |       |       |       |              |                     |                     |                     |                     |  |
| Monocyte   |  | Eosinophil   | Basophil            | PT                  | APTT  |       |       |              |                     |                     |                     |                     |  |
| Animal No.   |  | 10 <sup>2</sup> /µL  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |  |
| 50556  |  | 1.9  | 0.4                 | 0.0                 | 14.6  | 15.5  |       |              |                     |                     |                     |                     |  |
| 50557  |  | 1.2  | 1.1                 | 0.0                 | 14.3  | 15.3  |       |              |                     |                     |                     |                     |  |
| 50558  |  | 2.8  | 1.6                 | 0.0                 | 14.7  | 19.8  |       |              |                     |                     |                     |                     |  |
| 50559  |  | 1.3  | 0.7                 | 0.0                 | 15.4  | 18.0  |       |              |                     |                     |                     |                     |  |
| 50560  |  | 1.4  | 1.1                 | 0.0                 | 15.2  | 14.8  |       |              |                     |                     |                     |                     |  |
| n  |  | 5  | 5                   | 5                   | 5     | 5     |       |              |                     |                     |                     |                     |  |
| Mean   |  | 1.72   | 0.98                | 0.00                | 14.84 | 16.68 |       |              |                     |                     |                     |                     |  |
| S.D.   |  | 0.66   | 0.45                | 0.00                | 0.45  | 2.14  |       |              |                     |                     |                     |                     |  |

| Hematological findings<br>Sex : Female (satellite) |  | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 800 mg/kg |                     |                     |       |       |       |              |                     | Species : Rat       |                     |                     |
|--|--|--|---------------------|---------------------|-------|-------|-------|--------------|---------------------|---------------------|---------------------|---------------------|
|  |  | RBC  | HGB                 | HCT                 | MCV   | MCH   | MCHC  | Reticulocyte | Platelet            | WBC                 | Neutrophil          | Lymphocyte          |
| Animal No.   |  | 10 <sup>4</sup> /µL  | g/dL                | %                   | fL    | pg    | g/dL  | %            | 10 <sup>4</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL |
| 50656  |  | 859  | 15.3                | 42.5                | 49.5  | 17.8  | 36.0  | 2.43         | 116.3               | 63.4                | 10.3                | 49.9                |
| 50657  |  | 891  | 15.6                | 43.9                | 49.3  | 17.5  | 35.5  | 3.38         | 113.9               | 39.9                | 9.2                 | 28.2                |
| 50658  |  | 833  | 15.6                | 43.8                | 52.6  | 18.7  | 35.6  | 3.13         | 119.9               | 71.9                | 5.0                 | 64.6                |
| 50659  |  | 813  | 14.7                | 40.8                | 50.2  | 18.1  | 36.0  | 2.25         | 132.6               | 39.8                | 4.1                 | 34.2                |
| n  |  | 4  | 4                   | 4                   | 4     | 4     | 4     | 4            | 4                   | 4                   | 4                   | 4                   |
| Mean   |  | 849.0  | 15.30               | 42.75               | 50.40 | 18.03 | 35.78 | 2.798        | 120.68              | 53.75               | 7.15                | 44.23               |
| S.D.   |  | 33.7   | 0.42                | 1.45                | 1.52  | 0.51  | 0.26  | 0.543        | 8.32                | 16.42               | 3.06                | 16.38               |
| <hr/>  |  |  |                     |                     |       |       |       |              |                     |                     |                     |                     |
|  |  | Monocyte   | Eosinophil          | Basophil            | PT    | APTT  |       |              |                     |                     |                     |                     |
| Animal No.   |  | 10 <sup>2</sup> /µL  | 10 <sup>2</sup> /µL | 10 <sup>2</sup> /µL | sec   | sec   |       |              |                     |                     |                     |                     |
| 50656  |  | 2.1  | 1.1                 | 0.0                 | 16.6  | 16.1  |       |              |                     |                     |                     |                     |
| 50657  |  | 1.5  | 1.0                 | 0.0                 | 17.3  | 13.4  |       |              |                     |                     |                     |                     |
| 50658  |  | 1.6  | 0.7                 | 0.0                 | 14.7  | 16.1  |       |              |                     |                     |                     |                     |
| 50659  |  | 0.8  | 0.7                 | 0.0                 | 13.9  | 15.6  |       |              |                     |                     |                     |                     |
| n  |  | 4  | 4                   | 4                   | 4     | 4     |       |              |                     |                     |                     |                     |
| Mean   |  | 1.50   | 0.88                | 0.00                | 15.63 | 15.30 |       |              |                     |                     |                     |                     |
| S.D.   |  | 0.54   | 0.21                | 0.00                | 1.59  | 1.29  |       |              |                     |                     |                     |                     |

| Biochemical findings |       |   |       |       |       |        |         |         |         | Species : Rat |       |  |
|----------------------|-------|---|-------|-------|-------|--------|---------|---------|---------|---------------|-------|--|
| Sex : Male           |       | Stage : Day 29<br>Dose : PTSA Monohydrate 0 mg/kg |       |       |       |        |         |         |         |               |       |  |
|                      | AST   | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho   | TG      | TP            | UN    |  |
| Animal No.           | IU/L  | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL   | mg/dL   | g/dL          | mg/dL |  |
| 10101                | 65    | 30  | 451   | 0.5   | 0.08  | 20.2   | 154     | 62      | 69      | 5.2           | 13.7  |  |
| 10102                | 68    | 29  | 505   | 0.5   | 0.05  | 5.7    | 151     | 35      | 37      | 4.8           | 15.0  |  |
| 10107                | 58    | 27  | 406   | 0.3   | 0.05  | 11.4   | 145     | 37      | 32      | 5.0           | 17.8  |  |
| 10108                | 54    | 23  | 451   | 0.0   | 0.06  | 6.4    | 130     | 44      | 13      | 5.0           | 16.9  |  |
| 10109                | 53    | 27  | 305   | 0.1   | 0.04  | 3.3    | 149     | 51      | 27      | 5.2           | 11.0  |  |
| n                    | 5     | 5   | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |  |
| Mean                 | 59.6  | 27.2  | 423.6 | 0.28  | 0.056 | 9.40   | 145.8   | 45.8    | 35.6    | 5.04          | 14.88 |  |
| S.D.                 | 6.7   | 2.7   | 75.0  | 0.23  | 0.015 | 6.72   | 9.4     | 11.0    | 20.7    | 0.17          | 2.70  |  |
|                      |       |   |       |       |       |        |         |         |         |               |       |  |
| Crea                 |       | Na  | K     | Cl    | Ca    | IP     | A/G     | Albumin | Albumin | α1-G          | α2-G  |  |
| Animal No.           | mg/dL | mEq/L   | mEq/L | mEq/L | mg/dL | mg/dL  |         | g/dL    | %       | %             | %     |  |
| 10101                | 0.30  | 143   | 4.11  | 103   | 9.2   | 6.6    | 1.21    | 2.85    | 54.9    | 15.7          | 8.3   |  |
| 10102                | 0.33  | 145   | 3.99  | 107   | 9.1   | 7.5    | 1.07    | 2.49    | 51.8    | 21.9          | 6.8   |  |
| 10107                | 0.36  | 145   | 4.29  | 106   | 9.5   | 8.3    | 1.01    | 2.52    | 50.3    | 23.1          | 6.4   |  |
| 10108                | 0.29  | 146   | 4.01  | 108   | 9.3   | 8.7    | 1.11    | 2.63    | 52.6    | 19.5          | 7.9   |  |
| 10109                | 0.27  | 145   | 4.22  | 105   | 9.9   | 8.1    | 0.88    | 2.43    | 46.8    | 26.0          | 7.0   |  |
| n                    | 5     | 5   | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |  |
| Mean                 | 0.310 | 144.8   | 4.124 | 105.8 | 9.40  | 7.84   | 1.056   | 2.584   | 51.28   | 21.24         | 7.28  |  |
| S.D.                 | 0.035 | 1.1   | 0.130 | 1.9   | 0.32  | 0.82   | 0.122   | 0.165   | 3.01    | 3.88          | 0.79  |  |
|                      |       |   |       |       |       |        |         |         |         |               |       |  |
| β-G                  |       | γ-G   |       |       |       |        |         |         |         |               |       |  |
| Animal No.           | %     | %   |       |       |       |        |         |         |         |               |       |  |
| 10101                | 17.2  | 3.9   |       |       |       |        |         |         |         |               |       |  |
| 10102                | 15.8  | 3.7   |       |       |       |        |         |         |         |               |       |  |
| 10107                | 15.5  | 4.7   |       |       |       |        |         |         |         |               |       |  |
| 10108                | 16.1  | 3.9   |       |       |       |        |         |         |         |               |       |  |
| 10109                | 16.6  | 3.6   |       |       |       |        |         |         |         |               |       |  |
| n                    | 5     | 5   |       |       |       |        |         |         |         |               |       |  |
| Mean                 | 16.24 | 3.96  |       |       |       |        |         |         |         |               |       |  |
| S.D.                 | 0.67  | 0.43  |       |       |       |        |         |         |         |               |       |  |

| Biochemical findings |       |  |       |       |       |        |         |         |         | Species : Rat |       |
|----------------------|-------|--|-------|-------|-------|--------|---------|---------|---------|---------------|-------|
| Sex : Male           |       | Stage : Day 29<br>Dose : PTSA Monohydrate 50 mg/kg |       |       |       |        |         |         |         |               |       |
|                      | AST   | ALT  | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho   | TG      | TP            | UN    |
| Animal No.           | IU/L  | IU/L   | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL   | mg/dL   | g/dL          | mg/dL |
| 10201                | 65    | 36   | 692   | 0.4   | 0.06  | 5.7    | 131     | 34      | 28      | 5.3           | 13.6  |
| 10203                | 59    | 29   | 462   | 0.3   | 0.05  | 4.0    | 144     | 44      | 39      | 5.1           | 13.2  |
| 10205                | 139   | 28   | 429   | 0.2   | 0.05  | 4.2    | 141     | 53      | 25      | 4.9           | 13.8  |
| 10206                | 64    | 28   | 485   | 0.0   | 0.05  | 15.2   | 138     | 29      | 15      | 5.1           | 14.7  |
| 10208                | 62    | 26   | 366   | 0.3   | 0.07  | 2.7    | 152     | 35      | 13      | 5.0           | 14.2  |
| n                    | 5     | 5  | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |
| Mean                 | 77.8  | 29.4   | 486.8 | 0.24  | 0.056 | 6.36   | 141.2   | 39.0    | 24.0    | 5.08          | 13.90 |
| S.D.                 | 34.3  | 3.8  | 123.1 | 0.15  | 0.009 | 5.05   | 7.7     | 9.5     | 10.5    | 0.15          | 0.57  |
|                      |       |  |       |       |       |        |         |         |         |               |       |
|                      | Crea  | Na   | K     | Cl    | Ca    | IP     | A/G     | Albumin | Albumin | α1-G          | α2-G  |
| Animal No.           | mg/dL | mEq/L  | mEq/L | mEq/L | mg/dL | mg/dL  |         | g/dL    | %       | %             | %     |
| 10201                | 0.29  | 144  | 4.18  | 106   | 9.3   | 6.6    | 1.08    | 2.76    | 52.0    | 22.9          | 6.7   |
| 10203                | 0.27  | 144  | 3.98  | 105   | 9.2   | 7.6    | 0.97    | 2.50    | 49.1    | 23.0          | 6.7   |
| 10205                | 0.26  | 145  | 3.97  | 106   | 9.4   | 7.3    | 1.01    | 2.46    | 50.2    | 19.8          | 7.9   |
| 10206                | 0.32  | 147  | 4.11  | 108   | 9.3   | 7.7    | 1.06    | 2.62    | 51.3    | 22.3          | 7.4   |
| 10208                | 0.27  | 147  | 4.03  | 107   | 9.1   | 7.7    | 1.01    | 2.52    | 50.3    | 24.6          | 6.5   |
| n                    | 5     | 5  | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |
| Mean                 | 0.282 | 145.4  | 4.054 | 106.4 | 9.26  | 7.38   | 1.026   | 2.572   | 50.58   | 22.52         | 7.04  |
| S.D.                 | 0.024 | 1.5  | 0.090 | 1.1   | 0.11  | 0.47   | 0.044   | 0.120   | 1.11    | 1.74          | 0.59  |
|                      |       |  |       |       |       |        |         |         |         |               |       |
|                      | β-G   | γ-G  |       |       |       |        |         |         |         |               |       |
| Animal No.           | %     | %  |       |       |       |        |         |         |         |               |       |
| 10201                | 14.2  | 4.2  |       |       |       |        |         |         |         |               |       |
| 10203                | 15.9  | 5.3  |       |       |       |        |         |         |         |               |       |
| 10205                | 17.8  | 4.3  |       |       |       |        |         |         |         |               |       |
| 10206                | 14.8  | 4.2  |       |       |       |        |         |         |         |               |       |
| 10208                | 15.1  | 3.5  |       |       |       |        |         |         |         |               |       |
| n                    | 5     | 5  |       |       |       |        |         |         |         |               |       |
| Mean                 | 15.56 | 4.30   |       |       |       |        |         |         |         |               |       |
| S.D.                 | 1.39  | 0.64   |       |       |       |        |         |         |         |               |       |

| Biochemical findings   |       |   |       |       |       |        |         |       |       | Species : Rat |       |
|--|-------|---|-------|-------|-------|--------|---------|-------|-------|---------------|-------|
| Sex : Male   |       | Stage : Day 29<br>Dose : PTSA Monohydrate 200 mg/kg |       |       |       |        |         |       |       |               |       |
|  | AST   | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho | TG    | TP            | UN    |
| Animal No.   | IU/L  | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL | mg/dL | g/dL          | mg/dL |
| 10301  | 103   | 34  | 420   | 0.3   | 0.09  | 7.3    | 161     | 46    | 37    | 5.2           | 12.9  |
| 10304  | 71    | 31  | 473   | 0.3   | 0.04  | 5.6    | 143     | 36    | 22    | 4.8           | 14.2  |
| 10306  | 57    | 31  | 462   | 0.2   | 0.05  | 3.6    | 144     | 49    | 70    | 5.3           | 13.7  |
| 10309  | 78    | 30  | 475   | 0.2   | 0.06  | 5.3    | 136     | 58    | 56    | 4.8           | 14.6  |
| 10310  | 64    | 31  | 487   | 0.1   | 0.05  | 6.1    | 154     | 38    | 29    | 5.4           | 14.0  |
| n  | 5     | 5   | 5     | 5     | 5     | 5      | 5       | 5     | 5     | 5             | 5     |
| Mean   | 74.6  | 31.4  | 463.4 | 0.22  | 0.058 | 5.58   | 147.6   | 45.4  | 42.8  | 5.10          | 13.88 |
| S.D.   | 17.7  | 1.5   | 25.8  | 0.08  | 0.019 | 1.34   | 9.9     | 8.9   | 19.8  | 0.28          | 0.64  |
|  |       |   |       |       |       |        |         |       |       |               |       |
| Crea      Na      K      Cl      Ca      IP      A/G      Albumin      Albumin      α1-G      α2-G |       |   |       |       |       |        |         |       |       |               |       |
| Animal No.   | mg/dL | mEq/L   | mEq/L | mEq/L | mg/dL | mg/dL  |         | g/dL  | %     | %             | %     |
| 10301  | 0.32  | 143   | 4.45  | 105   | 9.2   | 7.4    | 0.99    | 2.58  | 49.7  | 23.4          | 7.0   |
| 10304  | 0.30  | 144   | 3.85  | 105   | 9.1   | 7.6    | 1.10    | 2.51  | 52.3  | 20.8          | 7.5   |
| 10306  | 0.25  | 145   | 4.25  | 106   | 9.6   | 7.8    | 1.08    | 2.76  | 52.0  | 19.3          | 8.1   |
| 10309  | 0.31  | 146   | 4.16  | 108   | 9.3   | 7.6    | 1.17    | 2.59  | 53.9  | 16.6          | 8.1   |
| 10310  | 0.29  | 147   | 4.01  | 106   | 9.3   | 8.3    | 0.97    | 2.65  | 49.1  | 24.1          | 7.4   |
| n  | 5     | 5   | 5     | 5     | 5     | 5      | 5       | 5     | 5     | 5             | 5     |
| Mean   | 0.294 | 145.0   | 4.144 | 106.0 | 9.30  | 7.74   | 1.062   | 2.618 | 51.40 | 20.84         | 7.62  |
| S.D.   | 0.027 | 1.6   | 0.229 | 1.2   | 0.19  | 0.34   | 0.082   | 0.094 | 1.97  | 3.06          | 0.48  |
|  |       |   |       |       |       |        |         |       |       |               |       |
| β-G      γ-G   |       |   |       |       |       |        |         |       |       |               |       |
| Animal No.   | %     | %   |       |       |       |        |         |       |       |               |       |
| 10301  | 17.1  | 2.8   |       |       |       |        |         |       |       |               |       |
| 10304  | 15.5  | 3.9   |       |       |       |        |         |       |       |               |       |
| 10306  | 17.0  | 3.6   |       |       |       |        |         |       |       |               |       |
| 10309  | 17.0  | 4.4   |       |       |       |        |         |       |       |               |       |
| 10310  | 14.8  | 4.6   |       |       |       |        |         |       |       |               |       |
| n  | 5     | 5   |       |       |       |        |         |       |       |               |       |
| Mean   | 16.28 | 3.86  |       |       |       |        |         |       |       |               |       |
| S.D.   | 1.06  | 0.71  |       |       |       |        |         |       |       |               |       |

| Biochemical findings |       |   |       |       |       |        |         |         |         | Species : Rat |       |
|----------------------|-------|---|-------|-------|-------|--------|---------|---------|---------|---------------|-------|
| Sex : Male           |       | Stage : Day 29<br>Dose : PTSA Monohydrate 800 mg/kg |       |       |       |        |         |         |         |               |       |
|                      | AST   | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho   | TG      | TP            | UN    |
| Animal No.           | IU/L  | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL   | mg/dL   | g/dL          | mg/dL |
| 10401                | 83    | 48  | 651   | 0.5   | 0.06  | 6.0    | 147     | 74      | 25      | 4.9           | 15.6  |
| 10404                | 61    | 26  | 444   | 0.4   | 0.05  | 17.4   | 142     | 46      | 26      | 4.9           | 16.1  |
| 10405                | 76    | 44  | 399   | 0.9   | 0.06  | 3.8    | 134     | 57      | 41      | 4.9           | 14.6  |
| 10406                | 93    | 55  | 566   | 0.9   | 0.06  | 6.8    | 141     | 53      | 39      | 5.1           | 14.5  |
| 10408                | 60    | 24  | 368   | 0.0   | 0.07  | 4.4    | 126     | 54      | 36      | 5.0           | 11.9  |
| n                    | 5     | 5   | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |
| Mean                 | 74.6  | 39.4  | 485.6 | 0.54  | 0.060 | 7.68   | 138.0   | 56.8    | 33.4    | 4.96          | 14.54 |
| S.D.                 | 14.2  | 13.7  | 119.2 | 0.38  | 0.007 | 5.57   | 8.2     | 10.4    | 7.4     | 0.09          | 1.62  |
|                      |       |   |       |       |       |        |         |         |         |               |       |
|                      | Crea  | Na  | K     | Cl    | Ca    | IP     | A/G     | Albumin | Albumin | α1-G          | α2-G  |
| Animal No.           | mg/dL | mEq/L   | mEq/L | mEq/L | mg/dL | mg/dL  |         | g/dL    | %       | %             | %     |
| 10401                | 0.28  | 143   | 4.06  | 105   | 9.0   | 7.0    | 1.10    | 2.57    | 52.4    | 18.7          | 8.0   |
| 10404                | 0.27  | 143   | 4.45  | 107   | 9.2   | 7.6    | 1.14    | 2.61    | 53.3    | 17.8          | 8.2   |
| 10405                | 0.28  | 146   | 4.55  | 107   | 9.3   | 7.5    | 1.08    | 2.54    | 51.8    | 20.6          | 8.3   |
| 10406                | 0.25  | 145   | 4.32  | 106   | 9.6   | 8.0    | 1.13    | 2.71    | 53.2    | 17.0          | 8.3   |
| 10408                | 0.24  | 145   | 4.11  | 107   | 9.3   | 8.0    | 1.07    | 2.59    | 51.7    | 20.3          | 7.6   |
| n                    | 5     | 5   | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |
| Mean                 | 0.264 | 144.4   | 4.298 | 106.4 | 9.28  | 7.62   | 1.104   | 2.604   | 52.48   | 18.88         | 8.08  |
| S.D.                 | 0.018 | 1.3   | 0.212 | 0.9   | 0.22  | 0.41   | 0.030   | 0.065   | 0.75    | 1.56          | 0.29  |
|                      |       |   |       |       |       |        |         |         |         |               |       |
|                      | β-G   | γ-G   |       |       |       |        |         |         |         |               |       |
| Animal No.           | %     | %   |       |       |       |        |         |         |         |               |       |
| 10401                | 17.5  | 3.4   |       |       |       |        |         |         |         |               |       |
| 10404                | 16.6  | 4.1   |       |       |       |        |         |         |         |               |       |
| 10405                | 16.0  | 3.3   |       |       |       |        |         |         |         |               |       |
| 10406                | 18.3  | 3.2   |       |       |       |        |         |         |         |               |       |
| 10408                | 16.2  | 4.2   |       |       |       |        |         |         |         |               |       |
| n                    | 5     | 5   |       |       |       |        |         |         |         |               |       |
| Mean                 | 16.92 | 3.64  |       |       |       |        |         |         |         |               |       |
| S.D.                 | 0.96  | 0.47  |       |       |       |        |         |         |         |               |       |

| Biochemical findings<br>Sex : Female   |             |             |             |               |                |               |                  |                |             |            | Species : Rat |  |
|--|-------------|-------------|-------------|---------------|----------------|---------------|------------------|----------------|-------------|------------|---------------|--|
| Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 0 mg/kg                     |             |             |             |               |                |               |                  |                |             |            |               |  |
| Animal No.   | AST<br>IU/L | ALT<br>IU/L | ALP<br>IU/L | γ-GTP<br>IU/L | T-Bil<br>mg/dL | TBA<br>μmol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL | TG<br>mg/dL | TP<br>g/dL | UN<br>mg/dL   |  |
| 50151  | 173         | 54          | 240         | 0.1           | 0.07           | 5.3           | 132              | 50             | 44          | 5.8        | 18.9          |  |
| 50152  | 72          | 44          | 182         | 0.5           | 0.04           | 11.3          | 130              | 52             | 18          | 5.3        | 18.3          |  |
| 50153  | 87          | 59          | 276         | 0.1           | 0.06           | 9.7           | 130              | 61             | 44          | 5.9        | 23.1          |  |
| 50155  | 93          | 47          | 227         | 0.2           | 0.05           | 7.0           | 131              | 35             | 49          | 5.4        | 20.4          |  |
| 50161  | 87          | 58          | 169         | 0.1           | 0.06           | 23.6          | 116              | 63             | 55          | 5.6        | 22.7          |  |
| n  | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5          | 5             |  |
| Mean   | 102.4       | 52.4        | 218.8       | 0.20          | 0.056          | 11.38         | 127.8            | 52.2           | 42.0        | 5.60       | 20.68         |  |
| S.D.   | 40.2        | 6.7         | 43.7        | 0.17          | 0.011          | 7.22          | 6.6              | 11.1           | 14.2        | 0.25       | 2.17          |  |
| Crea<br>Na<br>K<br>Cl<br>Ca<br>IP<br>A/G<br>Albumin<br>Albumin<br>α1-G<br>α2-G |             |             |             |               |                |               |                  |                |             |            |               |  |
| Animal No.   | mg/dL       | mEq/L       | mEq/L       | mEq/L         | mg/dL          | mg/dL         | g/dL             | %              | %           | %          | %             |  |
| 50151  | 0.35        | 142         | 4.41        | 103           | 10.5           | 10.3          | 1.11             | 3.05           | 52.5        | 19.7       | 8.3           |  |
| 50152  | 0.39        | 143         | 4.18        | 105           | 10.1           | 9.5           | 0.95             | 2.59           | 48.9        | 21.4       | 7.6           |  |
| 50153  | 0.37        | 143         | 4.56        | 104           | 10.3           | 9.4           | 0.98             | 2.92           | 49.5        | 22.2       | 7.1           |  |
| 50155  | 0.38        | 143         | 4.00        | 105           | 10.2           | 10.6          | 1.15             | 2.88           | 53.4        | 15.0       | 9.6           |  |
| 50161  | 0.33        | 143         | 3.95        | 104           | 10.6           | 11.3          | 1.01             | 2.82           | 50.3        | 22.1       | 6.1           |  |
| n  | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5          | 5             |  |
| Mean   | 0.364       | 142.8       | 4.220       | 104.2         | 10.34          | 10.22         | 1.040            | 2.852          | 50.92       | 20.08      | 7.74          |  |
| S.D.   | 0.024       | 0.4         | 0.262       | 0.8           | 0.21           | 0.79          | 0.086            | 0.169          | 1.94        | 3.01       | 1.31          |  |
| β-G<br>γ-G   |             |             |             |               |                |               |                  |                |             |            |               |  |
| Animal No.   | %           | %           |             |               |                |               |                  |                |             |            |               |  |
| 50151  | 16.3        | 3.2         |             |               |                |               |                  |                |             |            |               |  |
| 50152  | 16.4        | 5.7         |             |               |                |               |                  |                |             |            |               |  |
| 50153  | 17.4        | 3.8         |             |               |                |               |                  |                |             |            |               |  |
| 50155  | 17.8        | 4.2         |             |               |                |               |                  |                |             |            |               |  |
| 50161  | 16.6        | 4.9         |             |               |                |               |                  |                |             |            |               |  |
| n  | 5           | 5           |             |               |                |               |                  |                |             |            |               |  |
| Mean   | 16.90       | 4.36        |             |               |                |               |                  |                |             |            |               |  |
| S.D.   | 0.66        | 0.97        |             |               |                |               |                  |                |             |            |               |  |

| Biochemical findings<br>Sex : Female                        |             |             |             |               |                |               |                  |                |             | Species : Rat |             |
|---|-------------|-------------|-------------|---------------|----------------|---------------|------------------|----------------|-------------|---------------|-------------|
| Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 50 mg/kg |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.  | AST<br>IU/L | ALT<br>IU/L | ALP<br>IU/L | γ-GTP<br>IU/L | T-Bil<br>mg/dL | TBA<br>μmol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL | TG<br>mg/dL | TP<br>g/dL    | UN<br>mg/dL |
| 50251   | 209         | 150         | 201         | 1.2           | 0.12           | 22.7          | 143              | 76             | 73          | 6.0           | 14.9        |
| 50252   | 78          | 54          | 212         | 0.1           | 0.07           | 12.3          | 152              | 64             | 53          | 5.8           | 20.7        |
| 50253   | 114         | 56          | 296         | 0.0           | 0.07           | 9.8           | 131              | 73             | 32          | 5.4           | 21.6        |
| 50256   | 87          | 50          | 233         | 0.3           | 0.06           | 12.0          | 130              | 63             | 36          | 5.9           | 22.0        |
| 50258   | 84          | 62          | 264         | 0.3           | 0.07           | 14.8          | 118              | 49             | 25          | 5.3           | 17.9        |
| n   | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5             | 5           |
| Mean  | 114.4       | 74.4        | 241.2       | 0.38          | 0.078          | 14.32         | 134.8            | 65.0           | 43.8        | 5.68          | 19.42       |
| S.D.  | 54.7        | 42.5        | 38.9        | 0.48          | 0.024          | 5.01          | 13.1             | 10.6           | 19.3        | 0.31          | 2.99        |
|   |             |             |             |               |                |               |                  |                |             |               |             |
| Crea<br>mg/dL   |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.  | Na<br>mEq/L | K<br>mEq/L  | Cl<br>mEq/L | Ca<br>mEq/L   | IP<br>mg/dL    | A/G<br>mg/dL  | Albumin<br>g/dL  | Albumin<br>%   | α1-G<br>%   | α2-G<br>%     |             |
| 50251   | 0.32        | 143         | 4.95        | 103           | 10.0           | 7.0           | 1.01             | 3.02           | 50.3        | 20.2          | 7.8         |
| 50252   | 0.39        | 142         | 4.02        | 103           | 10.0           | 7.5           | 1.11             | 3.05           | 52.5        | 18.8          | 6.3         |
| 50253   | 0.36        | 144         | 3.98        | 105           | 10.2           | 8.8           | 1.04             | 2.75           | 51.0        | 19.0          | 8.4         |
| 50256   | 0.41        | 142         | 4.59        | 103           | 10.1           | 8.4           | 1.10             | 3.09           | 52.4        | 20.0          | 7.0         |
| 50258   | 0.33        | 142         | 4.55        | 105           | 9.7            | 8.2           | 1.05             | 2.71           | 51.2        | 22.6          | 6.3         |
| n   | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5             | 5           |
| Mean  | 0.362       | 142.6       | 4.418       | 103.8         | 10.00          | 7.98          | 1.062            | 2.924          | 51.48       | 20.12         | 7.16        |
| S.D.  | 0.038       | 0.9         | 0.412       | 1.1           | 0.19           | 0.72          | 0.042            | 0.179          | 0.95        | 1.51          | 0.93        |
|   |             |             |             |               |                |               |                  |                |             |               |             |
| β-G<br>%  |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.  | β-G<br>%    | γ-G<br>%    |             |               |                |               |                  |                |             |               |             |
| 50251   | 17.6        | 4.1         |             |               |                |               |                  |                |             |               |             |
| 50252   | 17.8        | 4.6         |             |               |                |               |                  |                |             |               |             |
| 50253   | 17.8        | 3.8         |             |               |                |               |                  |                |             |               |             |
| 50256   | 16.1        | 4.5         |             |               |                |               |                  |                |             |               |             |
| 50258   | 15.6        | 4.3         |             |               |                |               |                  |                |             |               |             |
| n   | 5           | 5           |             |               |                |               |                  |                |             |               |             |
| Mean  | 16.98       | 4.26        |             |               |                |               |                  |                |             |               |             |
| S.D.  | 1.05        | 0.32        |             |               |                |               |                  |                |             |               |             |

| Biochemical findings |       |  |       |               |       |             |         |         |         | Species : Rat |              |  |  |
|----------------------|-------|--|-------|---------------|-------|-------------|---------|---------|---------|---------------|--------------|--|--|
| Sex : Female         |       | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 200 mg/kg |       |               |       |             |         |         |         |               |              |  |  |
| Animal No.           | AST   | ALT  | ALP   | $\gamma$ -GTP | T-Bil | TBA         | Glucose | T-Cho   | TG      | TP            | UN           |  |  |
|                      | IU/L  | IU/L   | IU/L  | IU/L          | mg/dL | $\mu$ mol/L | mg/dL   | mg/dL   | mg/dL   | g/dL          | mg/dL        |  |  |
| 50353                | 111   | 51   | 248   | 0.1           | 0.06  | 11.8        | 148     | 41      | 27      | 5.4           | 19.9         |  |  |
| 50354                | 84    | 57   | 376   | 0.6           | 0.07  | 7.5         | 127     | 64      | 35      | 5.6           | 15.4         |  |  |
| 50355                | 89    | 46   | 220   | 0.2           | 0.07  | 11.7        | 131     | 44      | 56      | 5.5           | 19.2         |  |  |
| 50360                | 67    | 35   | 229   | 0.2           | 0.06  | 11.9        | 114     | 51      | 39      | 5.3           | 19.7         |  |  |
| 50362                | 86    | 46   | 215   | 0.5           | 0.05  | 3.4         | 121     | 63      | 36      | 5.5           | 18.4         |  |  |
| n                    | 5     | 5  | 5     | 5             | 5     | 5           | 5       | 5       | 5       | 5             | 5            |  |  |
| Mean                 | 87.4  | 47.0   | 257.6 | 0.32          | 0.062 | 9.26        | 128.2   | 52.6    | 38.6    | 5.46          | 18.52        |  |  |
| S.D.                 | 15.7  | 8.1  | 67.4  | 0.22          | 0.008 | 3.77        | 12.8    | 10.6    | 10.7    | 0.11          | 1.84         |  |  |
|                      |       |  |       |               |       |             |         |         |         |               |              |  |  |
| Crea                 |       | Na   | K     | Cl            | Ca    | IP          | A/G     | Albumin | Albumin | $\alpha$ 1-G  | $\alpha$ 2-G |  |  |
| Animal No.           | mg/dL | mEq/L  | mEq/L | mEq/L         | mg/dL | mg/dL       |         | g/dL    | %       | %             | %            |  |  |
|                      | 0.39  | 142  | 4.08  | 105           | 9.7   | 7.5         | 0.97    | 2.66    | 49.2    | 19.9          | 7.3          |  |  |
| 50353                | 0.35  | 142  | 3.99  | 106           | 9.7   | 9.0         | 0.98    | 2.77    | 49.5    | 18.0          | 7.9          |  |  |
| 50354                | 0.33  | 143  | 4.10  | 105           | 10.3  | 10.6        | 0.97    | 2.71    | 49.2    | 22.7          | 5.6          |  |  |
| 50355                | 0.35  | 143  | 4.41  | 106           | 10.0  | 9.0         | 1.08    | 2.75    | 51.9    | 21.1          | 6.6          |  |  |
| 50360                | 0.34  | 142  | 4.49  | 105           | 10.2  | 10.6        | 1.01    | 2.77    | 50.3    | 19.5          | 6.8          |  |  |
| n                    | 5     | 5  | 5     | 5             | 5     | 5           | 5       | 5       | 5       | 5             | 5            |  |  |
| Mean                 | 0.352 | 142.4  | 4.214 | 105.4         | 9.98  | 9.34        | 1.002   | 2.732   | 50.02   | 20.24         | 6.84         |  |  |
| S.D.                 | 0.023 | 0.5  | 0.221 | 0.5           | 0.28  | 1.30        | 0.047   | 0.047   | 1.14    | 1.77          | 0.86         |  |  |
|                      |       |  |       |               |       |             |         |         |         |               |              |  |  |
| $\beta$ -G           |       | $\gamma$ -G  |       |               |       |             |         |         |         |               |              |  |  |
| Animal No.           |       | %  | %     |               |       |             |         |         |         |               |              |  |  |
| 50353                | 18.6  | 5.0  |       |               |       |             |         |         |         |               |              |  |  |
| 50354                | 18.4  | 6.2  |       |               |       |             |         |         |         |               |              |  |  |
| 50355                | 17.4  | 5.1  |       |               |       |             |         |         |         |               |              |  |  |
| 50360                | 16.6  | 3.8  |       |               |       |             |         |         |         |               |              |  |  |
| 50362                | 17.5  | 5.9  |       |               |       |             |         |         |         |               |              |  |  |
| n                    | 5     | 5  |       |               |       |             |         |         |         |               |              |  |  |
| Mean                 | 17.70 | 5.20   |       |               |       |             |         |         |         |               |              |  |  |
| S.D.                 | 0.81  | 0.94   |       |               |       |             |         |         |         |               |              |  |  |

| Biochemical findings<br>Sex : Female                         |             |             |             |               |                |               |                  |                |             | Species : Rat |             |
|--|-------------|-------------|-------------|---------------|----------------|---------------|------------------|----------------|-------------|---------------|-------------|
| Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 800 mg/kg |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.   | AST<br>IU/L | ALT<br>IU/L | ALP<br>IU/L | γ-GTP<br>IU/L | T-Bil<br>mg/dL | TBA<br>μmol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL | TG<br>mg/dL | TP<br>g/dL    | UN<br>mg/dL |
| 50451  | 81          | 54          | 255         | 0.1           | 0.06           | 17.1          | 133              | 56             | 29          | 5.4           | 18.7        |
| 50452  | 104         | 63          | 416         | 0.2           | 0.05           | 19.8          | 134              | 55             | 22          | 5.6           | 19.4        |
| 50454  | 71          | 48          | 200         | 0.1           | 0.06           | 13.4          | 118              | 48             | 85          | 5.5           | 20.5        |
| 50457  | 73          | 50          | 206         | 0.6           | 0.06           | 5.7           | 136              | 58             | 51          | 5.2           | 13.5        |
| 50461  | 90          | 42          | 268         | 0.1           | 0.05           | 9.7           | 122              | 50             | 84          | 5.3           | 17.0        |
| n  | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5             | 5           |
| Mean   | 83.8        | 51.4        | 269.0       | 0.22          | 0.056          | 13.14         | 128.6            | 53.4           | 54.2        | 5.40          | 17.82       |
| S.D.   | 13.6        | 7.8         | 87.4        | 0.22          | 0.005          | 5.64          | 8.0              | 4.2            | 29.7        | 0.16          | 2.73        |
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| Biochemical findings<br>Sex : Female (satellite) |               |             |             | Stage : Day 29<br>Dose : PTSA Monohydrate 0 mg/kg |                |               |                  |                 |              | Species : Rat |             |  |
|--|---------------|-------------|-------------|---|----------------|---------------|------------------|-----------------|--------------|---------------|-------------|--|
|  | AST<br>IU/L   | ALT<br>IU/L | ALP<br>IU/L | γ-GTP<br>IU/L                                     | T-Bil<br>mg/dL | TBA<br>μmol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL  | TG<br>mg/dL  | TP<br>g/dL    | UN<br>mg/dL |  |
| Animal No.                                       |               |             |             |   |                |               |                  |                 |              |               |             |  |
| 50551  | 68            | 23          | 242         | 0.3   | 0.08           | 5.3           | 101              | 50              | 15           | 5.4           | 15.1        |  |
| 50552  | 62            | 29          | 343         | 0.1   | 0.08           | 5.9           | 138              | 52              | 13           | 5.5           | 13.9        |  |
| 50553  | 49            | 18          | 345         | 0.4   | 0.07           | 8.4           | 150              | 38              | 7            | 5.4           | 14.3        |  |
| 50554  | 56            | 25          | 217         | 0.8   | 0.07           | 7.9           | 123              | 68              | 16           | 5.7           | 13.0        |  |
| 50555  | 56            | 27          | 286         | 0.9   | 0.06           | 4.9           | 132              | 56              | 24           | 6.0           | 12.7        |  |
| n  | 5             | 5           | 5           | 5   | 5              | 5             | 5                | 5               | 5            | 5             | 5           |  |
| Mean   | 58.2          | 24.4        | 286.6       | 0.50  | 0.072          | 6.48          | 128.8            | 52.8            | 15.0         | 5.60          | 13.80       |  |
| S.D.   | 7.2           | 4.2         | 57.9        | 0.34  | 0.008          | 1.58          | 18.4             | 10.8            | 6.1          | 0.25          | 0.97        |  |
| <hr/>  |               |             |             |   |                |               |                  |                 |              |               |             |  |
|  | Crea<br>mg/dL | Na<br>mEq/L | K<br>mEq/L  | Cl<br>mEq/L                                       | Ca<br>mg/dL    | IP<br>mg/dL   | A/G              | Albumin<br>g/dL | Albumin<br>% | α1-G          | α2-G        |  |
| Animal No.                                       |               |             |             |   |                |               |                  |                 |              |               |             |  |
| 50551  | 0.32          | 145         | 4.48        | 107   | 9.8            | 7.7           | 1.13             | 2.87            | 53.1         | 17.4          | 7.0         |  |
| 50552  | 0.34          | 144         | 4.45        | 107   | 9.7            | 7.8           | 1.18             | 2.98            | 54.2         | 15.7          | 7.1         |  |
| 50553  | 0.31          | 146         | 3.94        | 108   | 9.6            | 7.7           | 1.13             | 2.87            | 53.1         | 17.7          | 7.6         |  |
| 50554  | 0.33          | 145         | 4.54        | 108   | 10.0           | 7.1           | 1.30             | 3.23            | 56.6         | 15.3          | 7.4         |  |
| 50555  | 0.28          | 144         | 4.21        | 107   | 10.1           | 7.1           | 1.33             | 3.43            | 57.1         | 16.3          | 6.7         |  |
| n  | 5             | 5           | 5           | 5   | 5              | 5             | 5                | 5               | 5            | 5             | 5           |  |
| Mean   | 0.316         | 144.8       | 4.324       | 107.4   | 9.84           | 7.48          | 1.214            | 3.076           | 54.82        | 16.48         | 7.16        |  |
| S.D.   | 0.023         | 0.8         | 0.249       | 0.5   | 0.21           | 0.35          | 0.095            | 0.247           | 1.91         | 1.04          | 0.35        |  |
| <hr/>  |               |             |             |   |                |               |                  |                 |              |               |             |  |
|  | β-G<br>%      | γ-G<br>%    |             |   |                |               |                  |                 |              |               |             |  |
| Animal No.                                       |               |             |             |   |                |               |                  |                 |              |               |             |  |
| 50551  | 15.8          | 6.7         |             |   |                |               |                  |                 |              |               |             |  |
| 50552  | 16.5          | 6.5         |             |   |                |               |                  |                 |              |               |             |  |
| 50553  | 16.1          | 5.5         |             |   |                |               |                  |                 |              |               |             |  |
| 50554  | 16.1          | 4.6         |             |   |                |               |                  |                 |              |               |             |  |
| 50555  | 14.3          | 5.6         |             |   |                |               |                  |                 |              |               |             |  |
| n  | 5             | 5           |             |   |                |               |                  |                 |              |               |             |  |
| Mean   | 15.76         | 5.78        |             |   |                |               |                  |                 |              |               |             |  |
| S.D.   | 0.85          | 0.85        |             |   |                |               |                  |                 |              |               |             |  |

| Biochemical findings<br>Sex : Female (satellite)    |             |             |             |               |                |               |                  |                |             | Species : Rat |             |
|---|-------------|-------------|-------------|---------------|----------------|---------------|------------------|----------------|-------------|---------------|-------------|
| Stage : Day 29<br>Dose : PTSA Monohydrate 800 mg/kg |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.  | AST<br>IU/L | ALT<br>IU/L | ALP<br>IU/L | γ-GTP<br>IU/L | T-Bil<br>mg/dL | TBA<br>μmol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL | TG<br>mg/dL | TP<br>g/dL    | UN<br>mg/dL |
| 50651   | 47          | 15          | 162         | 0.2           | 0.05           | 14.3          | 123              | 49             | 31          | 5.5           | 16.7        |
| 50652   | 127         | 51          | 203         | 0.7           | 0.04           | 8.0           | 138              | 62             | 9           | 5.2           | 15.6        |
| 50653   | 54          | 21          | 210         | 0.2           | 0.07           | 5.8           | 131              | 62             | 44          | 5.6           | 15.0        |
| 50654   | 68          | 21          | 293         | 0.6           | 0.05           | 3.5           | 126              | 41             | 14          | 5.0           | 13.8        |
| 50655   | 64          | 22          | 256         | 0.8           | 0.04           | 2.9           | 120              | 65             | 25          | 4.8           | 12.2        |
| n   | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5             | 5           |
| Mean  | 72.0        | 26.0        | 224.8       | 0.50          | 0.050          | 6.90          | 127.6            | 55.8           | 24.6        | 5.22          | 14.66       |
| S.D.  | 31.8        | 14.2        | 50.7        | 0.28          | 0.012          | 4.60          | 7.1              | 10.3           | 13.9        | 0.33          | 1.73        |
|   |             |             |             |               |                |               |                  |                |             |               |             |
| Crea<br>mg/dL                                       |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.  | Na<br>mEq/L | K<br>mEq/L  | Cl<br>mEq/L | Ca<br>mEq/L   | IP<br>mg/dL    | A/G           | Albumin<br>g/dL  | Albumin<br>%   | α1-G        | α2-G          |             |
| 50651   | 0.33        | 146         | 4.28        | 108           | 9.6            | 8.2           | 1.15             | 2.94           | 53.5        | 19.8          | 7.9         |
| 50652   | 0.37        | 143         | 4.16        | 108           | 9.5            | 7.2           | 1.11             | 2.73           | 52.5        | 16.1          | 7.5         |
| 50653   | 0.36        | 144         | 4.14        | 106           | 9.8            | 7.6           | 1.28             | 3.15           | 56.3        | 17.7          | 7.0         |
| 50654   | 0.32        | 145         | 3.69        | 108           | 9.7            | 8.6           | 1.06             | 2.58           | 51.6        | 18.7          | 7.0         |
| 50655   | 0.31        | 145         | 4.08        | 110           | 9.5            | 7.7           | 1.03             | 2.42           | 50.5        | 19.2          | 8.0         |
| n   | 5           | 5           | 5           | 5             | 5              | 5             | 5                | 5              | 5           | 5             | 5           |
| Mean  | 0.338       | 144.6       | 4.070       | 108.0         | 9.62           | 7.86          | 1.126            | 2.764          | 52.88       | 18.30         | 7.48        |
| S.D.  | 0.026       | 1.1         | 0.224       | 1.4           | 0.13           | 0.55          | 0.098            | 0.289          | 2.21        | 1.45          | 0.48        |
|   |             |             |             |               |                |               |                  |                |             |               |             |
| β-G<br>%  |             |             |             |               |                |               |                  |                |             |               |             |
| Animal No.  | β-G<br>%    | γ-G<br>%    |             |               |                |               |                  |                |             |               |             |
| 50651   | 14.6        | 4.2         |             |               |                |               |                  |                |             |               |             |
| 50652   | 17.5        | 6.4         |             |               |                |               |                  |                |             |               |             |
| 50653   | 15.1        | 3.9         |             |               |                |               |                  |                |             |               |             |
| 50654   | 14.8        | 7.9         |             |               |                |               |                  |                |             |               |             |
| 50655   | 16.1        | 6.2         |             |               |                |               |                  |                |             |               |             |
| n   | 5           | 5           |             |               |                |               |                  |                |             |               |             |
| Mean  | 15.62       | 5.72        |             |               |                |               |                  |                |             |               |             |
| S.D.  | 1.20        | 1.66        |             |               |                |               |                  |                |             |               |             |

| Biochemical findings            |               |             |             |               |                |               |                  |                 |              |             |
|---------------------------------|---------------|-------------|-------------|---------------|----------------|---------------|------------------|-----------------|--------------|-------------|
| Sex : Male                      |               |             |             |               |                |               |                  |                 |              |             |
| Stage : Recovery Day 15         |               |             |             |               |                |               |                  |                 |              |             |
| Dose : PTSA Monohydrate 0 mg/kg |               |             |             |               |                |               |                  |                 |              |             |
| Species : Rat                   |               |             |             |               |                |               |                  |                 |              |             |
| Animal No.                      | AST<br>IU/L   | ALT<br>IU/L | ALP<br>IU/L | γ-GTP<br>IU/L | T-Bil<br>mg/dL | TBA<br>μmol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL  | TG<br>g/dL   | TP<br>mg/dL |
| 10103                           | 58            | 26          | 303         | 0.2           | 0.05           | 5.1           | 141              | 45              | 37           | 5.2         |
| 10104                           | 64            | 27          | 370         | 0.5           | 0.06           | 8.2           | 130              | 52              | 32           | 5.0         |
| 10105                           | 65            | 30          | 376         | 0.1           | 0.08           | 4.6           | 148              | 51              | 25           | 5.3         |
| 10106                           | 78            | 33          | 318         | 0.7           | 0.07           | 5.9           | 129              | 59              | 17           | 4.6         |
| 10111                           | 82            | 35          | 375         | 0.1           | 0.07           | 5.2           | 137              | 57              | 33           | 5.0         |
| n                               | 5             | 5           | 5           | 5             | 5              | 5             | 5                | 5               | 5            | 5           |
| Mean                            | 69.4          | 30.2        | 348.4       | 0.32          | 0.066          | 5.80          | 137.0            | 52.8            | 28.8         | 5.02        |
| S.D.                            | 10.1          | 3.8         | 35.1        | 0.27          | 0.011          | 1.42          | 7.9              | 5.5             | 7.9          | 1.65        |
| Animal No.                      | Crea<br>mg/dL | Na<br>mEq/L | K<br>mEq/L  | Cl<br>mEq/L   | Ca<br>mg/dL    | IP<br>mg/dL   | A/G              | Albumin<br>g/dL | Albumin<br>% | α1-G<br>%   |
| 10103                           | 0.28          | 145         | 4.95        | 106           | 9.4            | 7.3           | 0.97             | 2.56            | 49.3         | 23.9        |
| 10104                           | 0.27          | 145         | 4.37        | 107           | 9.5            | 8.2           | 1.14             | 2.66            | 53.1         | 18.4        |
| 10105                           | 0.27          | 142         | 4.71        | 104           | 9.7            | 8.1           | 1.00             | 2.64            | 49.9         | 22.2        |
| 10106                           | 0.26          | 144         | 4.25        | 104           | 9.5            | 8.9           | 1.00             | 2.30            | 49.9         | 22.6        |
| 10111                           | 0.23          | 146         | 4.26        | 107           | 9.5            | 8.3           | 0.99             | 2.50            | 49.9         | 22.9        |
| n                               | 5             | 5           | 5           | 5             | 5              | 5             | 5                | 5               | 5            | 5           |
| Mean                            | 0.262         | 144.4       | 4.508       | 105.6         | 9.52           | 8.16          | 1.020            | 2.532           | 50.42        | 22.00       |
| S.D.                            | 0.019         | 1.5         | 0.310       | 1.5           | 0.11           | 0.57          | 0.068            | 0.145           | 1.52         | 2.11        |
| Animal No.                      | β-G<br>%      | γ-G<br>%    |             |               |                |               |                  |                 |              |             |
| 10103                           | 16.4          | 3.2         |             |               |                |               |                  |                 |              |             |
| 10104                           | 16.6          | 5.0         |             |               |                |               |                  |                 |              |             |
| 10105                           | 16.0          | 4.8         |             |               |                |               |                  |                 |              |             |
| 10106                           | 16.2          | 3.9         |             |               |                |               |                  |                 |              |             |
| 10111                           | 16.2          | 3.2         |             |               |                |               |                  |                 |              |             |
| n                               | 5             | 5           |             |               |                |               |                  |                 |              |             |
| Mean                            | 16.28         | 4.02        |             |               |                |               |                  |                 |              |             |
| S.D.                            | 0.23          | 0.86        |             |               |                |               |                  |                 |              |             |

| Biochemical findings |       |  |       |       |       |        |         |         |         | Species : Rat |       |
|----------------------|-------|--|-------|-------|-------|--------|---------|---------|---------|---------------|-------|
| Sex : Male           |       | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 800 mg/kg |       |       |       |        |         |         |         |               |       |
|                      | AST   | ALT  | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho   | TG      | TP            | UN    |
| Animal No.           | IU/L  | IU/L   | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL   | mg/dL   | g/dL          | mg/dL |
| 10402                | 73    | 30   | 287   | 0.2   | 0.06  | 9.5    | 134     | 42      | 23      | 5.1           | 12.6  |
| 10403                | 70    | 33   | 294   | 0.2   | 0.06  | 15.0   | 127     | 57      | 33      | 5.1           | 12.9  |
| 10407                | 71    | 29   | 392   | 0.2   | 0.06  | 7.7    | 128     | 47      | 28      | 5.2           | 11.5  |
| 10409                | 88    | 25   | 304   | 0.4   | 0.07  | 5.7    | 147     | 47      | 16      | 4.8           | 15.6  |
| 10411                | 68    | 29   | 307   | 0.2   | 0.05  | 5.7    | 144     | 40      | 33      | 5.1           | 13.1  |
| n                    | 5     | 5  | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |
| Mean                 | 74.0  | 29.2   | 316.8 | 0.24  | 0.060 | 8.72   | 136.0   | 46.6    | 26.6    | 5.06          | 13.14 |
| S.D.                 | 8.0   | 2.9  | 42.8  | 0.09  | 0.007 | 3.85   | 9.1     | 6.6     | 7.2     | 0.15          | 1.51  |
|                      |       |  |       |       |       |        |         |         |         |               |       |
|                      | Crea  | Na   | K     | Cl    | Ca    | IP     | A/G     | Albumin | Albumin | α1-G          | α2-G  |
| Animal No.           | mg/dL | mEq/L  | mEq/L | mEq/L | mg/dL | mg/dL  |         | g/dL    | %       | %             | %     |
| 10402                | 0.31  | 143  | 4.72  | 106   | 9.5   | 7.3    | 0.98    | 2.53    | 49.6    | 22.0          | 6.7   |
| 10403                | 0.27  | 144  | 4.80  | 106   | 9.4   | 8.4    | 1.15    | 2.73    | 53.5    | 19.9          | 6.9   |
| 10407                | 0.26  | 145  | 4.57  | 106   | 9.3   | 8.3    | 1.02    | 2.63    | 50.6    | 21.9          | 7.6   |
| 10409                | 0.29  | 144  | 4.68  | 106   | 9.2   | 8.0    | 1.13    | 2.54    | 52.9    | 19.3          | 7.5   |
| 10411                | 0.21  | 145  | 4.42  | 107   | 9.6   | 8.5    | 0.94    | 2.47    | 48.4    | 23.3          | 7.0   |
| n                    | 5     | 5  | 5     | 5     | 5     | 5      | 5       | 5       | 5       | 5             | 5     |
| Mean                 | 0.268 | 144.2  | 4.638 | 106.2 | 9.40  | 8.10   | 1.044   | 2.580   | 51.00   | 21.28         | 7.14  |
| S.D.                 | 0.038 | 0.8  | 0.147 | 0.4   | 0.16  | 0.48   | 0.092   | 0.101   | 2.16    | 1.64          | 0.39  |
|                      |       |  |       |       |       |        |         |         |         |               |       |
|                      | β-G   | γ-G  |       |       |       |        |         |         |         |               |       |
| Animal No.           | %     | %  |       |       |       |        |         |         |         |               |       |
| 10402                | 16.8  | 4.9  |       |       |       |        |         |         |         |               |       |
| 10403                | 16.2  | 3.5  |       |       |       |        |         |         |         |               |       |
| 10407                | 16.7  | 3.2  |       |       |       |        |         |         |         |               |       |
| 10409                | 16.2  | 4.1  |       |       |       |        |         |         |         |               |       |
| 10411                | 17.0  | 4.3  |       |       |       |        |         |         |         |               |       |
| n                    | 5     | 5  |       |       |       |        |         |         |         |               |       |
| Mean                 | 16.58 | 4.00   |       |       |       |        |         |         |         |               |       |
| S.D.                 | 0.36  | 0.67   |       |       |       |        |         |         |         |               |       |

| Biochemical findings<br>Sex : Female (satellite) |  | Stage : Recovery day 15<br>Dose : PTSA Monohydrate 0 mg/kg |       |       |       |       |        |         |         | Species : Rat |       |       |
|--|--|--|-------|-------|-------|-------|--------|---------|---------|---------------|-------|-------|
|  |  | AST  | ALT   | ALP   | γ-GTP | T-Bil | TBA    | Glucose | T-Cho   | TG            | TP    | UN    |
| Animal No.                                       |  | IU/L   | IU/L  | IU/L  | IU/L  | mg/dL | μmol/L | mg/dL   | mg/dL   | mg/dL         | g/dL  | mg/dL |
| 50556  |  | 46   | 18    | 181   | 0.4   | 0.06  | 8.5    | 169     | 49      | 19            | 5.9   | 12.2  |
| 50557  |  | 50   | 18    | 289   | 1.2   | 0.07  | 6.3    | 149     | 53      | 17            | 5.5   | 11.6  |
| 50558  |  | 51   | 22    | 130   | 0.0   | 0.06  | 6.7    | 137     | 32      | 18            | 5.7   | 14.1  |
| 50559  |  | 66   | 26    | 216   | 0.5   | 0.08  | 10.2   | 123     | 44      | 14            | 5.4   | 12.7  |
| 50560  |  | 54   | 26    | 165   | 0.0   | 0.07  | 15.0   | 142     | 80      | 35            | 6.5   | 18.9  |
| n  |  | 5  | 5     | 5     | 5     | 5     | 5      | 5       | 5       | 5             | 5     | 5     |
| Mean   |  | 53.4   | 22.0  | 196.2 | 0.42  | 0.068 | 9.34   | 144.0   | 51.6    | 20.6          | 5.80  | 13.90 |
| S.D.   |  | 7.6  | 4.0   | 60.4  | 0.49  | 0.008 | 3.52   | 16.9    | 17.7    | 8.3           | 0.44  | 2.94  |
|  |  | Crea   | Na    | K     | Cl    | Ca    | IP     | A/G     | Albumin | Albumin       | α1-G  | α2-G  |
| Animal No.                                       |  | mg/dL  | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL  |         | g/dL    | %             | %     | %     |
| 50556  |  | 0.28   | 143   | 4.04  | 103   | 9.8   | 7.7    | 1.46    | 3.50    | 59.4          | 14.2  | 7.7   |
| 50557  |  | 0.30   | 144   | 3.86  | 106   | 9.5   | 8.5    | 1.07    | 2.85    | 51.8          | 18.0  | 7.7   |
| 50558  |  | 0.32   | 144   | 4.20  | 105   | 10.2  | 8.3    | 1.34    | 3.26    | 57.2          | 17.8  | 7.2   |
| 50559  |  | 0.28   | 143   | 3.71  | 104   | 10.1  | 8.5    | 1.10    | 2.83    | 52.4          | 17.0  | 7.9   |
| 50560  |  | 0.35   | 143   | 4.04  | 104   | 10.5  | 8.3    | 1.37    | 3.76    | 57.9          | 15.6  | 7.3   |
| n  |  | 5  | 5     | 5     | 5     | 5     | 5      | 5       | 5       | 5             | 5     | 5     |
| Mean   |  | 0.306  | 143.4 | 3.970 | 104.4 | 10.02 | 8.26   | 1.268   | 3.240   | 55.74         | 16.52 | 7.56  |
| S.D.   |  | 0.030  | 0.5   | 0.189 | 1.1   | 0.38  | 0.33   | 0.173   | 0.406   | 3.42          | 1.60  | 0.30  |
|  |  | β-G  | γ-G   |       |       |       |        |         |         |               |       |       |
| Animal No.                                       |  | %  | %     |       |       |       |        |         |         |               |       |       |
| 50556  |  | 13.4   | 5.3   |       |       |       |        |         |         |               |       |       |
| 50557  |  | 16.3   | 6.2   |       |       |       |        |         |         |               |       |       |
| 50558  |  | 12.9   | 4.9   |       |       |       |        |         |         |               |       |       |
| 50559  |  | 15.0   | 7.7   |       |       |       |        |         |         |               |       |       |
| 50560  |  | 14.3   | 4.9   |       |       |       |        |         |         |               |       |       |
| n  |  | 5  | 5     |       |       |       |        |         |         |               |       |       |
| Mean   |  | 14.38  | 5.80  |       |       |       |        |         |         |               |       |       |
| S.D.   |  | 1.34   | 1.19  |       |       |       |        |         |         |               |       |       |

| Biochemical findings<br>Sex : Female (satellite) |                 |                  |             | Stage : Recovery day 15<br>Dose : PTSA Monohydrate 800 mg/kg |                |                    |                  |                |                   | Species : Rat     |             |  |
|--|-----------------|------------------|-------------|--|----------------|--------------------|------------------|----------------|-------------------|-------------------|-------------|--|
|  | AST<br>IU/L     | ALT<br>IU/L      | ALP<br>IU/L | $\gamma$ -GTP<br>IU/L  | T-Bil<br>mg/dL | TBA<br>$\mu$ mol/L | Glucose<br>mg/dL | T-Cho<br>mg/dL | TG<br>mg/dL       | TP<br>g/dL        | UN<br>mg/dL |  |
| Animal No.                                       |                 |                  |             |  |                |                    |                  |                |                   |                   |             |  |
| 50656  | 66              | 20               | 205         | 0.2  | 0.07           | 10.4               | 109              | 53             | 9                 | 5.7               | 17.6        |  |
| 50657  | 65              | 18               | 235         | 0.5  | 0.10           | 16.9               | 144              | 43             | 13                | 5.6               | 14.8        |  |
| 50658  | 56              | 18               | 347         | 0.8  | 0.07           | 11.2               | 124              | 57             | 12                | 5.3               | 12.6        |  |
| 50659  | 59              | 26               | 143         | 0.2  | 0.06           | 7.6                | 142              | 89             | 35                | 5.9               | 15.5        |  |
| n  | 4               | 4                | 4           | 4  | 4              | 4                  | 4                | 4              | 4                 | 4                 | 4           |  |
| Mean   | 61.5            | 20.5             | 232.5       | 0.43   | 0.075          | 11.53              | 129.8            | 60.5           | 17.3              | 5.63              | 15.13       |  |
| S.D.   | 4.8             | 3.8              | 85.4        | 0.29   | 0.017          | 3.90               | 16.5             | 19.9           | 12.0              | 0.25              | 2.06        |  |
|  |                 |                  |             |  |                |                    |                  |                |                   |                   |             |  |
| Crea<br>mg/dL                                    |                 |                  |             |  |                |                    |                  |                |                   |                   |             |  |
| Animal No.                                       | Na<br>mEq/L     | K<br>mEq/L       | Cl<br>mEq/L | Ca<br>mg/dL  | IP<br>mg/dL    | A/G                | Albumin<br>g/dL  | Albumin<br>%   | $\alpha$ 1-G<br>% | $\alpha$ 2-G<br>% |             |  |
| 50656  | 0.35            | 145              | 4.33        | 107  | 9.9            | 8.6                | 1.23             | 3.14           | 55.1              | 17.4              | 7.1         |  |
| 50657  | 0.36            | 141              | 5.14        | 105  | 9.5            | 6.4                | 1.27             | 3.13           | 55.9              | 14.5              | 8.0         |  |
| 50658  | 0.31            | 144              | 4.16        | 106  | 9.6            | 8.5                | 1.35             | 3.05           | 57.5              | 16.2              | 7.5         |  |
| 50659  | 0.32            | 143              | 4.28        | 105  | 10.4           | 8.1                | 1.38             | 3.42           | 58.0              | 15.1              | 7.6         |  |
| n  | 4               | 4                | 4           | 4  | 4              | 4                  | 4                | 4              | 4                 | 4                 | 4           |  |
| Mean   | 0.335           | 143.3            | 4.478       | 105.8  | 9.85           | 7.90               | 1.308            | 3.185          | 56.63             | 15.80             | 7.55        |  |
| S.D.   | 0.024           | 1.7              | 0.447       | 1.0  | 0.40           | 1.02               | 0.069            | 0.162          | 1.35              | 1.28              | 0.37        |  |
|  |                 |                  |             |  |                |                    |                  |                |                   |                   |             |  |
| $\beta$ -G<br>%                                  |                 |                  |             |  |                |                    |                  |                |                   |                   |             |  |
| Animal No.                                       | $\beta$ -G<br>% | $\gamma$ -G<br>% |             |  |                |                    |                  |                |                   |                   |             |  |
| 50656  | 13.2            | 7.2              |             |  |                |                    |                  |                |                   |                   |             |  |
| 50657  | 16.4            | 5.2              |             |  |                |                    |                  |                |                   |                   |             |  |
| 50658  | 14.1            | 4.7              |             |  |                |                    |                  |                |                   |                   |             |  |
| 50659  | 13.8            | 5.5              |             |  |                |                    |                  |                |                   |                   |             |  |
| n  | 4               | 4                |             |  |                |                    |                  |                |                   |                   |             |  |
| Mean   | 14.38           | 5.65             |             |  |                |                    |                  |                |                   |                   |             |  |
| S.D.   | 1.40            | 1.08             |             |  |                |                    |                  |                |                   |                   |             |  |

| Necropsy findings               |   |                    |                |               |
|---------------------------------|---|--------------------|----------------|---------------|
| Sex : Male                      |   |                    | Stage : Day 29 | Species : Rat |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10101 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10102 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10107 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10108 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10109 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10110 | Infertility    |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                              | Animal No. : 10112 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |

| Necropsy findings               |   | Stage : Day 29     | Species : Rat |
|---------------------------------|---|--------------------|---------------|
| Sex : Male                      |   |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10201 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10202 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10203 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10204 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10205 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10206 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10207 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10208 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10209 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10210 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10211 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                             | Animal No. : 10212 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |

| Necropsy findings               |   | Stage : Day 29     | Species : Rat |
|---------------------------------|---|--------------------|---------------|
| Sex : Male                      |   |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10301 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10302 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10303 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10304 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10305 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10306 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10307 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10308 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10309 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10310 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10311 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                            | Animal No. : 10312 |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |               |

| Necropsy findings               |   |                    | Stage : Day 29 | Species : Rat |
|---------------------------------|---|--------------------|----------------|---------------|
| Sex : Male                      |   |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10401 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10404 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10405 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10406 | Infertility    |               |
| Stomach                         |   |                    |                |               |
| Findings :                      | Finding present                             |                    |                |               |
|                                 | Thickening, limiting ridge                  |                    |                |               |
|                                 | Non-graded change                           |                    |                |               |
| Finding absent :                | Epididymis, Other organs & tissues          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10408 |                |               |
| Stomach                         |   |                    |                |               |
| Findings :                      | Finding present                             |                    |                |               |
|                                 | Thickening, limiting ridge                  |                    |                |               |
|                                 | Non-graded change                           |                    |                |               |
| Epididymis                      |   |                    |                |               |
| Findings :                      | Finding present                             |                    |                |               |
|                                 | Yellowish white focus, cauda, unilateral    |                    |                |               |
|                                 | Non-graded change                           |                    |                |               |
| Finding Comment :               | right, 4 x 3, mm                            |                    |                |               |
| Finding absent :                | Other organs & tissues                      |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10410 |                |               |
| Stomach                         |   |                    |                |               |
| Findings :                      | Finding present                             |                    |                |               |
|                                 | Thickening, limiting ridge                  |                    |                |               |
|                                 | Non-graded change                           |                    |                |               |
| Finding absent :                | Epididymis, Other organs & tissues          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                            | Animal No. : 10412 |                |               |
| Finding absent :                | Stomach, Epididymis, Other organs & tissues |                    |                |               |

| Necropsy findings               |                                 | Species : Rat                         |
|---------------------------------|---------------------------------|---------------------------------------|
| Sex : Female                    |                                 | Stage : Lactation Day 5               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50151                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50152                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50153                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50154                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50155                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50156                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50157                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50158                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50159                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50160      Non-pregnancy |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50161                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50162                    |
| Finding absent :                | Stomach, Other organs & tissues |                                       |

| Necropsy findings               |                                 | Sex : Female       | Stage : Lactation Day 5 | Species : Rat |
|---------------------------------|---------------------------------|--------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50251 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50252 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50253 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50254 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50255 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50256 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50257 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50258 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50259 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50260 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50261 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg                 | Animal No. : 50262 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |

| Necropsy findings               |                                 | Sex : Female       | Stage : Lactation Day 5 | Species : Rat |
|---------------------------------|---------------------------------|--------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50351 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50352 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50353 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50354 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50355 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50356 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50357 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50358 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50359 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50360 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50361 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg                | Animal No. : 50362 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |

| Necropsy findings               |                                 |                    | Stage : Lactation Day 5 | Species : Rat |
|---------------------------------|---------------------------------|--------------------|-------------------------|---------------|
| Sex : Female                    |                                 |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50451 |                         |               |
| Stomach                         |                                 |                    |                         |               |
| Findings : Finding present      |                                 |                    |                         |               |
| Thickening, limiting ridge      |                                 |                    |                         |               |
| Non-graded change               |                                 |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50452 |                         |               |
| Stomach                         |                                 |                    |                         |               |
| Findings : Finding present      |                                 |                    |                         |               |
| Thickening, limiting ridge      |                                 |                    |                         |               |
| Non-graded change               |                                 |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50453 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50454 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50455 | Total litter loss       |               |
| Stomach                         |                                 |                    |                         |               |
| Findings : Finding present      |                                 |                    |                         |               |
| Thickening, limiting ridge      |                                 |                    |                         |               |
| Non-graded change               |                                 |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50456 | Non-pregnancy           |               |
| Stomach                         |                                 |                    |                         |               |
| Findings : Finding present      |                                 |                    |                         |               |
| Thickening, limiting ridge      |                                 |                    |                         |               |
| Non-graded change               |                                 |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50457 |                         |               |
| Stomach                         |                                 |                    |                         |               |
| Findings : Finding present      |                                 |                    |                         |               |
| Thickening, limiting ridge      |                                 |                    |                         |               |
| Non-graded change               |                                 |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |

| Necropsy findings               |                                 | Sex : Female       | Stage : Lactation Day 5 | Species : Rat |
|---------------------------------|---------------------------------|--------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50458 | Died on lactation day 0 |               |
| Stomach                         |                                 |                    |                         |               |
| Findings :                      | Finding present                 |                    |                         |               |
|                                 | Thickening, limiting ridge      |                    |                         |               |
|                                 | Non-graded change               |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50459 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50460 |                         |               |
| Stomach                         |                                 |                    |                         |               |
| Findings :                      | Finding present                 |                    |                         |               |
|                                 | Thickening, limiting ridge      |                    |                         |               |
|                                 | Non-graded change               |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50461 |                         |               |
| Stomach                         |                                 |                    |                         |               |
| Findings :                      | Finding present                 |                    |                         |               |
|                                 | Thickening, limiting ridge      |                    |                         |               |
|                                 | Non-graded change               |                    |                         |               |
| Finding absent :                | Other organs & tissues          |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg                | Animal No. : 50462 |                         |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |                         |               |

| Necropsy findings               |                                 | Stage : Day 29     | Species : Rat |
|---------------------------------|---------------------------------|--------------------|---------------|
| Sex : Female (satellite)        |                                 |                    |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50551 |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                 | Diestrus                        |                    |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50552 |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                 | Proestrus                       |                    |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50553 |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                 | Proestrus                       |                    |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50554 |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                 | Proestrus                       |                    |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg                  | Animal No. : 50555 |               |
| Finding absent :                | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                 | Estrus                          |                    |               |

| Necropsy findings<br>Sex : Female (satellite) |                                 | Stage : Day 29     | Species : Rat |
|---|---------------------------------|--------------------|---------------|
| Test article : PTSA Monohydrate               | Dose : 800 mg/kg                | Animal No. : 50651 |               |
| Finding absent :                              | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                               | Proestrus                       |                    |               |
| Test article : PTSA Monohydrate               | Dose : 800 mg/kg                | Animal No. : 50652 |               |
| Finding absent :                              | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                               | Estrus                          |                    |               |
| Test article : PTSA Monohydrate               | Dose : 800 mg/kg                | Animal No. : 50653 |               |
| Stomach                                       |                                 |                    |               |
| Findings :                                    | Finding present                 |                    |               |
|   | Thickening, limiting ridge      |                    |               |
|   | Non-graded change               |                    |               |
| Finding absent :                              | Other organs & tissues          |                    |               |
| Estrous cycle :                               | Diestrus                        |                    |               |
| Test article : PTSA Monohydrate               | Dose : 800 mg/kg                | Animal No. : 50654 |               |
| Finding absent :                              | Stomach, Other organs & tissues |                    |               |
| Estrous cycle :                               | Estrus                          |                    |               |
| Test article : PTSA Monohydrate               | Dose : 800 mg/kg                | Animal No. : 50655 |               |
| Stomach                                       |                                 |                    |               |
| Findings :                                    | Finding present                 |                    |               |
|   | Thickening, limiting ridge      |                    |               |
|   | Non-graded change               |                    |               |
| Finding absent :                              | Other organs & tissues          |                    |               |
| Estrous cycle :                               | Estrus                          |                    |               |

| Necropsy findings               |                      |                         |               |
|---------------------------------|----------------------|-------------------------|---------------|
| Sex : Male                      |                      | Stage : Recovery Day 15 | Species : Rat |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg       | Animal No. : 10103      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg       | Animal No. : 10104      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg       | Animal No. : 10105      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg       | Animal No. : 10106      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg       | Animal No. : 10111      |               |
| Finding absent :                | All organs & tissues |                         |               |

| Necropsy findings               |                      |                         |               |
|---------------------------------|----------------------|-------------------------|---------------|
| Sex : Male                      |                      | Stage : Recovery Day 15 | Species : Rat |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg     | Animal No. : 10402      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg     | Animal No. : 10403      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg     | Animal No. : 10407      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg     | Animal No. : 10409      |               |
| Finding absent :                | All organs & tissues |                         |               |
| Test article : PTSA Monohydrate | Dose : 800 mg/kg     | Animal No. : 10411      |               |
| Finding absent :                | All organs & tissues |                         |               |

| Necropsy findings<br>Sex : Female (satellite) |                      | Stage : Recovery Day 15 | Species : Rat |
|---|----------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate               | Dose : 0 mg/kg       | Animal No. : 50556      |               |
| Finding absent :                              | All organs & tissues |                         |               |
| Estrous cycle :                               | Estrus               |                         |               |
| Test article : PTSA Monohydrate               | Dose : 0 mg/kg       | Animal No. : 50557      |               |
| Finding absent :                              | All organs & tissues |                         |               |
| Estrous cycle :                               | Estrus               |                         |               |
| Test article : PTSA Monohydrate               | Dose : 0 mg/kg       | Animal No. : 50558      |               |
| Finding absent :                              | All organs & tissues |                         |               |
| Estrous cycle :                               | Diestrus             |                         |               |
| Test article : PTSA Monohydrate               | Dose : 0 mg/kg       | Animal No. : 50559      |               |
| Finding absent :                              | All organs & tissues |                         |               |
| Estrous cycle :                               | Diestrus             |                         |               |
| Test article : PTSA Monohydrate               | Dose : 0 mg/kg       | Animal No. : 50560      |               |
| Finding absent :                              | All organs & tissues |                         |               |
| Estrous cycle :                               | Estrus               |                         |               |

| Necropsy findings                                |  | Stage : Recovery Day 15 | Species : Rat                |
|--|--|-------------------------|------------------------------|
| Sex : Female (satellite)                         |  |                         |                              |
| Test article : PTSA Monohydrate Dose : 800 mg/kg |  | Animal No. : 50656      |                              |
| Finding absent : All organs & tissues            |  |                         |                              |
| Estrous cycle : Diestrus                         |  |                         |                              |
| Test article : PTSA Monohydrate Dose : 800 mg/kg |  | Animal No. : 50657      |                              |
| Finding absent : All organs & tissues            |  |                         |                              |
| Estrous cycle : Estrus                           |  |                         |                              |
| Test article : PTSA Monohydrate Dose : 800 mg/kg |  | Animal No. : 50658      |                              |
| Finding absent : All organs & tissues            |  |                         |                              |
| Estrous cycle : Estrus                           |  |                         |                              |
| Test article : PTSA Monohydrate Dose : 800 mg/kg |  | Animal No. : 50659      |                              |
| Finding absent : All organs & tissues            |  |                         |                              |
| Estrous cycle : Metestrus                        |  |                         |                              |
| Test article : PTSA Monohydrate Dose : 800 mg/kg |  | Animal No. : 50660      | Died on administration day 3 |
| Stomach  |  |                         |                              |
| Findings : Finding present                       |  |                         |                              |
| Red focus, mucosa, multifocal, glandular stomach |  |                         |                              |
| Non-graded change                                |  |                         |                              |
| Finding Comment : less than 3 x 2, mm            |  |                         |                              |
| Red, mucosa, pyloric part                        |  |                         |                              |
| Non-graded change                                |  |                         |                              |
| Finding absent : Other organs & tissues          |  |                         |                              |

| Organ weight<br>Sex : Male |                  | Stage : Day 29<br>Dose : PTSA Monohydrate 0 mg/kg |               |          |               |                 |               | Species : Rat |               |
|----------------------------|------------------|---|---------------|----------|---------------|-----------------|---------------|---------------|---------------|
| Animal No.                 | Body weight<br>g | Liver   |               | Kidney   |               | Heart           |               | Spleen        |               |
|                            |                  | AB<br>g   | RE<br>g/100g  | AB<br>g  | RE<br>g/100g  | AB<br>g         | RE<br>g/100g  | AB<br>mg      | RE<br>mg/100g |
| 10101                      | 422              | 10.94   | 2.59          | 3.11     | 0.74          | 1.53            | 0.36          | 613           | 145.26        |
| 10102                      | 483              | 12.16   | 2.52          | 3.09     | 0.64          | 1.55            | 0.32          | 762           | 157.76        |
| 10107                      | 505              | 12.15   | 2.41          | 3.45     | 0.68          | 1.62            | 0.32          | 824           | 163.17        |
| 10108                      | 401              | 9.84  | 2.45          | 2.69     | 0.67          | 1.30            | 0.32          | 586           | 146.13        |
| 10109                      | 521              | 14.35   | 2.75          | 3.61     | 0.69          | 1.68            | 0.32          | 865           | 166.03        |
| 10110                      | 421              | 10.11   | 2.40          | 3.52     | 0.84          | 1.27            | 0.30          | 822           | 195.25        |
| 10112                      | 487              | 13.42   | 2.76          | 3.72     | 0.76          | 1.49            | 0.31          | 707           | 145.17        |
| n                          | 7                | 7   | 7             | 7        | 7             | 7               | 7             | 7             | 7             |
| Mean                       | 462.9            | 11.853  | 2.554         | 3.313    | 0.717         | 1.491           | 0.321         | 739.9         | 159.824       |
| S.D.                       | 47.2             | 1.673   | 0.152         | 0.364    | 0.068         | 0.154           | 0.019         | 108.6         | 17.904        |
| <br>                       |                  |   |               |          |               |                 |               |               |               |
|                            |                  | Thymus  |               | Adrenal  |               | Pituitary gland |               | Thyroid       |               |
| Animal No.                 |                  | AB<br>mg  | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg      | RE<br>mg/100g |
|                            |                  | 471   | 111.61        | 54       | 12.80         | 10.7            | 2.54          | 23.6          | 5.59          |
| 10101                      |                  | 471   | 111.61        | 54       | 12.80         | 10.7            | 2.54          | 23.6          | 5.59          |
| 10102                      |                  | 253   | 52.38         | 80       | 16.56         | 12.1            | 2.51          | 19.4          | 4.02          |
| 10107                      |                  | 246   | 48.71         | 76       | 15.05         | 12.9            | 2.55          | 21.2          | 4.20          |
| 10108                      |                  | 348   | 86.78         | 61       | 15.21         | 9.9             | 2.47          | 28.0          | 6.98          |
| 10109                      |                  | 475   | 91.17         | 85       | 16.31         | 16.2            | 3.11          | 26.2          | 5.03          |
| 10110                      |                  | 345   | 81.95         | 66       | 15.68         | 12.4            | 2.95          | 17.0          | 4.04          |
| 10112                      |                  | 339   | 69.61         | 69       | 14.17         | 14.2            | 2.92          | 16.7          | 3.43          |
| n                          | 7                | 7   | 7             | 7        | 7             | 7               | 7             | 7             | 7             |
| Mean                       | 353.9            | 77.459  | 70.1          | 15.111   | 12.63         | 2.721           | 21.73         | 4.756         | 3.034         |
| S.D.                       | 91.8             | 22.280  | 10.9          | 1.297    | 2.11          | 0.262           | 4.40          | 1.214         | 0.134         |
| <br>                       |                  |   |               |          |               |                 |               |               |               |
|                            |                  | Epididymis  |               | Prostate |               | Seminal vesicle |               | Brain         |               |
| Animal No.                 |                  | AB<br>g   | RE<br>g/100g  | AB<br>mg | RE<br>mg/100g | AB<br>g         | RE<br>g/100g  | AB<br>g       | RE<br>g/100g  |
|                            |                  | 1.06  | 0.25          | 542      | 128.44        | 1.79            | 0.42          | 2.14          | 0.51          |
| 10101                      |                  | 1.06  | 0.25          | 542      | 128.44        | 1.79            | 0.42          | 2.14          | 0.51          |
| 10102                      |                  | 1.40  | 0.29          | 710      | 147.00        | 1.93            | 0.40          | 2.25          | 0.47          |
| 10107                      |                  | 1.27  | 0.25          | 834      | 165.15        | 1.85            | 0.37          | 2.35          | 0.47          |
| 10108                      |                  | 1.19  | 0.30          | 716      | 178.55        | 2.35            | 0.59          | 2.19          | 0.55          |
| 10109                      |                  | 1.27  | 0.24          | 541      | 103.84        | 2.37            | 0.45          | 2.17          | 0.42          |
| 10110                      |                  | 1.24  | 0.29          | 712      | 169.12        | 2.01            | 0.48          | 2.11          | 0.50          |
| 10112                      |                  | 1.24  | 0.25          | 740      | 151.95        | 1.89            | 0.39          | 2.18          | 0.45          |
| n                          | 7                | 7   | 7             | 7        | 7             | 7               | 7             | 7             | 7             |
| Mean                       | 1.239            | 0.267   | 685.0         | 149.150  | 2.027         | 0.443           | 2.199         | 0.481         |               |
| S.D.                       | 0.102            | 0.025   | 107.0         | 25.863   | 0.237         | 0.075           | 0.080         | 0.043         |               |

AB : Absolute weight, RE : Relative weight by body weight

| Animal No. | Sex : Male<br>Body weight<br>g | Stage : Day 29<br>Dose : PTSA Monohydrate 50 mg/kg |              |         |              |         |              |          |               | Species : Rat |  |
|------------|--------------------------------|--|--------------|---------|--------------|---------|--------------|----------|---------------|---------------|--|
|            |                                | Liver  |              | Kidney  |              | Heart   |              | Spleen   |               |               |  |
|            |                                | AB<br>g  | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>mg | RE<br>mg/100g |               |  |
| 10201      | 417                            | 10.16  | 2.44         | 2.67    | 0.64         | 1.13    | 0.27         | 578      | 138.61        |               |  |
| 10202      | 459                            | 12.27  | 2.67         | 3.56    | 0.78         | 1.48    | 0.32         | 1295     | 282.14        |               |  |
| 10203      | 427                            | 10.76  | 2.52         | 3.18    | 0.74         | 1.46    | 0.34         | 711      | 166.51        |               |  |
| 10204      | 455                            | 10.79  | 2.37         | 3.57    | 0.78         | 1.42    | 0.31         | 751      | 165.05        |               |  |
| 10205      | 477                            | 11.03  | 2.31         | 3.54    | 0.74         | 1.72    | 0.36         | 724      | 151.78        |               |  |
| 10206      | 428                            | 10.26  | 2.40         | 2.82    | 0.66         | 1.39    | 0.32         | 682      | 159.35        |               |  |
| 10207      | 462                            | 10.35  | 2.24         | 3.56    | 0.77         | 1.57    | 0.34         | 746      | 161.47        |               |  |
| 10208      | 430                            | 9.89   | 2.30         | 3.17    | 0.74         | 1.50    | 0.35         | 639      | 148.60        |               |  |
| 10209      | 452                            | 12.36  | 2.73         | 3.71    | 0.82         | 1.39    | 0.31         | 720      | 159.29        |               |  |
| 10210      | 448                            | 12.17  | 2.72         | 3.03    | 0.68         | 1.26    | 0.28         | 748      | 166.96        |               |  |
| 10211      | 506                            | 13.65  | 2.70         | 3.49    | 0.69         | 1.46    | 0.29         | 998      | 197.23        |               |  |
| 10212      | 458                            | 12.81  | 2.80         | 3.39    | 0.74         | 1.63    | 0.36         | 809      | 176.64        |               |  |
| n          | 12                             | 12   | 12           | 12      | 12           | 12      | 12           | 12       | 12            |               |  |
| Mean       | 451.6                          | 11.375   | 2.517        | 3.308   | 0.732        | 1.451   | 0.321        | 783.4    | 172.803       |               |  |
| S.D.       | 24.6                           | 1.223  | 0.198        | 0.332   | 0.054        | 0.157   | 0.030        | 190.3    | 37.403        |               |  |

| Animal No. | Thymus   |               | Adrenal  |               | Pituitary gland |               | Thyroid  |               | Testis  |              |
|------------|----------|---------------|----------|---------------|-----------------|---------------|----------|---------------|---------|--------------|
|            | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>g | RE<br>g/100g |
|            |          |               |          |               |                 |               |          |               |         |              |
| 10201      | 375      | 89.93         | 52       | 12.47         | 9.7             | 2.33          | 24.1     | 5.78          | 3.17    | 0.76         |
| 10202      | 284      | 61.87         | 72       | 15.69         | 11.4            | 2.48          | 18.9     | 4.12          | 3.01    | 0.66         |
| 10203      | 388      | 90.87         | 59       | 13.82         | 10.7            | 2.51          | 21.3     | 4.99          | 3.42    | 0.80         |
| 10204      | 330      | 72.53         | 74       | 16.26         | 8.7             | 1.91          | 20.4     | 4.48          | 3.23    | 0.71         |
| 10205      | 228      | 47.80         | 71       | 14.88         | 13.2            | 2.77          | 24.2     | 5.07          | 3.43    | 0.72         |
| 10206      | 324      | 75.70         | 62       | 14.49         | 9.7             | 2.27          | 17.5     | 4.09          | 2.94    | 0.69         |
| 10207      | 347      | 75.11         | 79       | 17.10         | 11.6            | 2.51          | 16.1     | 3.48          | 3.56    | 0.77         |
| 10208      | 293      | 68.14         | 71       | 16.51         | 11.6            | 2.70          | 18.9     | 4.40          | 3.10    | 0.72         |
| 10209      | 293      | 64.82         | 54       | 11.95         | 11.8            | 2.61          | 15.2     | 3.36          | 3.01    | 0.67         |
| 10210      | 361      | 80.58         | 90       | 20.09         | 11.2            | 2.50          | 17.7     | 3.95          | 3.22    | 0.72         |
| 10211      | 266      | 52.57         | 95       | 18.77         | 14.3            | 2.83          | 27.1     | 5.36          | 3.39    | 0.67         |
| 10212      | 431      | 94.10         | 66       | 14.41         | 11.7            | 2.55          | 16.2     | 3.54          | 3.54    | 0.77         |
| n          | 12       | 12            | 12       | 12            | 12              | 12            | 12       | 12            | 12      | 12           |
| Mean       | 326.7    | 72.835        | 70.4     | 15.537        | 11.30           | 2.498         | 19.80    | 4.385         | 3.252   | 0.722        |
| S.D.       | 57.3     | 14.731        | 13.2     | 2.396         | 1.52            | 0.246         | 3.73     | 0.779         | 0.214   | 0.045        |

AB : Absolute weight, RE : Relative weight by body weight

| Animal No. | Organ weight<br>Sex : Male |              | Stage : Day 29<br>Dose : PTSA Monohydrate 50 mg/kg |               |                 |              | Species : Rat |              |
|------------|----------------------------|--------------|--|---------------|-----------------|--------------|---------------|--------------|
|            | Epididymis                 |              | Prostate   |               | Seminal vesicle |              | Brain         |              |
|            | AB<br>g                    | RE<br>g/100g | AB<br>mg   | RE<br>mg/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g |
| 10201      | 1.28                       | 0.31         | 814  | 195.20        | 2.26            | 0.54         | 2.17          | 0.52         |
| 10202      | 1.19                       | 0.26         | 768  | 167.32        | 1.87            | 0.41         | 2.21          | 0.48         |
| 10203      | 1.36                       | 0.32         | 616  | 144.26        | 2.23            | 0.52         | 2.06          | 0.48         |
| 10204      | 1.14                       | 0.25         | 824  | 181.10        | 2.39            | 0.53         | 2.27          | 0.50         |
| 10205      | 1.34                       | 0.28         | 831  | 174.21        | 2.45            | 0.51         | 2.18          | 0.46         |
| 10206      | 1.23                       | 0.29         | 709  | 165.65        | 1.91            | 0.45         | 2.19          | 0.51         |
| 10207      | 1.37                       | 0.30         | 900  | 194.81        | 2.67            | 0.58         | 2.12          | 0.46         |
| 10208      | 1.17                       | 0.27         | 628  | 146.05        | 2.40            | 0.56         | 2.34          | 0.54         |
| 10209      | 1.23                       | 0.27         | 912  | 201.77        | 2.17            | 0.48         | 2.06          | 0.46         |
| 10210      | 1.33                       | 0.30         | 602  | 134.38        | 2.15            | 0.48         | 2.06          | 0.46         |
| 10211      | 1.37                       | 0.27         | 699  | 138.14        | 1.91            | 0.38         | 2.24          | 0.44         |
| 10212      | 1.32                       | 0.29         | 805  | 175.76        | 2.28            | 0.50         | 2.30          | 0.50         |
| n          | 12                         | 12           | 12   | 12            | 12              | 12           | 12            | 12           |
| Mean       | 1.278                      | 0.284        | 759.0  | 168.221       | 2.224           | 0.495        | 2.183         | 0.484        |
| S.D.       | 0.083                      | 0.021        | 107.1  | 23.242        | 0.242           | 0.059        | 0.095         | 0.030        |

AB : Absolute weight, RE : Relative weight by body weight

| Animal No. | Sex : Male<br>Body weight<br>g | Stage : Day 29<br>Dose : PTSA Monohydrate 200 mg/kg |              |         |              |         |              | Species : Rat |               |
|------------|--------------------------------|---|--------------|---------|--------------|---------|--------------|---------------|---------------|
|            |                                | Liver   |              | Kidney  |              | Heart   |              | Spleen        |               |
|            |                                | AB<br>g   | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |
| 10301      | 476                            | 12.03   | 2.53         | 2.81    | 0.59         | 1.53    | 0.32         | 844           | 177.31        |
| 10302      | 426                            | 8.60  | 2.02         | 2.97    | 0.70         | 1.33    | 0.31         | 567           | 133.10        |
| 10303      | 456                            | 12.01   | 2.63         | 3.63    | 0.80         | 1.55    | 0.34         | 877           | 192.32        |
| 10304      | 429                            | 9.68  | 2.26         | 2.98    | 0.69         | 1.44    | 0.34         | 725           | 169.00        |
| 10305      | 470                            | 12.75   | 2.71         | 3.34    | 0.71         | 1.42    | 0.30         | 924           | 196.60        |
| 10306      | 506                            | 14.12   | 2.79         | 3.54    | 0.70         | 1.80    | 0.36         | 1046          | 206.72        |
| 10307      | 473                            | 11.21   | 2.37         | 3.49    | 0.74         | 1.64    | 0.35         | 871           | 184.14        |
| 10308      | 437                            | 12.45   | 2.85         | 3.27    | 0.75         | 1.36    | 0.31         | 775           | 177.35        |
| 10309      | 516                            | 12.50   | 2.42         | 3.31    | 0.64         | 1.70    | 0.33         | 972           | 188.37        |
| 10310      | 427                            | 10.65   | 2.49         | 2.82    | 0.66         | 1.33    | 0.31         | 638           | 149.41        |
| 10311      | 488                            | 11.80   | 2.42         | 3.54    | 0.73         | 1.47    | 0.30         | 875           | 179.30        |
| 10312      | 508                            | 13.05   | 2.57         | 4.03    | 0.79         | 1.41    | 0.28         | 846           | 166.54        |
| n          | 12                             | 12  | 12           | 12      | 12           | 12      | 12           | 12            | 12            |
| Mean       | 467.7                          | 11.738  | 2.505        | 3.311   | 0.708        | 1.498   | 0.321        | 830.0         | 176.680       |
| S.D.       | 32.9                           | 1.514   | 0.232        | 0.366   | 0.060        | 0.151   | 0.024        | 135.5         | 20.335        |

| Animal No. | Thymus   |               | Adrenal  |               | Pituitary gland |               | Thyroid  |               | Testis  |              |
|------------|----------|---------------|----------|---------------|-----------------|---------------|----------|---------------|---------|--------------|
|            | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>g | RE<br>g/100g |
|            |          |               |          |               |                 |               |          |               |         |              |
| 10301      | 361      | 75.84         | 47       | 9.87          | 11.6            | 2.44          | 18.5     | 3.89          | 3.12    | 0.66         |
| 10302      | 483      | 113.38        | 53       | 12.44         | 12.9            | 3.03          | 14.3     | 3.36          | 3.23    | 0.76         |
| 10303      | 317      | 69.52         | 59       | 12.94         | 12.2            | 2.68          | 21.6     | 4.74          | 3.28    | 0.72         |
| 10304      | 332      | 77.39         | 77       | 17.95         | 10.0            | 2.33          | 23.2     | 5.41          | 3.05    | 0.71         |
| 10305      | 333      | 70.85         | 62       | 13.19         | 10.4            | 2.21          | 20.3     | 4.32          | 3.48    | 0.74         |
| 10306      | 361      | 71.34         | 73       | 14.43         | 12.5            | 2.47          | 26.6     | 5.26          | 3.71    | 0.73         |
| 10307      | 402      | 84.99         | 70       | 14.80         | 11.5            | 2.43          | 23.6     | 4.99          | 2.80    | 0.59         |
| 10308      | 266      | 60.87         | 74       | 16.93         | 18.8            | 4.30          | 19.8     | 4.53          | 3.43    | 0.78         |
| 10309      | 377      | 73.06         | 67       | 12.98         | 9.7             | 1.88          | 21.8     | 4.22          | 3.50    | 0.68         |
| 10310      | 320      | 74.94         | 79       | 18.50         | 15.6            | 3.65          | 22.5     | 5.27          | 3.01    | 0.70         |
| 10311      | 343      | 70.29         | 70       | 14.34         | 14.0            | 2.87          | 18.8     | 3.85          | 3.47    | 0.71         |
| 10312      | 388      | 76.38         | 106      | 20.87         | 13.1            | 2.58          | 22.4     | 4.41          | 3.01    | 0.59         |
| n          | 12       | 12            | 12       | 12            | 12              | 12            | 12       | 12            | 12      | 12           |
| Mean       | 356.9    | 76.571        | 69.8     | 14.937        | 12.69           | 2.739         | 21.12    | 4.521         | 3.258   | 0.698        |
| S.D.       | 53.9     | 12.926        | 15.0     | 3.080         | 2.56            | 0.663         | 3.10     | 0.640         | 0.267   | 0.060        |

AB : Absolute weight, RE : Relative weight by body weight

| Animal No. | Organ weight<br>Sex : Male |              | Stage : Day 29<br>Dose : PTSA Monohydrate 200 mg/kg |               |                 |              | Species : Rat |              |
|------------|----------------------------|--------------|---|---------------|-----------------|--------------|---------------|--------------|
|            | Epididymis                 |              | Prostate  |               | Seminal vesicle |              | Brain         |              |
|            | AB<br>g                    | RE<br>g/100g | AB<br>mg  | RE<br>mg/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g |
| 10301      | 1.16                       | 0.24         | 749   | 157.35        | 1.34            | 0.28         | 2.16          | 0.45         |
| 10302      | 1.16                       | 0.27         | 748   | 175.59        | 2.26            | 0.53         | 2.17          | 0.51         |
| 10303      | 1.37                       | 0.30         | 886   | 194.30        | 1.85            | 0.41         | 2.14          | 0.47         |
| 10304      | 1.10                       | 0.26         | 841   | 196.04        | 2.32            | 0.54         | 2.22          | 0.52         |
| 10305      | 1.28                       | 0.27         | 677   | 144.04        | 1.66            | 0.35         | 2.25          | 0.48         |
| 10306      | 1.35                       | 0.27         | 636   | 125.69        | 2.19            | 0.43         | 2.16          | 0.43         |
| 10307      | 1.10                       | 0.23         | 339   | 71.67         | 1.69            | 0.36         | 2.23          | 0.47         |
| 10308      | 1.28                       | 0.29         | 683   | 156.29        | 2.48            | 0.57         | 2.10          | 0.48         |
| 10309      | 1.49                       | 0.29         | 860   | 166.67        | 2.32            | 0.45         | 2.23          | 0.43         |
| 10310      | 1.16                       | 0.27         | 648   | 151.76        | 1.81            | 0.42         | 2.11          | 0.49         |
| 10311      | 1.35                       | 0.28         | 781   | 160.04        | 2.01            | 0.41         | 2.29          | 0.47         |
| 10312      | 1.16                       | 0.23         | 950   | 187.01        | 2.38            | 0.47         | 2.39          | 0.47         |
| n          | 12                         | 12           | 12  | 12            | 12              | 12           | 12            | 12           |
| Mean       | 1.247                      | 0.267        | 733.2   | 157.204       | 2.026           | 0.435        | 2.204         | 0.473        |
| S.D.       | 0.125                      | 0.023        | 159.1   | 34.007        | 0.354           | 0.084        | 0.082         | 0.027        |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Male |                  | Stage : Day 29<br>Dose : PTSA Monohydrate 800 mg/kg |               |          |               |                 |               | Species : Rat |               |
|----------------------------|------------------|---|---------------|----------|---------------|-----------------|---------------|---------------|---------------|
| Animal No.                 | Body weight<br>g | Liver   |               | Kidney   |               | Heart           |               | Spleen        |               |
|                            |                  | AB<br>g   | RE<br>g/100g  | AB<br>g  | RE<br>g/100g  | AB<br>g         | RE<br>g/100g  | AB<br>mg      | RE<br>mg/100g |
| 10401                      | 438              | 11.42   | 2.61          | 3.08     | 0.70          | 1.46            | 0.33          | 874           | 199.54        |
| 10404                      | 418              | 10.97   | 2.62          | 3.18     | 0.76          | 1.37            | 0.33          | 720           | 172.25        |
| 10405                      | 428              | 11.66   | 2.72          | 2.80     | 0.65          | 1.20            | 0.28          | 687           | 160.51        |
| 10406                      | 484              | 13.32   | 2.75          | 3.34     | 0.69          | 1.61            | 0.33          | 702           | 145.04        |
| 10408                      | 418              | 10.99   | 2.63          | 3.38     | 0.81          | 1.32            | 0.32          | 743           | 177.75        |
| 10410                      | 407              | 10.24   | 2.52          | 3.10     | 0.76          | 1.24            | 0.30          | 682           | 167.57        |
| 10412                      | 484              | 12.74   | 2.63          | 3.57     | 0.74          | 1.34            | 0.28          | 787           | 162.60        |
| n                          | 7                | 7   | 7             | 7        | 7             | 7               | 7             | 7             | 7             |
| Mean                       | 439.6            | 11.620  | 2.640         | 3.207    | 0.730         | 1.363           | 0.310         | 742.1         | 169.323       |
| S.D.                       | 31.8             | 1.073   | 0.076         | 0.249    | 0.054         | 0.138           | 0.023         | 68.5          | 16.873        |
| <br>                       |                  |   |               |          |               |                 |               |               |               |
|                            |                  | Thymus  |               | Adrenal  |               | Pituitary gland |               | Thyroid       |               |
| Animal No.                 |                  | AB<br>mg  | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg      | RE<br>mg/100g |
|                            |                  | 374   | 85.39         | 56       | 12.79         | 10.9            | 2.49          | 19.0          | 4.34          |
| 10401                      |                  | 374   | 85.39         | 56       | 12.79         | 10.9            | 2.49          | 19.0          | 4.34          |
| 10404                      |                  | 250   | 59.81         | 71       | 16.99         | 14.1            | 3.37          | 16.5          | 3.95          |
| 10405                      |                  | 283   | 66.12         | 87       | 20.33         | 12.4            | 2.90          | 20.5          | 4.79          |
| 10406                      |                  | 390   | 80.58         | 64       | 13.22         | 11.4            | 2.36          | 19.3          | 3.99          |
| 10408                      |                  | 366   | 87.56         | 83       | 19.86         | 12.5            | 2.99          | 22.0          | 5.26          |
| 10410                      |                  | 296   | 72.73         | 71       | 17.44         | 9.4             | 2.31          | 19.9          | 4.89          |
| 10412                      |                  | 226   | 46.69         | 81       | 16.74         | 14.9            | 3.08          | 20.3          | 4.19          |
| n                          |                  | 7   | 7             | 7        | 7             | 7               | 7             | 7             | 7             |
| Mean                       |                  | 312.1   | 71.269        | 73.3     | 16.767        | 12.23           | 2.786         | 19.64         | 4.487         |
| S.D.                       |                  | 64.8  | 14.808        | 11.1     | 2.920         | 1.88            | 0.404         | 1.69          | 0.499         |
| <br>                       |                  |   |               |          |               |                 |               |               |               |
|                            |                  | Epididymis  |               | Prostate |               | Seminal vesicle |               | Brain         |               |
| Animal No.                 |                  | AB<br>g   | RE<br>g/100g  | AB<br>mg | RE<br>mg/100g | AB<br>g         | RE<br>g/100g  | AB<br>g       | RE<br>g/100g  |
|                            |                  | 1.18  | 0.27          | 857      | 195.66        | 2.68            | 0.61          | 2.17          | 0.50          |
| 10401                      |                  | 1.18  | 0.27          | 857      | 195.66        | 2.68            | 0.61          | 2.17          | 0.50          |
| 10404                      |                  | 1.23  | 0.29          | 810      | 193.78        | 2.32            | 0.56          | 2.20          | 0.53          |
| 10405                      |                  | 1.21  | 0.28          | 868      | 202.80        | 1.63            | 0.38          | 2.17          | 0.51          |
| 10406                      |                  | 1.33  | 0.27          | 706      | 145.87        | 2.10            | 0.43          | 2.16          | 0.45          |
| 10408                      |                  | 1.30  | 0.31          | 857      | 205.02        | 2.48            | 0.59          | 2.25          | 0.54          |
| 10410                      |                  | 1.12  | 0.28          | 588      | 144.47        | 2.33            | 0.57          | 2.07          | 0.51          |
| 10412                      |                  | 1.18  | 0.24          | 793      | 163.84        | 2.24            | 0.46          | 2.13          | 0.44          |
| n                          |                  | 7   | 7             | 7        | 7             | 7               | 7             | 7             | 7             |
| Mean                       |                  | 1.221   | 0.277         | 782.7    | 178.777       | 2.254           | 0.514         | 2.164         | 0.497         |
| S.D.                       |                  | 0.073   | 0.021         | 102.4    | 26.642        | 0.331           | 0.090         | 0.056         | 0.038         |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female |                  | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 0 mg/kg |              |         |              |         |              | Species : Rat |               |
|------------------------------|------------------|--|--------------|---------|--------------|---------|--------------|---------------|---------------|
| Animal No.                   | Body weight<br>g | Liver  |              | Kidney  |              | Heart   |              | Spleen        |               |
|                              |                  | AB<br>g  | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |
| 50151                        | 279              | 8.98   | 3.22         | 2.09    | 0.75         | 0.98    | 0.35         | 567           | 203.23        |
| 50152                        | 295              | 9.61   | 3.26         | 1.92    | 0.65         | 0.91    | 0.31         | 735           | 249.15        |
| 50153                        | 300              | 9.34   | 3.11         | 1.93    | 0.64         | 0.98    | 0.33         | 582           | 194.00        |
| 50154                        | 302              | 9.50   | 3.15         | 2.19    | 0.73         | 0.95    | 0.31         | 672           | 222.52        |
| 50155                        | 331              | 11.09  | 3.35         | 2.16    | 0.65         | 1.07    | 0.32         | 954           | 288.22        |
| 50156                        | 294              | 11.45  | 3.89         | 2.39    | 0.81         | 0.96    | 0.33         | 745           | 253.40        |
| 50157                        | 394              | 12.05  | 3.06         | 2.54    | 0.64         | 1.19    | 0.30         | 740           | 187.82        |
| 50158                        | 342              | 11.50  | 3.36         | 2.62    | 0.77         | 1.24    | 0.36         | 1014          | 296.49        |
| 50159                        | 308              | 10.99  | 3.57         | 2.40    | 0.78         | 1.11    | 0.36         | 883           | 286.69        |
| 50160                        | 421 \$           | 10.45 \$   | 2.48 \$      | 2.62 \$ | 0.62 \$      | 1.23 \$ | 0.29 \$      | 636 \$        | 151.07 \$     |
| 50161                        | 288              | 10.46  | 3.63         | 2.19    | 0.76         | 0.99    | 0.34         | 683           | 237.15        |
| 50162                        | 334              | 10.96  | 3.28         | 2.56    | 0.77         | 1.13    | 0.34         | 991           | 296.71        |
| n                            | 11               | 11   | 11           | 11      | 11           | 11      | 11           | 11            | 11            |
| Mean                         | 315.2            | 10.539   | 3.353        | 2.272   | 0.723        | 1.046   | 0.332        | 778.7         | 246.853       |
| S.D.                         | 33.0             | 1.027  | 0.251        | 0.246   | 0.065        | 0.108   | 0.020        | 158.3         | 41.429        |

|            |          | Thymus   |               | Adrenal  |               | Pituitary gland |               | Thyroid  |               | Ovary    |               |
|------------|----------|----------|---------------|----------|---------------|-----------------|---------------|----------|---------------|----------|---------------|
| Animal No. | AB<br>mg | AB       | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g |
| 50151      | 204      | 73.12    | 65            | 23.30    | 16.9          | 6.06            | 15.5          | 5.56     | 104           | 37.28    |               |
| 50152      | 248      | 84.07    | 73            | 24.75    | 18.2          | 6.17            | 18.0          | 6.10     | 107           | 36.27    |               |
| 50153      | 164      | 54.67    | 63            | 21.00    | 10.2          | 3.40            | 15.1          | 5.03     | 79            | 26.33    |               |
| 50154      | 265      | 87.75    | 77            | 25.50    | 17.8          | 5.89            | 16.5          | 5.46     | 108           | 35.76    |               |
| 50155      | 234      | 70.69    | 80            | 24.17    | 18.4          | 5.56            | 21.3          | 6.44     | 98            | 29.61    |               |
| 50156      | 200      | 68.03    | 80            | 27.21    | 18.1          | 6.16            | 12.2          | 4.15     | 104           | 35.37    |               |
| 50157      | 310      | 78.68    | 82            | 20.81    | 21.3          | 5.41            | 19.2          | 4.87     | 138           | 35.03    |               |
| 50158      | 235      | 68.71    | 116           | 33.92    | 21.6          | 6.32            | 16.7          | 4.88     | 139           | 40.64    |               |
| 50159      | 230      | 74.68    | 70            | 22.73    | 16.5          | 5.36            | 16.5          | 5.36     | 128           | 41.56    |               |
| 50160      | 300 \$   | 71.26 \$ | 94 \$         | 22.33 \$ | 19.5 \$       | 4.63 \$         | 20.0 \$       | 4.75 \$  | 171 \$        | 40.62 \$ |               |
| 50161      | 231      | 80.21    | 93            | 32.29    | 15.7          | 5.45            | 15.4          | 5.35     | 101           | 35.07    |               |
| 50162      | 253      | 75.75    | 82            | 24.55    | 17.5          | 5.24            | 15.3          | 4.58     | 135           | 40.42    |               |
| n          | 11       | 11       | 11            | 11       | 11            | 11              | 11            | 11       | 11            | 11       | 11            |
| Mean       | 234.0    | 74.215   | 80.1          | 25.475   | 17.47         | 5.547           | 16.52         | 5.253    | 112.8         | 35.758   |               |
| S.D.       | 37.8     | 8.961    | 14.6          | 4.218    | 3.01          | 0.807           | 2.38          | 0.655    | 19.4          | 4.579    |               |

AB : Absolute weight, RE : Relative weight by body weight

Animal No. 50160 : Non-pregnancy

\$ : Excepted data from calculation

| Organ weight<br>Sex : Female |          | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 0 mg/kg |         | Species : Rat |
|------------------------------|----------|--|---------|---------------|
| Animal No.                   | Uterus   | Brain  |         |               |
|                              | AB<br>mg | RE<br>mg/100g  | AB<br>g | RE<br>g/100g  |
| 50151                        | 694      | 248.75   | 2.10    | 0.75          |
| 50152                        | 638      | 216.27   | 2.12    | 0.72          |
| 50153                        | 664      | 221.33   | 2.04    | 0.68          |
| 50154                        | 854      | 282.78   | 2.02    | 0.67          |
| 50155                        | 665      | 200.91   | 1.99    | 0.60          |
| 50156                        | 565      | 192.18   | 2.02    | 0.69          |
| 50157                        | 710      | 180.20   | 2.16    | 0.55          |
| 50158                        | 798      | 233.33   | 2.20    | 0.64          |
| 50159                        | 752      | 244.16   | 2.15    | 0.70          |
| 50160                        | 534 \$   | 126.84 \$  | 2.32 \$ | 0.55 \$       |
| 50161                        | 692      | 240.28   | 1.94    | 0.67          |
| 50162                        | 784      | 234.73   | 2.18    | 0.65          |
| n                            | 11       | 11   | 11      | 11            |
| Mean                         | 710.5    | 226.811  | 2.084   | 0.665         |
| S.D.                         | 81.6     | 28.957   | 0.086   | 0.055         |

AB : Absolute weight, RE : Relative weight by body weight

Animal No. 50160 : Non-pregnancy

\$ : Excepted data from calculation

| Animal No. | Organ weight<br>Sex : Female |        | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 50 mg/kg |              |         |              |         |              | Species : Rat |               |
|------------|------------------------------|--------|---|--------------|---------|--------------|---------|--------------|---------------|---------------|
|            | Body weight<br>g             | Liver  | Kidney  |              | Heart   |              | Spleen  |              |               |               |
|            |                              |        | AB<br>g   | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |
| 50251      | 290                          | 10.47  | 3.61  | 2.12         | 0.73    | 0.89         | 0.31    | 642          | 221.38        |               |
| 50252      | 312                          | 10.38  | 3.33  | 1.99         | 0.64    | 1.02         | 0.33    | 1061         | 340.06        |               |
| 50253      | 328                          | 10.18  | 3.10  | 2.30         | 0.70    | 1.04         | 0.32    | 703          | 214.33        |               |
| 50254      | 335                          | 10.99  | 3.28  | 2.26         | 0.67    | 1.04         | 0.31    | 894          | 266.87        |               |
| 50255      | 287                          | 9.29   | 3.24  | 1.91         | 0.67    | 1.00         | 0.35    | 766          | 266.90        |               |
| 50256      | 329                          | 10.22  | 3.11  | 2.13         | 0.65    | 1.09         | 0.33    | 677          | 205.78        |               |
| 50257      | 303                          | 8.80   | 2.90  | 2.10         | 0.69    | 0.98         | 0.32    | 627          | 206.93        |               |
| 50258      | 293                          | 8.48   | 2.89  | 2.09         | 0.71    | 0.82         | 0.28    | 597          | 203.75        |               |
| 50259      | 349                          | 10.92  | 3.13  | 2.67         | 0.77    | 1.30         | 0.37    | 861          | 246.70        |               |
| 50260      | 288                          | 9.71   | 3.37  | 2.39         | 0.83    | 0.97         | 0.34    | 756          | 262.50        |               |
| 50261      | 327                          | 11.98  | 3.66  | 2.35         | 0.72    | 1.20         | 0.37    | 881          | 269.42        |               |
| 50262      | 336                          | 11.85  | 3.53  | 2.42         | 0.72    | 1.27         | 0.38    | 660          | 196.43        |               |
| n          | 12                           | 12     | 12  | 12           | 12      | 12           | 12      | 12           | 12            |               |
| Mean       | 314.8                        | 10.273 | 3.263   | 2.228        | 0.708   | 1.052        | 0.334   | 760.4        | 241.754       |               |
| S.D.       | 21.9                         | 1.090  | 0.253   | 0.212        | 0.053   | 0.144        | 0.029   | 138.8        | 41.909        |               |

| Animal No. | Thymus   |               | Adrenal  |               | Pituitary gland |               | Thyroid  |               | Ovary    |               |
|------------|----------|---------------|----------|---------------|-----------------|---------------|----------|---------------|----------|---------------|
|            | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g |
|            |          |               |          |               |                 |               |          |               |          |               |
| 50251      | 241      | 83.10         | 70       | 24.14         | 20.2            | 6.97          | 20.4     | 7.03          | 124      | 42.76         |
| 50252      | 218      | 69.87         | 62       | 19.87         | 16.5            | 5.29          | 18.0     | 5.77          | 91       | 29.17         |
| 50253      | 385      | 117.38        | 75       | 22.87         | 17.9            | 5.46          | 15.3     | 4.66          | 98       | 29.88         |
| 50254      | 248      | 74.03         | 70       | 20.90         | 18.7            | 5.58          | 19.0     | 5.67          | 136      | 40.60         |
| 50255      | 241      | 83.97         | 83       | 28.92         | 17.6            | 6.13          | 15.6     | 5.44          | 121      | 42.16         |
| 50256      | 235      | 71.43         | 68       | 20.67         | 18.8            | 5.71          | 23.3     | 7.08          | 116      | 35.26         |
| 50257      | 203      | 67.00         | 62       | 20.46         | 15.6            | 5.15          | 15.6     | 5.15          | 96       | 31.68         |
| 50258      | 214      | 73.04         | 76       | 25.94         | 20.4            | 6.96          | 18.2     | 6.21          | 86       | 29.35         |
| 50259      | 261      | 74.79         | 75       | 21.49         | 23.3            | 6.68          | 21.6     | 6.19          | 116      | 33.24         |
| 50260      | 204      | 70.83         | 87       | 30.21         | 16.0            | 5.56          | 15.0     | 5.21          | 83       | 28.82         |
| 50261      | 243      | 74.31         | 91       | 27.83         | 18.6            | 5.69          | 16.6     | 5.08          | 136      | 41.59         |
| 50262      | 197      | 58.63         | 113      | 33.63         | 14.6            | 4.35          | 19.7     | 5.86          | 151      | 44.94         |
| n          | 12       | 12            | 12       | 12            | 12              | 12            | 12       | 12            | 12       | 12            |
| Mean       | 240.8    | 76.532        | 77.7     | 24.744        | 18.18           | 5.794         | 18.19    | 5.779         | 112.8    | 35.788        |
| S.D.       | 49.8     | 14.484        | 14.3     | 4.524         | 2.40            | 0.776         | 2.70     | 0.751         | 22.0     | 6.195         |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female |          | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 50 mg/kg |         | Species : Rat |
|------------------------------|----------|---|---------|---------------|
| Animal No.                   | Uterus   | Brain   |         |               |
|                              | AB<br>mg | RE<br>mg/100g   | AB<br>g | RE<br>g/100g  |
| 50251                        | 605      | 208.62  | 2.01    | 0.69          |
| 50252                        | 546      | 175.00  | 2.11    | 0.68          |
| 50253                        | 799      | 243.60  | 2.12    | 0.65          |
| 50254                        | 588      | 175.52  | 2.05    | 0.61          |
| 50255                        | 704      | 245.30  | 2.05    | 0.71          |
| 50256                        | 645      | 196.05  | 2.06    | 0.63          |
| 50257                        | 671      | 221.45  | 2.12    | 0.70          |
| 50258                        | 652      | 222.53  | 2.07    | 0.71          |
| 50259                        | 567      | 162.46  | 2.08    | 0.60          |
| 50260                        | 771      | 267.71  | 2.05    | 0.71          |
| 50261                        | 919      | 281.04  | 2.18    | 0.67          |
| 50262                        | 767      | 228.27  | 2.07    | 0.62          |
| n                            | 12       | 12  | 12      | 12            |
| Mean                         | 686.2    | 218.963   | 2.081   | 0.665         |
| S.D.                         | 110.4    | 37.271  | 0.045   | 0.041         |

AB : Absolute weight, RE : Relative weight by body weight

| Animal No. | Organ weight<br>Sex : Female |        | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 200 mg/kg |              |         |              |         |              | Species : Rat |               |
|------------|------------------------------|--------|--|--------------|---------|--------------|---------|--------------|---------------|---------------|
|            | Body weight<br>g             | Liver  | Kidney   |              | Heart   |              | Spleen  |              |               |               |
|            |                              |        | AB<br>g  | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>g | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |
| 50351      | 372                          | 11.41  | 3.07   | 2.29         | 0.62    | 1.07         | 0.29    | 647          | 173.92        |               |
| 50352      | 299                          | 11.02  | 3.69   | 2.44         | 0.82    | 1.03         | 0.34    | 753          | 251.84        |               |
| 50353      | 302                          | 9.09   | 3.01   | 1.97         | 0.65    | 0.98         | 0.32    | 574          | 190.07        |               |
| 50354      | 300                          | 8.97   | 2.99   | 1.85         | 0.62    | 0.97         | 0.32    | 760          | 253.33        |               |
| 50355      | 303                          | 10.28  | 3.39   | 2.19         | 0.72    | 1.02         | 0.34    | 959          | 316.50        |               |
| 50356      | 308                          | 9.77   | 3.17   | 2.07         | 0.67    | 1.06         | 0.34    | 798          | 259.09        |               |
| 50357      | 330                          | 11.09  | 3.36   | 2.30         | 0.70    | 0.97         | 0.29    | 812          | 246.06        |               |
| 50358      | 296                          | 10.06  | 3.40   | 2.04         | 0.69    | 1.00         | 0.34    | 918          | 310.14        |               |
| 50359      | 350                          | 11.56  | 3.30   | 2.48         | 0.71    | 1.29         | 0.37    | 965          | 275.71        |               |
| 50360      | 305                          | 9.95   | 3.26   | 2.11         | 0.69    | 0.99         | 0.32    | 671          | 220.00        |               |
| 50361      | 358                          | 11.23  | 3.14   | 2.25         | 0.63    | 1.19         | 0.33    | 704          | 196.65        |               |
| 50362      | 323                          | 10.54  | 3.26   | 2.45         | 0.76    | 1.08         | 0.33    | 1190         | 368.42        |               |
| n          | 12                           | 12     | 12   | 12           | 12      | 12           | 12      | 12           | 12            |               |
| Mean       | 320.5                        | 10.414 | 3.253  | 2.203        | 0.690   | 1.054        | 0.328   | 812.6        | 255.144       |               |
| S.D.       | 26.2                         | 0.875  | 0.197  | 0.201        | 0.059   | 0.097        | 0.022   | 170.8        | 56.925        |               |

| Animal No. | Thymus   |               | Adrenal  |               | Pituitary gland |               | Thyroid  |               | Ovary    |               |
|------------|----------|---------------|----------|---------------|-----------------|---------------|----------|---------------|----------|---------------|
|            | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g |
|            |          |               |          |               |                 |               |          |               |          |               |
| 50351      | 373      | 100.27        | 64       | 17.20         | 17.7            | 4.76          | 21.1     | 5.67          | 94       | 25.27         |
| 50352      | 177      | 59.20         | 71       | 23.75         | 16.3            | 5.45          | 18.8     | 6.29          | 124      | 41.47         |
| 50353      | 239      | 79.14         | 82       | 27.15         | 14.8            | 4.90          | 14.2     | 4.70          | 91       | 30.13         |
| 50354      | 297      | 99.00         | 60       | 20.00         | 13.1            | 4.37          | 23.2     | 7.73          | 96       | 32.00         |
| 50355      | 206      | 67.99         | 83       | 27.39         | 18.8            | 6.20          | 13.8     | 4.55          | 91       | 30.03         |
| 50356      | 262      | 85.06         | 78       | 25.32         | 14.5            | 4.71          | 13.2     | 4.29          | 89       | 28.90         |
| 50357      | 308      | 93.33         | 81       | 24.55         | 19.0            | 5.76          | 16.0     | 4.85          | 97       | 29.39         |
| 50358      | 316      | 106.76        | 67       | 22.64         | 13.9            | 4.70          | 13.7     | 4.63          | 88       | 29.73         |
| 50359      | 390      | 111.43        | 101      | 28.86         | 18.6            | 5.31          | 15.1     | 4.31          | 111      | 31.71         |
| 50360      | 277      | 90.82         | 85       | 27.87         | 16.0            | 5.25          | 14.0     | 4.59          | 101      | 33.11         |
| 50361      | 327      | 91.34         | 89       | 24.86         | 19.2            | 5.36          | 18.4     | 5.14          | 114      | 31.84         |
| 50362      | 264      | 81.73         | 89       | 27.55         | 16.2            | 5.02          | 19.3     | 5.98          | 124      | 38.39         |
| n          | 12       | 12            | 12       | 12            | 12              | 12            | 12       | 12            | 12       | 12            |
| Mean       | 286.3    | 88.839        | 79.2     | 24.762        | 16.51           | 5.149         | 16.73    | 5.228         | 101.7    | 31.831        |
| S.D.       | 62.7     | 15.279        | 11.8     | 3.472         | 2.14            | 0.512         | 3.33     | 1.024         | 13.2     | 4.325         |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female |          | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 200 mg/kg |         | Species : Rat |
|------------------------------|----------|--|---------|---------------|
| Animal No.                   | Uterus   | Brain  |         |               |
|                              | AB<br>mg | RE<br>mg/100g  | AB<br>g | RE<br>g/100g  |
| 50351                        | 688      | 184.95   | 2.07    | 0.56          |
| 50352                        | 775      | 259.20   | 2.12    | 0.71          |
| 50353                        | 686      | 227.15   | 2.05    | 0.68          |
| 50354                        | 541      | 180.33   | 1.90    | 0.63          |
| 50355                        | 761      | 251.16   | 2.00    | 0.66          |
| 50356                        | 655      | 212.66   | 1.97    | 0.64          |
| 50357                        | 541      | 163.94   | 1.92    | 0.58          |
| 50358                        | 639      | 215.88   | 2.11    | 0.71          |
| 50359                        | 868      | 248.00   | 2.00    | 0.57          |
| 50360                        | 552      | 180.98   | 2.09    | 0.69          |
| 50361                        | 752      | 210.06   | 2.13    | 0.59          |
| 50362                        | 692      | 214.24   | 2.08    | 0.64          |
| n                            | 12       | 12   | 12      | 12            |
| Mean                         | 679.2    | 212.379  | 2.037   | 0.638         |
| S.D.                         | 101.7    | 30.624   | 0.078   | 0.054         |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female |                  | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 800 mg/kg |               |          |               |                 |               | Species : Rat |               |
|------------------------------|------------------|--|---------------|----------|---------------|-----------------|---------------|---------------|---------------|
| Animal No.                   | Body weight<br>g | Liver  |               | Kidney   |               | Heart           |               | Spleen        |               |
|                              |                  | AB<br>g  | RE<br>g/100g  | AB<br>g  | RE<br>g/100g  | AB<br>g         | RE<br>g/100g  | AB<br>mg      | RE<br>mg/100g |
| 50451                        | 320              | 10.43  | 3.26          | 2.31     | 0.72          | 1.12            | 0.35          | 625           | 195.31        |
| 50452                        | 282              | 8.25   | 2.93          | 2.44     | 0.87          | 0.96            | 0.34          | 619           | 219.50        |
| 50453                        | 302              | 10.30  | 3.41          | 2.61     | 0.86          | 1.10            | 0.36          | 519           | 171.85        |
| 50454                        | 297              | 9.55   | 3.22          | 2.15     | 0.72          | 1.08            | 0.36          | 712           | 239.73        |
| 50455                        | 332 \$           | 11.29 \$   | 3.40 \$       | 2.52 \$  | 0.76 \$       | 1.09 \$         | 0.33 \$       | 516 \$        | 155.42 \$     |
| 50456                        | 289 \$           | 7.02 \$  | 2.43 \$       | 2.27 \$  | 0.79 \$       | 0.92 \$         | 0.32 \$       | 463 \$        | 160.21 \$     |
| 50457                        | 346              | 10.47  | 3.03          | 2.22     | 0.64          | 1.06            | 0.31          | 702           | 202.89        |
| 50459                        | 321              | 10.69  | 3.33          | 2.60     | 0.81          | 0.96            | 0.30          | 787           | 245.17        |
| 50460                        | 411              | 13.38  | 3.26          | 3.05     | 0.74          | 1.17            | 0.28          | 1005          | 244.53        |
| 50461                        | 366              | 13.19  | 3.60          | 2.43     | 0.66          | 1.29            | 0.35          | 943           | 257.65        |
| 50462                        | 286              | 9.44   | 3.30          | 2.34     | 0.82          | 0.94            | 0.33          | 655           | 229.02        |
| n                            | 9                | 9  | 9             | 9        | 9             | 9               | 9             | 9             | 9             |
| Mean                         | 325.7            | 10.633   | 3.260         | 2.461    | 0.760         | 1.076           | 0.331         | 729.7         | 222.850       |
| S.D.                         | 42.2             | 1.679  | 0.196         | 0.270    | 0.084         | 0.113           | 0.028         | 157.7         | 27.998        |
| I-598                        |                  |  |               |          |               |                 |               |               |               |
|                              |                  | Thymus   |               | Adrenal  |               | Pituitary gland |               | Thyroid       |               |
| Animal No.                   |                  | AB<br>mg   | RE<br>mg/100g | AB<br>mg | RE<br>mg/100g | AB<br>mg        | RE<br>mg/100g | AB<br>mg      | RE<br>mg/100g |
| 50451                        |                  | 212  | 66.25         | 85       | 26.56         | 19.4            | 6.06          | 15.7          | 4.91          |
| 50452                        |                  | 263  | 93.26         | 76       | 26.95         | 18.1            | 6.42          | 18.2          | 6.45          |
| 50453                        |                  | 199  | 65.89         | 77       | 25.50         | 18.8            | 6.23          | 16.4          | 5.43          |
| 50454                        |                  | 147  | 49.49         | 69       | 23.23         | 16.3            | 5.49          | 12.4          | 4.18          |
| 50455                        |                  | 301 \$   | 90.66 \$      | 96 \$    | 28.92 \$      | 17.7 \$         | 5.33 \$       | 18.0 \$       | 5.42 \$       |
| 50456                        |                  | 334 \$   | 115.57 \$     | 88 \$    | 30.45 \$      | 13.2 \$         | 4.57 \$       | 12.6 \$       | 4.36 \$       |
| 50457                        |                  | 256  | 73.99         | 78       | 22.54         | 19.3            | 5.58          | 14.6          | 4.22          |
| 50459                        |                  | 263  | 81.93         | 81       | 25.23         | 18.0            | 5.61          | 17.5          | 5.45          |
| 50460                        |                  | 228  | 55.47         | 91       | 22.14         | 16.3            | 3.97          | 19.7          | 4.79          |
| 50461                        |                  | 361  | 98.63         | 89       | 24.32         | 21.3            | 5.82          | 13.6          | 3.72          |
| 50462                        |                  | 191  | 66.78         | 72       | 25.17         | 17.0            | 5.94          | 16.2          | 5.66          |
| n                            |                  | 9  | 9             | 9        | 9             | 9               | 9             | 9             | 9             |
| Mean                         |                  | 235.6  | 72.410        | 79.8     | 24.627        | 18.28           | 5.680         | 16.03         | 4.979         |
| S.D.                         |                  | 60.7   | 16.355        | 7.4      | 1.701         | 1.63            | 0.712         | 2.28          | 0.858         |

AB : Absolute weight, RE : Relative weight by body weight

Animal No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

Animal No. 50456 : Non-pregnancy

\$ : Excepted data from calculation

| Organ weight<br>Sex : Female |          | Stage : Lactation Day 5<br>Dose : PTSA Monohydrate 800 mg/kg |         | Species : Rat |
|------------------------------|----------|--|---------|---------------|
| Animal No.                   | Uterus   |  | Brain   |               |
|                              | AB<br>mg | RE<br>mg/100g  | AB<br>g | RE<br>g/100g  |
| 50451                        | 711      | 222.19   | 2.06    | 0.64          |
| 50452                        | 616      | 218.44   | 2.04    | 0.72          |
| 50453                        | 675      | 223.51   | 2.00    | 0.66          |
| 50454                        | 697      | 234.68   | 1.98    | 0.67          |
| 50455                        | 724 \$   | 218.07 \$  | 2.02 \$ | 0.61 \$       |
| 50456                        | 397 \$   | 137.37 \$  | 1.99 \$ | 0.69 \$       |
| 50457                        | 764      | 220.81   | 2.17    | 0.63          |
| 50459                        | 564      | 175.70   | 2.10    | 0.65          |
| 50460                        | 793      | 192.94   | 2.03    | 0.49          |
| 50461                        | 798      | 218.03   | 2.14    | 0.58          |
| 50462                        | 688      | 240.56   | 1.97    | 0.69          |
| n                            | 9        | 9  | 9       | 9             |
| Mean                         | 700.7    | 216.318  | 2.054   | 0.637         |
| S.D.                         | 78.1     | 20.109   | 0.070   | 0.067         |

AB : Absolute weight, RE : Relative weight by body weight

Animal No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

Animal No. 50456 : Non-pregnancy

\$ : Excepted data from calculation

| Organ weight<br>Sex : Female (satellite) |                  | Stage : Day 29<br>Dose : PTSA Monohydrate 0 mg/kg |              |                 |              |               |              | Species : Rat |               |        |
|--|------------------|---|--------------|-----------------|--------------|---------------|--------------|---------------|---------------|--------|
| Animal No.                               | Body weight<br>g | Liver   |              | Kidney          |              | Heart         |              | Spleen        |               |        |
|  |                  | AB<br>g   | RE<br>g/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |        |
| 50551                                    | 249              | 5.31  | 2.13         | 1.90            | 0.76         | 0.88          | 0.35         | 466           | 187.15        |        |
| 50552                                    | 250              | 6.78  | 2.71         | 1.66            | 0.66         | 0.76          | 0.30         | 584           | 233.60        |        |
| 50553                                    | 263              | 6.59  | 2.51         | 2.03            | 0.77         | 0.94          | 0.36         | 445           | 169.20        |        |
| 50554                                    | 272              | 6.99  | 2.57         | 1.77            | 0.65         | 0.91          | 0.33         | 450           | 165.44        |        |
| 50555                                    | 279              | 8.48  | 3.04         | 2.00            | 0.72         | 1.05          | 0.38         | 511           | 183.15        |        |
| n  | 5                | 5   | 5            | 5               | 5            | 5             | 5            | 5             | 5             |        |
| Mean                                     | 262.6            | 6.830   | 2.592        | 1.872           | 0.712        | 0.908         | 0.344        | 491.2         | 187.708       |        |
| S.D.                                     | 13.2             | 1.131   | 0.330        | 0.156           | 0.055        | 0.105         | 0.030        | 58.0          | 27.229        |        |
| Thymus                                   |                  | Adrenal   |              | Pituitary gland |              | Thyroid       |              | Ovary         |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g                                     | AB<br>mg     | RE<br>mg/100g   | AB<br>mg     | RE<br>mg/100g | AB<br>mg     | RE<br>mg/100g | AB<br>mg      |        |
|  |                  |   |              |                 |              |               |              |               |               |        |
| 50551                                    | 365              | 146.59  | 83           | 33.33           | 12.6         | 5.06          | 22.4         | 9.00          | 110           | 44.18  |
| 50552                                    | 390              | 156.00  | 75           | 30.00           | 16.2         | 6.48          | 23.8         | 9.52          | 104           | 41.60  |
| 50553                                    | 305              | 115.97  | 86           | 32.70           | 14.5         | 5.51          | 14.0         | 5.32          | 117           | 44.49  |
| 50554                                    | 398              | 146.32  | 57           | 20.96           | 13.9         | 5.11          | 11.7         | 4.30          | 80            | 29.41  |
| 50555                                    | 362              | 129.75  | 89           | 31.90           | 15.0         | 5.38          | 17.7         | 6.34          | 115           | 41.22  |
| n  | 5                | 5   | 5            | 5               | 5            | 5             | 5            | 5             | 5             | 5      |
| Mean                                     | 364.0            | 138.926   | 78.0         | 29.778          | 14.44        | 5.508         | 17.92        | 6.896         | 105.2         | 40.180 |
| S.D.                                     | 36.5             | 15.938  | 12.8         | 5.086           | 1.33         | 0.575         | 5.21         | 2.283         | 15.0          | 6.198  |
| Uterus                                   |                  | Brain   |              |                 |              |               |              |               |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g                                     | AB<br>g      | RE<br>g/100g    |              |               |              |               |               |        |
|  |                  |   |              |                 |              |               |              |               |               |        |
| 50551                                    | 489              | 196.39  | 1.90         | 0.76            |              |               |              |               |               |        |
| 50552                                    | 786              | 314.40  | 1.91         | 0.76            |              |               |              |               |               |        |
| 50553                                    | 1054             | 400.76  | 1.93         | 0.73            |              |               |              |               |               |        |
| 50554                                    | 917              | 337.13  | 1.89         | 0.69            |              |               |              |               |               |        |
| 50555                                    | 654              | 234.41  | 1.96         | 0.70            |              |               |              |               |               |        |
| n  | 5                | 5   | 5            | 5               |              |               |              |               |               |        |
| Mean                                     | 780.0            | 296.618   | 1.918        | 0.728           |              |               |              |               |               |        |
| S.D.                                     | 220.5            | 81.729  | 0.028        | 0.033           |              |               |              |               |               |        |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female (satellite) |                  | Stage : Day 29<br>Dose : PTSA Monohydrate 800 mg/kg |              |                 |              |               |              | Species : Rat |               |        |
|--|------------------|---|--------------|-----------------|--------------|---------------|--------------|---------------|---------------|--------|
| Animal No.                               | Body weight<br>g | Liver   |              | Kidney          |              | Heart         |              | Spleen        |               |        |
|  |                  | AB<br>g   | RE<br>g/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |        |
| 50651                                    | 265              | 6.83  | 2.58         | 2.04            | 0.77         | 0.79          | 0.30         | 462           | 174.34        |        |
| 50652                                    | 258              | 7.31  | 2.83         | 1.86            | 0.72         | 0.99          | 0.38         | 633           | 245.35        |        |
| 50653                                    | 258              | 7.05  | 2.73         | 1.70            | 0.66         | 0.92          | 0.36         | 451           | 174.81        |        |
| 50654                                    | 243              | 6.38  | 2.63         | 1.88            | 0.77         | 0.84          | 0.35         | 435           | 179.01        |        |
| 50655                                    | 264              | 8.18  | 3.10         | 2.72            | 1.03         | 0.98          | 0.37         | 645           | 244.32        |        |
| n  | 5                | 5   | 5            | 5               | 5            | 5             | 5            | 5             | 5             |        |
| Mean                                     | 257.6            | 7.150   | 2.774        | 2.040           | 0.790        | 0.904         | 0.352        | 525.2         | 203.566       |        |
| S.D.                                     | 8.8              | 0.669   | 0.206        | 0.399           | 0.142        | 0.087         | 0.031        | 104.4         | 37.719        |        |
| Thymus                                   |                  | Adrenal   |              | Pituitary gland |              | Thyroid       |              | Ovary         |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g                                       | AB<br>mg     | RE<br>mg/100g   | AB<br>mg     | RE<br>mg/100g | AB<br>mg     | RE<br>mg/100g | AB<br>mg      |        |
|  |                  |   |              |                 |              |               |              |               |               |        |
| 50651                                    | 423              | 159.62  | 72           | 27.17           | 15.9         | 6.00          | 22.0         | 8.30          | 136           | 51.32  |
| 50652                                    | 423              | 163.95  | 66           | 25.58           | 19.7         | 7.64          | 16.7         | 6.47          | 96            | 37.21  |
| 50653                                    | 283              | 109.69  | 75           | 29.07           | 14.8         | 5.74          | 15.0         | 5.81          | 96            | 37.21  |
| 50654                                    | 216              | 88.89   | 78           | 32.10           | 14.4         | 5.93          | 12.9         | 5.31          | 88            | 36.21  |
| 50655                                    | 365              | 138.26  | 87           | 32.95           | 15.0         | 5.68          | 19.5         | 7.39          | 124           | 46.97  |
| n  | 5                | 5   | 5            | 5               | 5            | 5             | 5            | 5             | 5             | 5      |
| Mean                                     | 342.0            | 132.082   | 75.6         | 29.374          | 15.96        | 6.198         | 17.22        | 6.656         | 108.0         | 41.784 |
| S.D.                                     | 90.8             | 32.323  | 7.8          | 3.145           | 2.16         | 0.817         | 3.60         | 1.205         | 20.8          | 6.905  |
| Uterus                                   |                  | Brain   |              |                 |              |               |              |               |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g                                       | AB<br>g      | RE<br>g/100g    |              |               |              |               |               |        |
|  |                  |   |              |                 |              |               |              |               |               |        |
| 50651                                    | 783              | 295.47  | 1.98         | 0.75            |              |               |              |               |               |        |
| 50652                                    | 562              | 217.83  | 1.97         | 0.76            |              |               |              |               |               |        |
| 50653                                    | 781              | 302.71  | 1.94         | 0.75            |              |               |              |               |               |        |
| 50654                                    | 552              | 227.16  | 2.01         | 0.83            |              |               |              |               |               |        |
| 50655                                    | 611              | 231.44  | 2.09         | 0.79            |              |               |              |               |               |        |
| n  | 5                | 5   | 5            | 5               |              |               |              |               |               |        |
| Mean                                     | 657.8            | 254.922   | 1.998        | 0.776           |              |               |              |               |               |        |
| S.D.                                     | 115.6            | 40.699  | 0.057        | 0.034           |              |               |              |               |               |        |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Male |                  | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 0 mg/kg |              |                 |              |               |              | Species : Rat |               |       |
|----------------------------|------------------|--|--------------|-----------------|--------------|---------------|--------------|---------------|---------------|-------|
| Animal No.                 | Body weight<br>g | Liver  |              | Kidney          |              | Heart         |              | Spleen        |               |       |
|                            |                  | AB<br>g  | RE<br>g/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |       |
| 10103                      | 508              | 12.44  | 2.45         | 3.40            | 0.67         | 1.48          | 0.29         | 641           | 126.18        |       |
| 10104                      | 458              | 10.43  | 2.28         | 3.21            | 0.70         | 1.44          | 0.31         | 692           | 151.09        |       |
| 10105                      | 511              | 12.85  | 2.51         | 3.46            | 0.68         | 1.73          | 0.34         | 745           | 145.79        |       |
| 10106                      | 495              | 11.43  | 2.31         | 3.27            | 0.66         | 1.68          | 0.34         | 713           | 144.04        |       |
| 10111                      | 459              | 12.05  | 2.63         | 3.36            | 0.73         | 1.30          | 0.28         | 775           | 168.85        |       |
| n                          | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             | 5             |       |
| Mean                       | 486.2            | 11.840   | 2.436        | 3.340           | 0.688        | 1.526         | 0.312        | 713.2         | 147.190       |       |
| S.D.                       | 26.0             | 0.946  | 0.144        | 0.100           | 0.028        | 0.177         | 0.028        | 51.2          | 15.311        |       |
|                            |                  |  |              |                 |              |               |              |               |               |       |
| Thymus                     |                  | Adrenal  |              | Pituitary gland |              | Thyroid       |              | Testis        |               |       |
| Animal No.                 | AB<br>mg         | RE<br>mg/100g  | AB<br>mg     | RE<br>mg/100g   | AB<br>mg     | RE<br>mg/100g | AB<br>mg     | RE<br>mg/100g | AB<br>g       |       |
|                            |                  |  |              |                 |              |               |              |               |               |       |
| 10103                      | 454              | 89.37  | 52           | 10.24           | 14.4         | 2.83          | 28.8         | 5.67          | 3.21          | 0.63  |
| 10104                      | 289              | 63.10  | 75           | 16.38           | 13.5         | 2.95          | 19.3         | 4.21          | 3.57          | 0.78  |
| 10105                      | 418              | 81.80  | 61           | 11.94           | 12.5         | 2.45          | 21.7         | 4.25          | 3.32          | 0.65  |
| 10106                      | 317              | 64.04  | 86           | 17.37           | 13.1         | 2.65          | 20.8         | 4.20          | 3.48          | 0.70  |
| 10111                      | 309              | 67.32  | 78           | 16.99           | 10.9         | 2.37          | 28.1         | 6.12          | 3.42          | 0.75  |
| n                          | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             | 5             | 5     |
| Mean                       | 357.4            | 73.126   | 70.4         | 14.584          | 12.88        | 2.650         | 23.74        | 4.890         | 3.400         | 0.702 |
| S.D.                       | 73.6             | 11.789   | 13.7         | 3.265           | 1.30         | 0.245         | 4.39         | 0.931         | 0.140         | 0.064 |
|                            |                  |  |              |                 |              |               |              |               |               |       |
| Epididymis                 |                  | Prostate   |              | Seminal vesicle |              | Brain         |              |               |               |       |
| Animal No.                 | AB<br>g          | RE<br>g/100g   | AB<br>mg     | RE<br>mg/100g   | AB<br>g      | RE<br>g/100g  | AB<br>g      | RE<br>g/100g  |               |       |
|                            |                  |  |              |                 |              |               |              |               |               |       |
| 10103                      | 1.32             | 0.26   | 978          | 192.52          | 2.39         | 0.47          | 2.26         | 0.44          |               |       |
| 10104                      | 1.26             | 0.28   | 607          | 132.53          | 1.81         | 0.40          | 2.22         | 0.48          |               |       |
| 10105                      | 1.39             | 0.27   | 752          | 147.16          | 1.99         | 0.39          | 2.27         | 0.44          |               |       |
| 10106                      | 1.39             | 0.28   | 663          | 133.94          | 2.31         | 0.47          | 2.18         | 0.44          |               |       |
| 10111                      | 1.37             | 0.30   | 838          | 182.57          | 2.54         | 0.55          | 2.30         | 0.50          |               |       |
| n                          | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             |               |       |
| Mean                       | 1.346            | 0.278  | 767.6        | 157.744         | 2.208        | 0.456         | 2.246        | 0.460         |               |       |
| S.D.                       | 0.056            | 0.015  | 146.8        | 28.018          | 0.300        | 0.065         | 0.047        | 0.028         |               |       |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Male |                  | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 800 mg/kg |              |                 |              |               |              | Species : Rat |               |
|----------------------------|------------------|--|--------------|-----------------|--------------|---------------|--------------|---------------|---------------|
| Animal No.                 | Body weight<br>g | Liver  |              | Kidney          |              | Heart         |              | Spleen        |               |
|                            |                  | AB<br>g  | RE<br>g/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |
| 10402                      | 490              | 11.12  | 2.27         | 2.89            | 0.59         | 1.53          | 0.31         | 932           | 190.20        |
| 10403                      | 485              | 11.76  | 2.42         | 3.39            | 0.70         | 1.49          | 0.31         | 804           | 165.77        |
| 10407                      | 493              | 12.27  | 2.49         | 3.46            | 0.70         | 1.56          | 0.32         | 856           | 173.63        |
| 10409                      | 464              | 9.83   | 2.12         | 2.83            | 0.61         | 1.33          | 0.29         | 752           | 162.07        |
| 10411                      | 515              | 13.57  | 2.63         | 3.76            | 0.73         | 1.55          | 0.30         | 690           | 133.98        |
| n                          | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             | 5             |
| Mean                       | 489.4            | 11.710   | 2.386        | 3.266           | 0.666        | 1.492         | 0.306        | 806.8         | 165.130       |
| S.D.                       | 18.3             | 1.384  | 0.197        | 0.396           | 0.062        | 0.094         | 0.011        | 93.2          | 20.499        |
|                            |                  |  |              |                 |              |               |              |               |               |
| Thymus                     |                  | Adrenal  |              | Pituitary gland |              | Thyroid       |              | Testis        |               |
| Animal No.                 | AB<br>mg         | RE<br>mg/100g  | AB<br>mg     | RE<br>mg/100g   | AB<br>mg     | RE<br>mg/100g | AB<br>mg     | RE<br>mg/100g | AB<br>g       |
|                            |                  |  |              |                 |              |               |              |               |               |
| 10402                      | 392              | 80.00  | 59           | 12.04           | 11.8         | 2.41          | 20.0         | 4.08          | 3.34          |
| 10403                      | 489              | 100.82   | 60           | 12.37           | 11.8         | 2.43          | 16.0         | 3.30          | 3.81          |
| 10407                      | 230              | 46.65  | 79           | 16.02           | 15.0         | 3.04          | 21.4         | 4.34          | 3.69          |
| 10409                      | 317              | 68.32  | 80           | 17.24           | 10.5         | 2.26          | 18.8         | 4.05          | 3.17          |
| 10411                      | 262              | 50.87  | 56           | 10.87           | 10.0         | 1.94          | 18.9         | 3.67          | 3.95          |
| n                          | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             | 5             |
| Mean                       | 338.0            | 69.332   | 66.8         | 13.708          | 11.82        | 2.416         | 19.02        | 3.888         | 3.592         |
| S.D.                       | 104.4            | 22.145   | 11.7         | 2.759           | 1.95         | 0.400         | 1.99         | 0.406         | 0.327         |
|                            |                  |  |              |                 |              |               |              |               |               |
| Epididymis                 |                  | Prostate   |              | Seminal vesicle |              | Brain         |              |               |               |
| Animal No.                 | AB<br>g          | RE<br>g/100g   | AB<br>mg     | RE<br>mg/100g   | AB<br>g      | RE<br>g/100g  | AB<br>g      | RE<br>g/100g  | AB<br>g       |
|                            |                  |  |              |                 |              |               |              |               |               |
| 10402                      | 1.22             | 0.25   | 482          | 98.37           | 1.81         | 0.37          | 2.22         | 0.45          |               |
| 10403                      | 1.39             | 0.29   | 1014         | 209.07          | 2.02         | 0.42          | 2.19         | 0.45          |               |
| 10407                      | 1.49             | 0.30   | 906          | 183.77          | 2.18         | 0.44          | 2.48         | 0.50          |               |
| 10409                      | 1.16             | 0.25   | 678          | 146.12          | 2.24         | 0.48          | 2.24         | 0.48          |               |
| 10411                      | 1.42             | 0.28   | 549          | 106.60          | 2.57         | 0.50          | 2.16         | 0.42          |               |
| n                          | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             |               |
| Mean                       | 1.336            | 0.274  | 725.8        | 148.786         | 2.164        | 0.442         | 2.258        | 0.460         |               |
| S.D.                       | 0.140            | 0.023  | 228.3        | 47.923          | 0.281        | 0.051         | 0.128        | 0.031         |               |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female (satellite) |                  | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 0 mg/kg |              |                 |              |               |              | Species : Rat |               |        |
|--|------------------|--|--------------|-----------------|--------------|---------------|--------------|---------------|---------------|--------|
| Animal No.                               | Body weight<br>g | Liver  |              | Kidney          |              | Heart         |              | Spleen        |               |        |
|  |                  | AB<br>g  | RE<br>g/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |        |
| 50556                                    | 280              | 7.67   | 2.74         | 2.01            | 0.72         | 0.89          | 0.32         | 535           | 191.07        |        |
| 50557                                    | 264              | 7.10   | 2.69         | 1.83            | 0.69         | 0.89          | 0.34         | 419           | 158.71        |        |
| 50558                                    | 287              | 7.65   | 2.67         | 2.03            | 0.71         | 1.12          | 0.39         | 527           | 183.62        |        |
| 50559                                    | 276              | 5.75   | 2.08         | 1.92            | 0.70         | 0.89          | 0.32         | 493           | 178.62        |        |
| 50560                                    | 278              | 7.36   | 2.65         | 1.68            | 0.60         | 0.96          | 0.35         | 454           | 163.31        |        |
| n  | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             | 5             |        |
| Mean                                     | 277.0            | 7.106  | 2.566        | 1.894           | 0.684        | 0.950         | 0.344        | 485.6         | 175.066       |        |
| S.D.                                     | 8.4              | 0.793  | 0.274        | 0.144           | 0.048        | 0.100         | 0.029        | 49.1          | 13.672        |        |
| Thymus                                   |                  | Adrenal  |              | Pituitary gland |              | Thyroid       |              | Ovary         |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g  | AB<br>mg     | RE<br>mg/100g   | AB<br>mg     | RE<br>mg/100g | AB<br>mg     | RE<br>mg/100g | AB<br>mg      |        |
|  |                  |  |              |                 |              |               |              |               |               |        |
| 50556                                    | 237              | 84.64  | 97           | 34.64           | 19.0         | 6.79          | 12.7         | 4.54          | 79            | 28.21  |
| 50557                                    | 254              | 96.21  | 69           | 26.14           | 14.1         | 5.34          | 12.9         | 4.89          | 83            | 31.44  |
| 50558                                    | 273              | 95.12  | 58           | 20.21           | 14.3         | 4.98          | 12.6         | 4.39          | 99            | 34.49  |
| 50559                                    | 334              | 121.01   | 87           | 31.52           | 19.2         | 6.96          | 12.5         | 4.53          | 75            | 27.17  |
| 50560                                    | 335              | 120.50   | 62           | 22.30           | 19.5         | 7.01          | 16.5         | 5.94          | 46            | 16.55  |
| n  | 5                | 5  | 5            | 5               | 5            | 5             | 5            | 5             | 5             | 5      |
| Mean                                     | 286.6            | 103.496  | 74.6         | 26.962          | 17.22        | 6.216         | 13.44        | 4.858         | 76.4          | 27.572 |
| S.D.                                     | 45.5             | 16.391   | 16.7         | 6.077           | 2.76         | 0.976         | 1.72         | 0.632         | 19.3          | 6.798  |
| Uterus                                   |                  | Brain  |              |                 |              |               |              |               |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g  | AB<br>g      | RE<br>g/100g    |              |               |              |               |               |        |
|  |                  |  |              |                 |              |               |              |               |               |        |
| 50556                                    | 597              | 213.21   | 1.97         | 0.70            |              |               |              |               |               |        |
| 50557                                    | 744              | 281.82   | 2.00         | 0.76            |              |               |              |               |               |        |
| 50558                                    | 522              | 181.88   | 2.19         | 0.76            |              |               |              |               |               |        |
| 50559                                    | 647              | 234.42   | 2.06         | 0.75            |              |               |              |               |               |        |
| 50560                                    | 595              | 214.03   | 1.98         | 0.71            |              |               |              |               |               |        |
| n  | 5                | 5  | 5            | 5               |              |               |              |               |               |        |
| Mean                                     | 621.0            | 225.072  | 2.040        | 0.736           |              |               |              |               |               |        |
| S.D.                                     | 81.9             | 36.864   | 0.091        | 0.029           |              |               |              |               |               |        |

AB : Absolute weight, RE : Relative weight by body weight

| Organ weight<br>Sex : Female (satellite) |                  | Stage : Recovery Day 15<br>Dose : PTSA Monohydrate 800 mg/kg |              |                 |              |               |              | Species : Rat |               |        |
|--|------------------|--|--------------|-----------------|--------------|---------------|--------------|---------------|---------------|--------|
| Animal No.                               | Body weight<br>g | Liver  |              | Kidney          |              | Heart         |              | Spleen        |               |        |
|  |                  | AB<br>g  | RE<br>g/100g | AB<br>g         | RE<br>g/100g | AB<br>g       | RE<br>g/100g | AB<br>mg      | RE<br>mg/100g |        |
| 50656                                    | 234              | 5.76   | 2.46         | 1.81            | 0.77         | 0.78          | 0.33         | 465           | 198.72        |        |
| 50657                                    | 311              | 7.12   | 2.29         | 1.89            | 0.61         | 0.97          | 0.31         | 559           | 179.74        |        |
| 50658                                    | 263              | 6.92   | 2.63         | 2.28            | 0.87         | 0.87          | 0.33         | 578           | 219.77        |        |
| 50659                                    | 291              | 8.06   | 2.77         | 2.12            | 0.73         | 0.90          | 0.31         | 526           | 180.76        |        |
| n  | 4                | 4  | 4            | 4               | 4            | 4             | 4            | 4             | 4             |        |
| Mean                                     | 274.8            | 6.965  | 2.538        | 2.025           | 0.745        | 0.880         | 0.320        | 532.0         | 194.748       |        |
| S.D.                                     | 33.5             | 0.945  | 0.208        | 0.215           | 0.108        | 0.079         | 0.012        | 49.6          | 18.822        |        |
|  |                  |  |              |                 |              |               |              |               |               |        |
| Thymus                                   |                  | Adrenal  |              | Pituitary gland |              | Thyroid       |              | Ovary         |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g  | AB<br>mg     | RE<br>mg/100g   | AB<br>mg     | RE<br>mg/100g | AB<br>mg     | RE<br>mg/100g | AB<br>mg      |        |
|  |                  |  |              |                 |              |               |              |               |               |        |
| 50656                                    | 140              | 59.83  | 58           | 24.79           | 14.8         | 6.32          | 12.0         | 5.13          | 66            | 28.21  |
| 50657                                    | 463              | 148.87   | 74           | 23.79           | 21.8         | 7.01          | 13.8         | 4.44          | 100           | 32.15  |
| 50658                                    | 222              | 84.41  | 69           | 26.24           | 14.7         | 5.59          | 18.4         | 7.00          | 76            | 28.90  |
| 50659                                    | 304              | 104.47   | 74           | 25.43           | 20.6         | 7.08          | 16.5         | 5.67          | 47            | 16.15  |
| n  | 4                | 4  | 4            | 4               | 4            | 4             | 4            | 4             | 4             | 4      |
| Mean                                     | 282.3            | 99.395   | 68.8         | 25.063          | 17.98        | 6.500         | 15.18        | 5.560         | 72.3          | 26.353 |
| S.D.                                     | 137.9            | 37.698   | 7.5          | 1.035           | 3.76         | 0.697         | 2.84         | 1.084         | 22.1          | 7.015  |
|  |                  |  |              |                 |              |               |              |               |               |        |
| Uterus                                   |                  | Brain  |              |                 |              |               |              |               |               |        |
| Animal No.                               | AB<br>mg         | RE<br>mg/100g  | AB<br>g      | RE<br>g/100g    |              |               |              |               |               |        |
|  |                  |  |              |                 |              |               |              |               |               |        |
| 50656                                    | 608              | 259.83   | 2.13         | 0.91            |              |               |              |               |               |        |
| 50657                                    | 687              | 220.90   | 2.11         | 0.68            |              |               |              |               |               |        |
| 50658                                    | 842              | 320.15   | 2.05         | 0.78            |              |               |              |               |               |        |
| 50659                                    | 797              | 273.88   | 2.19         | 0.75            |              |               |              |               |               |        |
| n  | 4                | 4  | 4            | 4               |              |               |              |               |               |        |
| Mean                                     | 733.5            | 268.690  | 2.120        | 0.780           |              |               |              |               |               |        |
| S.D.                                     | 106.0            | 40.977   | 0.058        | 0.096           |              |               |              |               |               |        |

AB : Absolute weight, RE : Relative weight by body weight

| Histopathological findings  |                |                    |               |
|---|----------------|--------------------|---------------|
| Sex : Male  |                | Stage : Day 29     | Species : Rat |
| Test article : PTSA Monohydrate   | Dose : 0 mg/kg | Animal No. : 10101 |               |
| <b>Kidney</b>   |                |                    |               |
| Findings : Finding present  |                |                    |               |
| Basophilic change, renal tubule   |                |                    |               |
| Slight  |                |                    |               |
| <b>Prostate</b>   |                |                    |               |
| Findings : Finding present  |                |                    |               |
| Inflammation, interstitium  |                |                    |               |
| Slight  |                |                    |               |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Testis, Epididymis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur            |                |                    |               |
| Test article : PTSA Monohydrate   | Dose : 0 mg/kg | Animal No. : 10102 |               |
| <b>Liver</b>  |                |                    |               |
| Findings : Finding present  |                |                    |               |
| Microgranuloma  |                |                    |               |
| Slight  |                |                    |               |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                |                    |               |
| Test article : PTSA Monohydrate   | Dose : 0 mg/kg | Animal No. : 10107 |               |
| <b>Kidney</b>   |                |                    |               |
| Findings : Finding present  |                |                    |               |
| Basophilic change, renal tubule   |                |                    |               |
| Slight  |                |                    |               |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur  |                |                    |               |

| Histopathological findings   |                |                    |               |
|--|----------------|--------------------|---------------|
| Sex : Male   |                | Stage : Day 29     | Species : Rat |
| Test article : PTSA Monohydrate  | Dose : 0 mg/kg | Animal No. : 10108 |               |
| <b>Lung</b>  |                |                    |               |
| Findings : Finding present<br>Aggregation, macrophage, alveolar<br>Slight  |                |                    |               |
| <b>Liver</b>   |                |                    |               |
| Findings : Finding present<br>Microgranuloma<br>Slight   |                |                    |               |
| <b>Prostate</b>  |                |                    |               |
| Findings : Finding present<br>Inflammation, interstitium<br>Slight   |                |                    |               |
| <b>Thyroid</b>   |                |                    |               |
| Findings : Finding present<br>Ultimobranchial body<br>Slight   |                |                    |               |
| Finding absent : Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Testis, Epididymis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                |                    |               |

|  |                |                    |
|--|----------------|--------------------|
| Test article : PTSA Monohydrate  | Dose : 0 mg/kg | Animal No. : 10109 |
| <b>Prostate</b>  |                |                    |
| Findings : Finding present<br>Inflammation, interstitium<br>Slight   |                |                    |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Testis, Epididymis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                |                    |

| Histopathological findings                   |  | Sex : Male         | Stage : Day 29 | Species : Rat |
|--|--|--------------------|----------------|---------------|
| Test article : PTSA Monohydrate              | Dose : 0 mg/kg   | Animal No. : 10110 | Infertility    |               |
| Lung   |  |                    |                |               |
| Findings : Finding present                   |  |                    |                |               |
| Aggregation, macrophage, alveolar            |  |                    |                |               |
| Slight                                       |  |                    |                |               |
| Parathyroid                                  |  |                    |                |               |
| Findings : Finding absent                    |  |                    |                |               |
| Animal Comment : right parathyroid : missing |  |                    |                |               |
| Finding absent :                             | Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur   |                    |                |               |
| Test article : PTSA Monohydrate              | Dose : 0 mg/kg   | Animal No. : 10112 |                |               |
| Pancreas                                     |  |                    |                |               |
| Findings : Finding present                   |  |                    |                |               |
| Atrophy, acinar cell, focal                  |  |                    |                |               |
| Slight                                       |  |                    |                |               |
| Heart  |  |                    |                |               |
| Findings : Finding present                   |  |                    |                |               |
| Cardiomyopathy, focal                        |  |                    |                |               |
| Slight                                       |  |                    |                |               |
| Finding absent :                             | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Liver, Kidney, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                    |                |               |

| Histopathological findings      |                 | Sex : Male         | Stage : Day 29 | Species : Rat |
|---------------------------------|-----------------|--------------------|----------------|---------------|
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10201 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10202 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10203 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10204 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10205 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10206 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10207 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10208 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10209 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10210 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10211 |                |               |
| Finding absent :                | Stomach         |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 10212 |                |               |
| Finding absent :                | Stomach         |                    |                |               |

| Histopathological findings      |                  | Sex : Male         | Stage : Day 29 | Species : Rat |
|---------------------------------|------------------|--------------------|----------------|---------------|
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10301 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10302 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10303 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10304 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10305 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10306 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10307 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10308 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10309 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10310 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10311 |                |               |
| Finding absent :                | Stomach          |                    |                |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 10312 |                |               |
| Finding absent :                | Stomach          |                    |                |               |

| Histopathological findings   |  |                    |                |
|--|--|--------------------|----------------|
| Test article : PTSA Monohydrate  | Dose : 800 mg/kg   | Animal No. : 10401 | Stage : Day 29 |
| Species : Rat  |  |                    |                |
| <b>Stomach</b>   |  |                    |                |
| Findings : Finding present   |  |                    |                |
| Hyperplasia, squamous cell, limiting ridge                                 |  |                    |                |
| Slight   |  |                    |                |
| Finding absent :   | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                    |                |
| <b>Test article : PTSA Monohydrate Dose : 800 mg/kg Animal No. : 10404</b> |  |                    |                |
| <b>Stomach</b>   |  |                    |                |
| Findings : Finding present   |  |                    |                |
| Hyperplasia, squamous cell, limiting ridge                                 |  |                    |                |
| Slight   |  |                    |                |
| <b>Liver</b>   |  |                    |                |
| Findings : Finding present   |  |                    |                |
| Microgranuloma   |  |                    |                |
| Slight   |  |                    |                |
| <b>Kidney</b>  |  |                    |                |
| Findings : Finding present   |  |                    |                |
| Basophilic change, renal tubule  |  |                    |                |
| Slight   |  |                    |                |
| <b>Prostate</b>  |  |                    |                |
| Findings : Finding present   |  |                    |                |
| Inflammation, interstitium   |  |                    |                |
| Slight   |  |                    |                |
| Finding absent :   | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Urinary bladder, Testis, Epididymis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur                          |                    |                |

| Histopathological findings                 |  | Sex : Male         | Stage : Day 29 | Species : Rat |
|--|--|--------------------|----------------|---------------|
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 10405 |                |               |
| <b>Stomach</b>                             |  |                    |                |               |
| Findings : Finding present                 |  |                    |                |               |
| Hyperplasia, squamous cell, limiting ridge | Slight   |                    |                |               |
| <b>Kidney</b>                              |  |                    |                |               |
| Findings : Finding present                 |  |                    |                |               |
| Basophilic change, renal tubule            | Slight   |                    |                |               |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                    |                |               |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 10406 | Infertility    |               |
| <b>Lung</b>                                |  |                    |                |               |
| Findings : Finding present                 |  |                    |                |               |
| Aggregation, macrophage, alveolar          | Slight   |                    |                |               |
| <b>Stomach</b>                             |  |                    |                |               |
| Findings : Finding present                 |  |                    |                |               |
| Hyperplasia, squamous cell, limiting ridge | Slight   |                    |                |               |
| <b>Heart</b>                               |  |                    |                |               |
| Findings : Finding present                 |  |                    |                |               |
| Cardiomyopathy, focal                      | Slight   |                    |                |               |
| <b>Prostate</b>                            |  |                    |                |               |
| Findings : Finding present                 |  |                    |                |               |
| Inflammation, interstitium                 | Slight   |                    |                |               |
| Finding absent :                           | Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Kidney, Urinary bladder, Testis, Epididymis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur                |                    |                |               |

| Histopathological findings                 |  | Stage : Day 29     | Species : Rat |
|--|--|--------------------|---------------|
| Sex : Male                                 |  |                    |               |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 10408 |               |
| Stomach                                    |  |                    |               |
| Findings : Finding present                 |  |                    |               |
| Hyperplasia, squamous cell, limiting ridge |  |                    |               |
| Slight                                     |  |                    |               |
| Epididymis                                 |  |                    |               |
| Findings : Finding present                 |  |                    |               |
| Granuloma, spermatic                       |  |                    |               |
| Slight                                     |  |                    |               |
| Prostate                                   |  |                    |               |
| Findings : Finding present                 |  |                    |               |
| Inflammation, interstitium                 |  |                    |               |
| Slight                                     |  |                    |               |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Testis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur                       |                    |               |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 10410 |               |
| Stomach                                    |  |                    |               |
| Findings : Finding present                 |  |                    |               |
| Hyperplasia, squamous cell, limiting ridge |  |                    |               |
| Slight                                     |  |                    |               |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Testis, Epididymis, Prostate, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur |                    |               |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 10412 |               |
| Pancreas                                   |  |                    |               |
| Findings : Finding present                 |  |                    |               |
| Atrophy, acinar cell, focal                |  |                    |               |
| Slight                                     |  |                    |               |
| Prostate                                   |  |                    |               |
| Findings : Finding present                 |  |                    |               |
| Inflammation, interstitium                 |  |                    |               |
| Slight                                     |  |                    |               |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Liver, Heart, Kidney, Urinary bladder, Testis, Epididymis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur            |                    |               |

| Histopathological findings                   |   | Stage : Lactation Day 5 | Species : Rat |
|--|---|-------------------------|---------------|
| Sex : Female                                 |   |                         |               |
| Test article : PTSA Monohydrate              | Dose : 0 mg/kg  | Animal No. : 50151      |               |
| Finding absent :                             | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |
| Test article : PTSA Monohydrate              | Dose : 0 mg/kg  | Animal No. : 50152      |               |
| Lung   |   |                         |               |
| Findings : Finding present                   |   |                         |               |
| Aggregation, macrophage, alveolar            |   |                         |               |
| Slight                                       |   |                         |               |
| Parathyroid                                  |   |                         |               |
| Findings : Finding absent                    |   |                         |               |
| Animal Comment : right parathyroid : missing |   |                         |               |
| Finding absent :                             | Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland                    |                         |               |
| Test article : PTSA Monohydrate              | Dose : 0 mg/kg  | Animal No. : 50153      |               |
| Liver  |   |                         |               |
| Findings : Finding present                   |   |                         |               |
| Microgranuloma                               |   |                         |               |
| Slight                                       |   |                         |               |
| Finding absent :                             | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland        |                         |               |

| Histopathological findings      |   |                         |               |
|---------------------------------|---|-------------------------|---------------|
| Sex : Female                    |   | Stage : Lactation Day 5 | Species : Rat |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50154      |               |
| Liver                           |   |                         |               |
| Findings : Finding present      |   |                         |               |
| Microgranuloma                  |   |                         |               |
| Slight                          |   |                         |               |
| Kidney                          |   |                         |               |
| Findings : Finding present      |   |                         |               |
| Basophilic change, renal tubule |   |                         |               |
| Slight                          |   |                         |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland                |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50155      |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50156      |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50157      |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50158      |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |

| Histopathological findings      |   |                         |               |
|---------------------------------|---|-------------------------|---------------|
| Sex : Female                    |   | Stage : Lactation Day 5 | Species : Rat |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50159      |               |
| Thyroid                         |   |                         |               |
| Findings : Finding present      |   |                         |               |
| Ultimobranchial body            |   |                         |               |
| Slight                          |   |                         |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland          |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50160      | Non-pregnancy |
| Kidney                          |   |                         |               |
| Findings : Finding present      |   |                         |               |
| Basophilic change, renal tubule |   |                         |               |
| Slight                          |   |                         |               |
| Pituitary gland                 |   |                         |               |
| Findings : Finding present      |   |                         |               |
| Cyst, pars distalis             |   |                         |               |
| Slight                          |   |                         |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland                          |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50161      |               |
| Thyroid                         |   |                         |               |
| Findings : Finding present      |   |                         |               |
| Ultimobranchial body            |   |                         |               |
| Slight                          |   |                         |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland          |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg  | Animal No. : 50162      |               |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |

| Histopathological findings      |                 | Sex : Female       | Stage : Lactation Day 5 | Species : Rat |
|---------------------------------|-----------------|--------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50251 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50252 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50253 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50254 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50255 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50256 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50257 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50258 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50259 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50260 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50261 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 50 mg/kg | Animal No. : 50262 |                         |               |
| Finding absent :                | Stomach, Kidney |                    |                         |               |

| Histopathological findings      |                  | Stage : Lactation Day 5 | Species : Rat |
|---------------------------------|------------------|-------------------------|---------------|
| Sex : Female                    |                  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50351      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50352      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50353      |               |
| Kidney                          |                  |                         |               |
| Findings : Finding present      |                  |                         |               |
| Basophilic change, renal tubule |                  |                         |               |
| Slight                          |                  |                         |               |
| Finding absent :                | Stomach          |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50354      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50355      |               |
| Kidney                          |                  |                         |               |
| Findings : Finding present      |                  |                         |               |
| Basophilic change, renal tubule |                  |                         |               |
| Slight                          |                  |                         |               |
| Finding absent :                | Stomach          |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50356      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50357      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50358      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50359      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50360      |               |
| Kidney                          |                  |                         |               |
| Findings : Finding present      |                  |                         |               |
| Basophilic change, renal tubule |                  |                         |               |
| Slight                          |                  |                         |               |
| Finding absent :                | Stomach          |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50361      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |
| Test article : PTSA Monohydrate | Dose : 200 mg/kg | Animal No. : 50362      |               |
| Finding absent :                | Stomach, Kidney  |                         |               |

| Histopathological findings  |                  |                         |               |
|---|------------------|-------------------------|---------------|
| Sex : Female  |                  | Stage : Lactation Day 5 | Species : Rat |
| Test article : PTSA Monohydrate   | Dose : 800 mg/kg | Animal No. : 50451      |               |
| <b>Stomach</b>  |                  |                         |               |
| Findings : Finding present  |                  |                         |               |
| Hyperplasia, squamous cell, limiting ridge  |                  |                         |               |
| Slight  |                  |                         |               |
| <b>Kidney</b>   |                  |                         |               |
| Findings : Finding present  |                  |                         |               |
| Basophilic change, renal tubule   |                  |                         |               |
| Slight  |                  |                         |               |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                  |                         |               |

|  |                  |                    |
|--|------------------|--------------------|
| Test article : PTSA Monohydrate  | Dose : 800 mg/kg | Animal No. : 50452 |
| <b>Stomach</b>   |                  |                    |
| Findings : Finding present   |                  |                    |
| Hyperplasia, squamous cell, limiting ridge   |                  |                    |
| Slight   |                  |                    |
| Hyperkeratosis, limiting ridge   |                  |                    |
| Slight   |                  |                    |
| <b>Kidney</b>  |                  |                    |
| Findings : Finding present   |                  |                    |
| Basophilic change, renal tubule  |                  |                    |
| Slight   |                  |                    |
| <b>Thyroid</b>   |                  |                    |
| Findings : Finding present   |                  |                    |
| Ultimobranchial body   |                  |                    |
| Slight   |                  |                    |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                  |                    |

| Histopathological findings                 |   |                         |                   |
|--|---|-------------------------|-------------------|
| Sex : Female                               |   | Stage : Lactation Day 5 | Species : Rat     |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg  | Animal No. : 50453      |                   |
| Kidney                                     |   |                         |                   |
| Findings : Finding present                 |   |                         |                   |
| Basophilic change, renal tubule            |   |                         |                   |
| Slight                                     |   |                         |                   |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |                   |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg  | Animal No. : 50454      |                   |
| Kidney                                     |   |                         |                   |
| Findings : Finding present                 |   |                         |                   |
| Basophilic change, renal tubule            |   |                         |                   |
| Slight                                     |   |                         |                   |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |                   |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg  | Animal No. : 50455      | Total litter loss |
| Stomach                                    |   |                         |                   |
| Findings : Finding present                 |   |                         |                   |
| Hyperplasia, squamous cell, limiting ridge |   |                         |                   |
| Slight                                     |   |                         |                   |
| Hyperkeratosis, limiting ridge             |   |                         |                   |
| Slight                                     |   |                         |                   |
| Liver                                      |   |                         |                   |
| Findings : Finding present                 |   |                         |                   |
| Vacuolation, hepatocyte, periportal        |   |                         |                   |
| Slight                                     |   |                         |                   |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland         |                         |                   |

| Histopathological findings                 |  |                    |               | Stage : Lactation Day 5 | Species : Rat |
|--|--|--------------------|---------------|-------------------------|---------------|
| Sex : Female                               |  |                    |               |                         |               |
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 50456 | Non-pregnancy |                         |               |
| Stomach                                    |  |                    |               |                         |               |
| Findings : Finding present                 |  |                    |               |                         |               |
| Hyperplasia, squamous cell, limiting ridge |  |                    |               |                         |               |
| Slight                                     |  |                    |               |                         |               |
| Kidney                                     |  |                    |               |                         |               |
| Findings : Finding present                 |  |                    |               |                         |               |
| Basophilic change, renal tubule            |  |                    |               |                         |               |
| Mild                                       |  |                    |               |                         |               |
| Cast, hyaline                              |  |                    |               |                         |               |
| Slight                                     |  |                    |               |                         |               |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                    |               |                         |               |

|  |   |                    |  |  |  |
|--|---|--------------------|--|--|--|
| Test article : PTSA Monohydrate              | Dose : 800 mg/kg  | Animal No. : 50457 |  |  |  |
| Stomach                                      |   |                    |  |  |  |
| Findings : Finding present                   |   |                    |  |  |  |
| Hyperplasia, squamous cell, limiting ridge   |   |                    |  |  |  |
| Slight                                       |   |                    |  |  |  |
| Hyperkeratosis, limiting ridge               |   |                    |  |  |  |
| Slight                                       |   |                    |  |  |  |
| Kidney                                       |   |                    |  |  |  |
| Findings : Finding present                   |   |                    |  |  |  |
| Basophilic change, renal tubule              |   |                    |  |  |  |
| Slight                                       |   |                    |  |  |  |
| Parathyroid                                  |   |                    |  |  |  |
| Findings : Finding absent                    |   |                    |  |  |  |
| Animal Comment : right parathyroid : missing |   |                    |  |  |  |
| Finding absent :                             | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                    |  |  |  |

| Histopathological findings   |                  | Sex : Female       | Stage : Lactation Day 5 | Species : Rat |
|--|------------------|--------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate  | Dose : 800 mg/kg | Animal No. : 50458 | Died on lactation day 0 |               |
| <b>Lung</b>  |                  |                    |                         |               |
| Findings : Finding present   |                  |                    |                         |               |
| Necrosis, bronchial epithelial   | Moderate         |                    |                         |               |
| Edema, alveolar  | Moderate         |                    |                         |               |
| Edema, perivascular  | Mild             |                    |                         |               |
| Infiltration, neutrophil   | Mild             |                    |                         |               |
| <b>Stomach</b>   |                  |                    |                         |               |
| Findings : Finding present   |                  |                    |                         |               |
| Hyperplasia, squamous cell, limiting ridge   | Slight           |                    |                         |               |
| <b>Parathyroid</b>   |                  |                    |                         |               |
| Findings : Finding absent  |                  |                    |                         |               |
| Animal Comment : right parathyroid : missing   |                  |                    |                         |               |
| Finding absent : Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                  |                    |                         |               |

| Test article : PTSA Monohydrate   | Dose : 800 mg/kg | Animal No. : 50459 |
|---|------------------|--------------------|
| <b>Stomach</b>  |                  |                    |
| Findings : Finding present  |                  |                    |
| Hyperplasia, squamous cell, limiting ridge  |                  |                    |
| Slight  |                  |                    |
| <b>Kidney</b>   |                  |                    |
| Findings : Finding present  |                  |                    |
| Basophilic change, renal tubule   |                  |                    |
| Mild  |                  |                    |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                  |                    |

| Histopathological findings                   |   | Stage : Lactation Day 5 | Species : Rat |
|--|---|-------------------------|---------------|
| Sex : Female                                 |   |                         |               |
| Test article : PTSA Monohydrate              | Dose : 800 mg/kg  | Animal No. : 50460      |               |
| Stomach                                      |   |                         |               |
| Findings : Finding present                   |   |                         |               |
| Hyperplasia, squamous cell, limiting ridge   |   |                         |               |
| Slight                                       |   |                         |               |
| Kidney                                       |   |                         |               |
| Findings : Finding present                   |   |                         |               |
| Basophilic change, renal tubule              |   |                         |               |
| Slight                                       |   |                         |               |
| Parathyroid                                  |   |                         |               |
| Findings : Finding absent                    |   |                         |               |
| Animal Comment : right parathyroid : missing |   |                         |               |
| Finding absent :                             | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |               |

|  |  |                    |  |
|--|--|--------------------|--|
| Test article : PTSA Monohydrate            | Dose : 800 mg/kg   | Animal No. : 50461 |  |
| Stomach                                    |  |                    |  |
| Findings : Finding present                 |  |                    |  |
| Hyperplasia, squamous cell, limiting ridge |  |                    |  |
| Slight                                     |  |                    |  |
| Finding absent :                           | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                    |  |

|                                 |   |                    |  |
|---------------------------------|---|--------------------|--|
| Test article : PTSA Monohydrate | Dose : 800 mg/kg  | Animal No. : 50462 |  |
| Kidney                          |   |                    |  |
| Findings : Finding present      |   |                    |  |
| Basophilic change, renal tubule |   |                    |  |
| Slight                          |   |                    |  |
| Finding absent :                | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                    |  |

| Histopathological findings<br>Sex : Female (satellite) |  | Stage : Day 29     | Species : Rat |
|--|--|--------------------|---------------|
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg   | Animal No. : 50551 |               |
| Kidney   |  |                    |               |
| Findings : Finding present                             |  |                    |               |
| Basophilic change, renal tubule                        |  |                    |               |
| Slight   |  |                    |               |
| Pituitary gland  |  |                    |               |
| Findings : Finding present                             |  |                    |               |
| Craniopharyngeal tissue, aberrant                      |  |                    |               |
| Slight   |  |                    |               |
| Finding absent :                                       | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland                   |                    |               |
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg   | Animal No. : 50552 |               |
| Liver  |  |                    |               |
| Findings : Finding present                             |  |                    |               |
| Microgranuloma   |  |                    |               |
| Slight   |  |                    |               |
| Parathyroid  |  |                    |               |
| Findings : Finding absent                              |  |                    |               |
| Animal Comment : right parathyroid : missing           |  |                    |               |
| Finding absent :                                       | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland              |                    |               |
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg   | Animal No. : 50553 |               |
| Liver  |  |                    |               |
| Findings : Finding present                             |  |                    |               |
| Microgranuloma   |  |                    |               |
| Slight   |  |                    |               |
| Finding absent :                                       | Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                    |               |

| Histopathological findings<br>Sex : Female (satellite)   |                | Stage : Day 29     | Species : Rat |
|--|----------------|--------------------|---------------|
| Test article : PTSA Monohydrate  | Dose : 0 mg/kg | Animal No. : 50554 |               |
| <b>Kidney</b>  |                |                    |               |
| Findings : Finding present   |                |                    |               |
| Basophilic change, renal tubule  |                |                    |               |
| Slight   |                |                    |               |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                |                    |               |
| Test article : PTSA Monohydrate  | Dose : 0 mg/kg | Animal No. : 50555 |               |
| <b>Thyroid</b>   |                |                    |               |
| Findings : Finding present   |                |                    |               |
| Ultimobranchial body   |                |                    |               |
| Slight   |                |                    |               |
| Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland  |                |                    |               |

| Histopathological findings<br>Sex : Female (satellite)   | Stage : Day 29 | Species : Rat |
|--|----------------|---------------|
| Test article : PTSA Monohydrate Dose : 800 mg/kg Animal No. : 50651  |                |               |
| <p>Stomach</p> <p>Findings : Finding present</p> <p>Hyperplasia, squamous cell, limiting ridge</p> <p>Slight</p> <p>Fibrosis, lamina propria, glandular stomach</p> <p>Slight</p>  |                |               |
| <p>Kidney</p> <p>Findings : Finding present</p> <p>Basophilic change, renal tubule</p> <p>Slight</p>   |                |               |
| <p>Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland</p> |                |               |

| Test article : PTSA Monohydrate Dose : 800 mg/kg   | Animal No. : 50652 |
|--|--------------------|
| <p>Stomach</p> <p>Findings : Finding present</p> <p>Hyperplasia, squamous cell, limiting ridge</p> <p>Slight</p>   |                    |
| <p>Kidney</p> <p>Findings : Finding present</p> <p>Basophilic change, renal tubule</p> <p>Slight</p>   |                    |
| <p>Finding absent : Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland</p> |                    |

| Histopathological findings<br>Sex : Female (satellite)  |                  | Stage : Day 29     | Species : Rat |
|---|------------------|--------------------|---------------|
| Test article : PTSA Monohydrate   | Dose : 800 mg/kg | Animal No. : 50653 |               |
| <b>Stomach</b>  |                  |                    |               |
| Findings : Finding present  |                  |                    |               |
| Hyperplasia, squamous cell, limiting ridge  |                  |                    |               |
| Slight  |                  |                    |               |
| Hyperkeratosis, limiting ridge  |                  |                    |               |
| Slight  |                  |                    |               |
| <b>Thyroid</b>  |                  |                    |               |
| Findings : Finding present  |                  |                    |               |
| Ultimobranchial body  |                  |                    |               |
| Slight  |                  |                    |               |
| Finding absent :  |                  |                    |               |
| Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                  |                    |               |

| Test article : PTSA Monohydrate   |  | Dose : 800 mg/kg | Animal No. : 50654 |
|---|--|------------------|--------------------|
| <b>Stomach</b>  |  |                  |                    |
| Findings : Finding present  |  |                  |                    |
| Hyperplasia, squamous cell, limiting ridge  |  |                  |                    |
| Slight  |  |                  |                    |
| Hyperkeratosis, limiting ridge  |  |                  |                    |
| Slight  |  |                  |                    |
| <b>Liver</b>  |  |                  |                    |
| Findings : Finding present  |  |                  |                    |
| Microgranuloma  |  |                  |                    |
| Slight  |  |                  |                    |
| Finding absent :  |  |                  |                    |
| Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |  |                  |                    |

| Histopathological findings<br>Sex : Female (satellite)   |                  | Stage : Day 29     | Species : Rat |
|--|------------------|--------------------|---------------|
| Test article : PTSA Monohydrate  | Dose : 800 mg/kg | Animal No. : 50655 |               |
| <b>Stomach</b>   |                  |                    |               |
| Findings : Finding present   |                  |                    |               |
| Hyperplasia, squamous cell, limiting ridge   |                  |                    |               |
| Slight   |                  |                    |               |
| Hyperkeratosis, limiting ridge   |                  |                    |               |
| Slight   |                  |                    |               |
| <b>Kidney</b>  |                  |                    |               |
| Findings : Finding present   |                  |                    |               |
| Basophilic change, renal tubule  |                  |                    |               |
| Moderate   |                  |                    |               |
| Mineralization, cortex   |                  |                    |               |
| Mild   |                  |                    |               |
| Finding absent :   |                  |                    |               |
| Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland |                  |                    |               |

| Histopathological findings      |                | Sex : Male         | Stage : Recovery Day 15 | Species : Rat |
|---------------------------------|----------------|--------------------|-------------------------|---------------|
| Test article : PTSA Monohydrate | Dose : 0 mg/kg | Animal No. : 10103 |                         |               |
| Finding absent :                | Stomach        |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg | Animal No. : 10104 |                         |               |
| Finding absent :                | Stomach        |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg | Animal No. : 10105 |                         |               |
| Finding absent :                | Stomach        |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg | Animal No. : 10106 |                         |               |
| Finding absent :                | Stomach        |                    |                         |               |
| Test article : PTSA Monohydrate | Dose : 0 mg/kg | Animal No. : 10111 |                         |               |
| Finding absent :                | Stomach        |                    |                         |               |

| Histopathological findings                 |           |                 |         |
|--|-----------|-----------------|---------|
| Test article                               | Dose      | Animal No.      | Species |
| PTSA Monohydrate                           | 800 mg/kg | 10402           | Rat     |
| Stomach                                    |           | Recovery Day 15 |         |
| Findings : Finding present                 |           |                 |         |
| Hyperplasia, squamous cell, limiting ridge |           |                 |         |
| Slight                                     |           |                 |         |
| PTSA Monohydrate                           | 800 mg/kg | 10403           |         |
| Stomach                                    |           |                 |         |
| Findings : Finding present                 |           |                 |         |
| Hyperplasia, squamous cell, limiting ridge |           |                 |         |
| Slight                                     |           |                 |         |
| PTSA Monohydrate                           | 800 mg/kg | 10407           |         |
| Finding absent :                           | Stomach   |                 |         |
| PTSA Monohydrate                           | 800 mg/kg | 10409           |         |
| Finding absent :                           | Stomach   |                 |         |
| PTSA Monohydrate                           | 800 mg/kg | 10411           |         |
| Finding absent :                           | Stomach   |                 |         |

| Histopathological findings<br>Sex : Female (satellite) |                 | Stage : Recovery Day 15 | Species : Rat |
|--|-----------------|-------------------------|---------------|
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg  | Animal No. : 50556      |               |
| Finding absent :                                       | Stomach, Kidney |                         |               |
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg  | Animal No. : 50557      |               |
| Finding absent :                                       | Stomach, Kidney |                         |               |
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg  | Animal No. : 50558      |               |
| Finding absent :                                       | Stomach, Kidney |                         |               |
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg  | Animal No. : 50559      |               |
| Finding absent :                                       | Stomach, Kidney |                         |               |
| Test article : PTSA Monohydrate                        | Dose : 0 mg/kg  | Animal No. : 50560      |               |
| Finding absent :                                       | Stomach, Kidney |                         |               |

| Histopathological findings<br>Sex : Female (satellite) | Stage : Recovery Day 15 | Species : Rat |
|--|-------------------------|---------------|
| Test article : PTSA Monohydrate Dose : 800 mg/kg       | Animal No. : 50656      |               |
| Finding absent : Stomach, Kidney                       |                         |               |
| Test article : PTSA Monohydrate Dose : 800 mg/kg       | Animal No. : 50657      |               |
| Kidney   |                         |               |
| Findings : Finding present                             |                         |               |
| Basophilic change, renal tubule                        |                         |               |
| Slight   |                         |               |
| Hyperplasia, tubular epithelium                        |                         |               |
| Slight   |                         |               |
| Finding absent : Stomach                               |                         |               |
| Test article : PTSA Monohydrate Dose : 800 mg/kg       | Animal No. : 50658      |               |
| Kidney   |                         |               |
| Findings : Finding present                             |                         |               |
| Basophilic change, renal tubule                        |                         |               |
| Slight   |                         |               |
| Finding absent : Stomach                               |                         |               |
| Test article : PTSA Monohydrate Dose : 800 mg/kg       | Animal No. : 50659      |               |
| Kidney   |                         |               |
| Findings : Finding present                             |                         |               |
| Cyst   |                         |               |
| Slight   |                         |               |
| Finding absent : Stomach                               |                         |               |

| Histopathological findings<br>Sex : Female (satellite) |   | Stage : Recovery Day 15 |                              | Species : Rat |
|--|---|-------------------------|------------------------------|---------------|
| Test article : PTSA Monohydrate                        | Dose : 800 mg/kg  | Animal No. : 50660      | Died on administration day 3 |               |
| Stomach  |   |                         |                              |               |
| Findings : Finding present                             |   |                         |                              |               |
| Erosion, glandular stomach                             |   |                         |                              |               |
| Slight   |   |                         |                              |               |
| Necrosis, mucosa, pyloric part                         |   |                         |                              |               |
| Moderate   |   |                         |                              |               |
| Kidney   |   |                         |                              |               |
| Findings : Finding present                             |   |                         |                              |               |
| Necrosis, renal tubule, cortex                         |   |                         |                              |               |
| Severe   |   |                         |                              |               |
| Spleen   |   |                         |                              |               |
| Findings : Finding present                             |   |                         |                              |               |
| Atrophy, white pulp                                    |   |                         |                              |               |
| Mild   |   |                         |                              |               |
| Pituitary gland  |   |                         |                              |               |
| Findings : Finding present                             |   |                         |                              |               |
| Cyst, pars distalis                                    |   |                         |                              |               |
| Slight   |   |                         |                              |               |
| Parathyroid  |   |                         |                              |               |
| Findings : Finding absent                              |   |                         |                              |               |
| Animal Comment : left thyroid : missing                |   |                         |                              |               |
| Finding absent :                                       | Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart,<br>Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve,<br>Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Thyroid, Adrenal, Eyeball,<br>Harderian gland, Skeletal muscle, Femur, Mammary gland |                         |                              |               |

| Animal No. | Estrous cycles and copulation<br>Generation : F0<br>/Before mating (day) |   |   |   |   |   |   |   |   |    |    |    |    |    | Dose : PTSA Monohydrate 0 mg/kg   |   |      | Species : Rat       |   |  |
|------------|--|---|---|---|---|---|---|---|---|----|----|----|----|----|-----------------------------------|---|------|---------------------|---|--|
|            | 1  | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | Length of estrous cycle<br>(days) |   | Mean | Number of<br>estrus | Animal with acyclic<br>or irregular cycle |  |
|            | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |      |                     |   |  |
| 50151      |  |   |   |   |   |   |   |   |   |    |    |    |    |    |                                   |   | 4.0  | 3                   | -   |  |
| 50152      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 | 4.0  | 3                   | -   |  |
| 50153      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | M  | D  | 4                                 | 4 | 4.0  | 3                   | -   |  |
| 50154      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4.0  | 4                   | -   |  |
| 50155      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 | 4.0  | 3                   | -   |  |
| 50156      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4.0  | 4                   | -   |  |
| 50157      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4.0  | 4                   | -   |  |
| 50158      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4.0  | 4                   | -   |  |
| 50159      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4.0  | 4                   | -   |  |
| 50160      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | E  | M  | 4                                 | 4 | 4.0  | 3                   | -   |  |
| 50161      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 | 4.0  | 3                   | -   |  |
| 50162      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4.0  | 4                   | -   |  |

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with acyclic or irregular cycle, - : Animal with normal and regular cycle

| Animal No. | Estrous cycles and copulation<br>Generation : F0<br>/Before mating (day) |   |   |   |   |   |   |   |   |    |    |    |    |    | Dose : PTSA Monohydrate 50 mg/kg  |   |   | Species : Rat |                     |   |
|------------|--|---|---|---|---|---|---|---|---|----|----|----|----|----|-----------------------------------|---|---|---------------|---------------------|---|
|            | 1  | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | Length of estrous cycle<br>(days) |   |   | Mean          | Number of<br>estrus | Animal with acyclic<br>or irregular cycle |
|            | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 |               |                     |   |
| 50251      |  |   |   |   |   |   |   |   |   |    |    |    |    |    |                                   |   |   | 4.0           | 4                   | -   |
| 50252      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50253      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | M  | D  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50254      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50255      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50256      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50257      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50258      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50259      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50260      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50261      | E  | M | D | P | E | M | D | P | E | M  | D  | P  | E  | M  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50262      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with acyclic or irregular cycle, - : Animal with normal and regular cycle

| Animal No. | Estrous cycles and copulation<br>Generation : F0<br>/Before mating (day) |   |   |   |   |   |   |   |   |    |    |    |    |    | Dose : PTSA Monohydrate 200 mg/kg |   |   | Species : Rat |                     |   |
|------------|--|---|---|---|---|---|---|---|---|----|----|----|----|----|-----------------------------------|---|---|---------------|---------------------|---|
|            | 1  | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | Length of estrous cycle<br>(days) |   |   | Mean          | Number of<br>estrus | Animal with acyclic<br>or irregular cycle |
|            | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 |               |                     |   |
| 50351      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50352      | E  | M | D | P | E | M | D | P | E | M  | D  | P  | E  | M  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50353      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | M  | D  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50354      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50355      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50356      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | M  | D  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50357      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50358      | E  | M | D | P | E | M | D | P | E | M  | D  | P  | E  | M  | 4                                 | 4 | 4 | 4.0           | 4                   | -   |
| 50359      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | M  | D  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50360      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50361      | M  | D | P | E | M | D | P | E | M | D  | P  | E  | M  | D  | 4                                 | 4 |   | 4.0           | 3                   | -   |
| 50362      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |   | 4.0           | 3                   | -   |

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with acyclic or irregular cycle, - : Animal with normal and regular cycle

| Animal No. | Estrous cycles and copulation<br>Generation : F0<br>/Before mating (day) |   |   |   |   |   |   |   |   |    |    |    |    |    | Dose : PTSA Monohydrate 800 mg/kg |   |      | Species : Rat       |   |   |
|------------|--|---|---|---|---|---|---|---|---|----|----|----|----|----|-----------------------------------|---|------|---------------------|---|---|
|            | 1  | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | Length of estrous cycle<br>(days) |   | Mean | Number of<br>estrus | Animal with acyclic<br>or irregular cycle |   |
|            | D  | P | E | E | M | D | P | E | M | D  | P  | E  | M  | D  | 5                                 | 4 |      |                     |   |   |
| 50451      |  |   |   |   |   |   |   |   |   |    |    |    |    |    |                                   |   | 4.5  | 3                   | -   |   |
| 50452      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4    | 4.0                 | 4   | - |
| 50453      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4    | 4.0                 | 4   | - |
| 50454      | D  | P | E | E | M | D | P | E | M | D  | P  | E  | M  | D  | 5                                 | 4 |      | 4.5                 | 3   | - |
| 50455      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |      | 4.0                 | 3   | - |
| 50456      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4    | 4.0                 | 4   | - |
| 50457      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |      | 4.0                 | 3   | - |
| 50458      | D  | P | M | D | E | M | D | P | E | M  | D  | P  | E  | M  | 4                                 | 4 |      | 4.0                 | 3   | - |
| 50459      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4    | 4.0                 | 4   | - |
| 50460      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4    | 4.0                 | 4   | - |
| 50461      | D  | P | E | M | D | P | E | M | D | P  | E  | M  | D  | P  | 4                                 | 4 |      | 4.0                 | 3   | - |
| 50462      | P  | E | M | D | P | E | M | D | P | E  | M  | D  | P  | E  | 4                                 | 4 | 4    | 4.0                 | 4   | - |

P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

+ : Animal with acyclic or irregular cycle, - : Animal with normal and regular cycle

## Estrous cycles and copulation

| Animal No. | Generation : F0<br>/1st mating (times) |   |   |   |   |   |   |   |   |    |    |    |    |    | Species : Rat |
|------------|--|---|---|---|---|---|---|---|---|----|----|----|----|----|---------------|
|            | 1                                      | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |               |
| 50151      | E                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
|            | Y                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
| 50152      | E                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
|            | Y                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
| 50153      | P                                      | E |   |   |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | Y |   |   |   |   |   |   |   |    |    |    |    |    |               |
| 50154      | M                                      | D | P | E |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | N | N | Y |   |   |   |   |   |    |    |    |    |    |               |
| 50155      | E                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
|            | Y                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
| 50156      | M                                      | D | P | E |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | N | N | Y |   |   |   |   |   |    |    |    |    |    |               |
| 50157      | M                                      | D | P | E |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | N | N | Y |   |   |   |   |   |    |    |    |    |    |               |
| 50158      | M                                      | D | P | E |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | N | N | Y |   |   |   |   |   |    |    |    |    |    |               |
| 50159      | M                                      | D | P | E |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | N | N | Y |   |   |   |   |   |    |    |    |    |    |               |
| 50160      | D                                      | P | D | D | D | D | D | E |   |    |    |    |    |    |               |
|            | N                                      | N | N | N | N | N | N | N | Y |    |    |    |    |    |               |
| 50161      | E                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
|            | Y                                      |   |   |   |   |   |   |   |   |    |    |    |    |    |               |
| 50162      | M                                      | D | P | E |   |   |   |   |   |    |    |    |    |    |               |
|            | N                                      | N | N | Y |   |   |   |   |   |    |    |    |    |    |               |

Upper / P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Lower / Y : Completion in copulation, N : Incompletion in copulation

| Animal No. | Estrous cycles and copulation |   |   |   |   |   |   |                                  |    |    |    |    |    |  | Species : Rat |  |
|------------|-------------------------------|---|---|---|---|---|---|----------------------------------|----|----|----|----|----|--|---------------|--|
|            | Generation : F0               |   |   |   |   |   |   | Dose : PTSA Monohydrate 50 mg/kg |    |    |    |    |    |  |               |  |
|            | /1st mating (times)           |   |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 1          | 2                             | 3 | 4 | 5 | 6 | 7 | 8 | 9                                | 10 | 11 | 12 | 13 | 14 |  |               |  |
| 50251      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50252      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50253      | P                             | E |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | Y |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50254      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50255      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50256      | E                             |   |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | Y                             |   |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50257      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50258      | E                             |   |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | Y                             |   |   |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50259      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50260      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50261      | D                             | P | E |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | Y |   |   |   |   |                                  |    |    |    |    |    |  |               |  |
| 50262      | M                             | D | P | E |   |   |   |                                  |    |    |    |    |    |  |               |  |
|            | N                             | N | N | Y |   |   |   |                                  |    |    |    |    |    |  |               |  |

Upper / P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Lower / Y : Completion in copulation, N : Incompletion in copulation

| Animal No. | Estrous cycles and copulation |   |   |   |   |   |   |                                   |    |    |    |    |    |   | Species : Rat |  |
|------------|-------------------------------|---|---|---|---|---|---|-----------------------------------|----|----|----|----|----|---|---------------|--|
|            | Generation : F0               |   |   |   |   |   |   | Dose : PTSA Monohydrate 200 mg/kg |    |    |    |    |    |   |               |  |
|            | /1st mating (times)           |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 1          | 2                             | 3 | 4 | 5 | 6 | 7 | 8 | 9                                 | 10 | 11 | 12 | 13 | 14 |   |               |  |
| 50351      | M                             | D | D | D | D | D | D | D                                 | D  | D  | D  | P  | E  |   |               |  |
|            | N                             | N | N | N | N | N | N | N                                 | N  | N  | N  | N  | N  | Y |               |  |
| 50352      | D                             | P | E |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | N | Y |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50353      | P                             | E |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | Y |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50354      | E                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50355      | E                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50356      | P                             | E |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | Y |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50357      | M                             | D | P | E |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | N | N | Y |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50358      | D                             | P | E |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | N | Y |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50359      | P                             | E |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | Y |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50360      | E                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50361      | P                             | E |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | N                             | Y |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
| 50362      | E                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |    |    |    |    |    |   |               |  |

Upper / P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Lower / Y : Completion in copulation, N : Incompletion in copulation

| Animal No. | Estrous cycles and copulation |   |   |   |   |   |   |                                   |   |    |    |    |    |    | Species : Rat |  |
|------------|-------------------------------|---|---|---|---|---|---|-----------------------------------|---|----|----|----|----|----|---------------|--|
|            | Generation : F0               |   |   |   |   |   |   | Dose : PTSA Monohydrate 800 mg/kg |   |    |    |    |    |    |               |  |
|            | /1st mating (times)           |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| Animal No. | 1                             | 2 | 3 | 4 | 5 | 6 | 7 | 8                                 | 9 | 10 | 11 | 12 | 13 | 14 |               |  |
| 50451      | P                             | E |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | Y |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50452      | M                             | D | P | E |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | N | N | Y |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50453      | M                             | D | P | E |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | N | N | Y |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50454      | P                             | E |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | Y |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50455      | E                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50456      | E                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50457      | E                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50458      | D                             | P | E |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | N | Y |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50459      | M                             | D | P | E |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | N | N | Y |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50460      | M                             | D | P | E |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | N | N | Y |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50461      | E                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | Y                             |   |   |   |   |   |   |                                   |   |    |    |    |    |    |               |  |
| 50462      | M                             | D | P | E |   |   |   |                                   |   |    |    |    |    |    |               |  |
|            | N                             | N | N | Y |   |   |   |                                   |   |    |    |    |    |    |               |  |

Upper / P : Proestrus, E : Estrus, M : Metestrus, D : Diestrus

Lower / Y : Completion in copulation, N : Incompletion in copulation

| Animal No.       | Day of conceiving | Reproductive performance |            |            | Dose : PTSA Monohydrate 0 mg/kg |            |            | Species : Rat |           |  |
|------------------|-------------------|--------------------------|------------|------------|---------------------------------|------------|------------|---------------|-----------|--|
|                  |                   | Generation : F0          |            | Sex : Male | 1st mating                      |            | 2nd mating |               | Total     |  |
|                  |                   | Paired animal            | Copulation | Fertility  | Paired animal                   | Copulation | Fertility  | Copulation    | Fertility |  |
| 10101            | 1                 | 50151                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10102            | 1                 | 50152                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10103            | 2                 | 50153                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10104            | 4                 | 50154                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10105            | 1                 | 50155                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10106            | 4                 | 50156                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10107            | 4                 | 50157                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10108            | 4                 | 50158                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10109            | 4                 | 50159                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10110            | 8                 | 50160                    | +          | -          | ///                             | ///        | ///        | +             | -         |  |
| 10111            | 1                 | 50161                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| 10112            | 4                 | 50162                    | +          | +          | ///                             | ///        | ///        | +             | +         |  |
| n                | 12                |                          | 12         | 12         |                                 | 0          | 0          | 12            | 12        |  |
| Mean             | 3.2               |                          |            |            |                                 |            |            |               |           |  |
| S.D.             | 2.1               |                          |            |            |                                 |            |            |               |           |  |
| No. of positives |                   |                          | 12         | 11         |                                 |            |            | 12            | 11        |  |
| %                |                   |                          | 100.0      | 91.7       |                                 |            |            | 100.0         | 91.7      |  |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance |            |               | Dose : PTSA Monohydrate 50 mg/kg |           |               | Species : Rat |           |       |
|------------------|-------------------|--------------------------|------------|---------------|----------------------------------|-----------|---------------|---------------|-----------|-------|
|                  |                   | Generation : F0          | Sex : Male | 1st mating    |                                  |           | 2nd mating    |               |           |       |
|                  |                   |                          |            | Paired animal | Copulation                       | Fertility | Paired animal | Copulation    | Fertility |       |
| 10201            | 4                 | 50251                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10202            | 4                 | 50252                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10203            | 2                 | 50253                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10204            | 4                 | 50254                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10205            | 4                 | 50255                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10206            | 1                 | 50256                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10207            | 4                 | 50257                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10208            | 1                 | 50258                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10209            | 4                 | 50259                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10210            | 4                 | 50260                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10211            | 3                 | 50261                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| 10212            | 4                 | 50262                    |            | +             | +                                | ///       | ///           | ///           | +         | +     |
| n                | 12                |                          |            | 12            | 12                               |           | 0             | 0             | 12        | 12    |
| Mean             | 3.3               |                          |            |               |                                  |           |               |               |           |       |
| S.D.             | 1.2               |                          |            |               |                                  |           |               |               |           |       |
| No. of positives |                   |                          |            | 12            | 12                               |           |               |               | 12        | 12    |
| %                |                   |                          |            | 100.0         | 100.0                            |           |               |               | 100.0     | 100.0 |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance |            |            | Dose : PTSA Monohydrate 200 mg/kg |            |           | Species : Rat |           |
|------------------|-------------------|--------------------------|------------|------------|-----------------------------------|------------|-----------|---------------|-----------|
|                  |                   | Generation : F0          |            | Sex : Male | 1st mating                        |            |           | 2nd mating    |           |
|                  |                   | Paired animal            | Copulation | Fertility  | Paired animal                     | Copulation | Fertility | Copulation    | Fertility |
| 10301            | 14                | 50351                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10302            | 3                 | 50352                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10303            | 2                 | 50353                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10304            | 1                 | 50354                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10305            | 1                 | 50355                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10306            | 2                 | 50356                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10307            | 4                 | 50357                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10308            | 3                 | 50358                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10309            | 2                 | 50359                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10310            | 1                 | 50360                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10311            | 2                 | 50361                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10312            | 1                 | 50362                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| n                | 12                |                          | 12         | 12         |                                   | 0          | 0         | 12            | 12        |
| Mean             | 3.0               |                          |            |            |                                   |            |           |               |           |
| S.D.             | 3.6               |                          |            |            |                                   |            |           |               |           |
| No. of positives |                   |                          | 12         | 12         |                                   |            |           | 12            | 12        |
| %                |                   |                          | 100.0      | 100.0      |                                   |            |           | 100.0         | 100.0     |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance |            |            | Dose : PTSA Monohydrate 800 mg/kg |            |           | Species : Rat |           |
|------------------|-------------------|--------------------------|------------|------------|-----------------------------------|------------|-----------|---------------|-----------|
|                  |                   | Generation : F0          |            | Sex : Male | 1st mating                        |            |           | 2nd mating    |           |
|                  |                   | Paired animal            | Copulation | Fertility  | Paired animal                     | Copulation | Fertility | Copulation    | Fertility |
| 10401            | 2                 | 50451                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10402            | 4                 | 50452                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10403            | 4                 | 50453                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10404            | 2                 | 50454                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10405            | 1                 | 50455                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10406            | 1                 | 50456                    | +          | -          | ///                               | ///        | ///       | +             | -         |
| 10407            | 1                 | 50457                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10408            | 3                 | 50458                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10409            | 4                 | 50459                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10410            | 4                 | 50460                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10411            | 1                 | 50461                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| 10412            | 4                 | 50462                    | +          | +          | ///                               | ///        | ///       | +             | +         |
| n                | 12                |                          | 12         | 12         |                                   | 0          | 0         | 12            | 12        |
| Mean             | 2.6               |                          |            |            |                                   |            |           |               |           |
| S.D.             | 1.4               |                          |            |            |                                   |            |           |               |           |
| No. of positives |                   |                          | 12         | 11         |                                   |            |           | 12            | 11        |
| %                |                   |                          | 100.0      | 91.7       |                                   |            |           | 100.0         | 91.7      |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance |            |              | Dose : PTSA Monohydrate 0 mg/kg |            |           | Species : Rat |           |
|------------------|-------------------|--------------------------|------------|--------------|---------------------------------|------------|-----------|---------------|-----------|
|                  |                   | Generation : F0          |            | Sex : Female | 1st mating                      |            |           | Total         |           |
|                  |                   | Paired animal            | Copulation | Fertility    | Paired animal                   | Copulation | Fertility | Copulation    | Fertility |
| 50151            | 1                 | 10101                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50152            | 1                 | 10102                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50153            | 2                 | 10103                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50154            | 4                 | 10104                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50155            | 1                 | 10105                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50156            | 4                 | 10106                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50157            | 4                 | 10107                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50158            | 4                 | 10108                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50159            | 4                 | 10109                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50160            | 8                 | 10110                    | +          | -            | ///                             | ///        | ///       | +             | -         |
| 50161            | 1                 | 10111                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| 50162            | 4                 | 10112                    | +          | +            | ///                             | ///        | ///       | +             | +         |
| n                | 12                |                          | 12         | 12           |                                 | 0          | 0         | 12            | 12        |
| Mean             | 3.2               |                          |            |              |                                 |            |           |               |           |
| S.D.             | 2.1               |                          |            |              |                                 |            |           |               |           |
| No. of positives |                   |                          | 12         | 11           |                                 |            |           | 12            | 11        |
| %                |                   |                          | 100.0      | 91.7         |                                 |            |           | 100.0         | 91.7      |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance     |            |           | Dose : PTSA Monohydrate 50 mg/kg |            |           | Species : Rat |           |
|------------------|-------------------|------------------------------|------------|-----------|----------------------------------|------------|-----------|---------------|-----------|
|                  |                   | Generation : F0 Sex : Female |            |           | 1st mating                       |            |           | 2nd mating    |           |
|                  |                   | Paired animal                | Copulation | Fertility | Paired animal                    | Copulation | Fertility | Copulation    | Fertility |
| 50251            | 4                 | 10201                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50252            | 4                 | 10202                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50253            | 2                 | 10203                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50254            | 4                 | 10204                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50255            | 4                 | 10205                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50256            | 1                 | 10206                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50257            | 4                 | 10207                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50258            | 1                 | 10208                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50259            | 4                 | 10209                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50260            | 4                 | 10210                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50261            | 3                 | 10211                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| 50262            | 4                 | 10212                        | +          | +         | ///                              | ///        | ///       | +             | +         |
| n                | 12                |                              | 12         | 12        |                                  | 0          | 0         | 12            | 12        |
| Mean             | 3.3               |                              |            |           |                                  |            |           |               |           |
| S.D.             | 1.2               |                              |            |           |                                  |            |           |               |           |
| No. of positives |                   | 12                           | 12         |           |                                  |            |           | 12            | 12        |
| %                |                   | 100.0                        | 100.0      |           |                                  |            |           | 100.0         | 100.0     |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance     |            |           | Dose : PTSA Monohydrate 200 mg/kg |            |           | Species : Rat |           |
|------------------|-------------------|------------------------------|------------|-----------|-----------------------------------|------------|-----------|---------------|-----------|
|                  |                   | Generation : F0 Sex : Female |            |           | 1st mating                        |            |           | 2nd mating    |           |
|                  |                   | Paired animal                | Copulation | Fertility | Paired animal                     | Copulation | Fertility | Copulation    | Fertility |
| 50351            | 14                | 10301                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50352            | 3                 | 10302                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50353            | 2                 | 10303                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50354            | 1                 | 10304                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50355            | 1                 | 10305                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50356            | 2                 | 10306                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50357            | 4                 | 10307                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50358            | 3                 | 10308                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50359            | 2                 | 10309                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50360            | 1                 | 10310                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50361            | 2                 | 10311                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50362            | 1                 | 10312                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| n                | 12                |                              | 12         | 12        |                                   | 0          | 0         | 12            | 12        |
| Mean             | 3.0               |                              |            |           |                                   |            |           |               |           |
| S.D.             | 3.6               |                              |            |           |                                   |            |           |               |           |
| No. of positives |                   |                              | 12         | 12        |                                   |            |           | 12            | 12        |
| %                |                   |                              | 100.0      | 100.0     |                                   |            |           | 100.0         | 100.0     |

/// : No need to input/measure

| Animal No.       | Day of conceiving | Reproductive performance     |            |           | Dose : PTSA Monohydrate 800 mg/kg |            |           | Species : Rat |           |
|------------------|-------------------|------------------------------|------------|-----------|-----------------------------------|------------|-----------|---------------|-----------|
|                  |                   | Generation : F0 Sex : Female |            |           | 1st mating                        |            |           | 2nd mating    |           |
|                  |                   | Paired animal                | Copulation | Fertility | Paired animal                     | Copulation | Fertility | Copulation    | Fertility |
| 50451            | 2                 | 10401                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50452            | 4                 | 10402                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50453            | 4                 | 10403                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50454            | 2                 | 10404                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50455            | 1                 | 10405                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50456            | 1                 | 10406                        | +          | -         | ///                               | ///        | ///       | +             | -         |
| 50457            | 1                 | 10407                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50458            | 3                 | 10408                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50459            | 4                 | 10409                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50460            | 4                 | 10410                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50461            | 1                 | 10411                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| 50462            | 4                 | 10412                        | +          | +         | ///                               | ///        | ///       | +             | +         |
| n                | 12                |                              | 12         | 12        |                                   | 0          | 0         | 12            | 12        |
| Mean             | 2.6               |                              |            |           |                                   |            |           |               |           |
| S.D.             | 1.4               |                              |            |           |                                   |            |           |               |           |
| No. of positives |                   |                              | 12         | 11        |                                   |            |           | 12            | 11        |
| %                |                   |                              | 100.0      | 91.7      |                                   |            |           | 100.0         | 91.7      |

/// : No need to input/measure

| Dam No. | Gestation period (day) | Delivery data Generation : F0 |                 |                     |                         | Dose : PTSA Monohydrate 0 mg/kg |       |                         |     | Species : Rat |       |             |     |     |       |       |     |     |       |
|---------|------------------------|-------------------------------|-----------------|---------------------|-------------------------|---------------------------------|-------|-------------------------|-----|---------------|-------|-------------|-----|-----|-------|-------|-----|-----|-------|
|         |                        | Number of implantation        | Birth index (%) | Number of offspring | Number of live newborns |                                 |       | Number of dead newborns |     |               |       | Cannibalism |     |     |       | Total |     |     |       |
|         |                        |                               |                 |                     | M                       | F                               | Total | M                       | F   | U             | Total | M           | F   | U   | Total | M     | F   | U   | Total |
| 50151   | 22                     | 16(10/6)                      | 75.0            | 13                  | 8                       | 4                               | 12    | 0                       | 1   | 0             | 1     | 0           | 0   | 0   | 0     | 0     | 1   | 0   | 1     |
| 50152   | 22                     | 15(8/7)                       | 100.0           | 15                  | 8                       | 7                               | 15    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50153   | 22                     | 15(7/8)                       | 93.3            | 14                  | 8                       | 6                               | 14    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50154   | 22                     | 15(5/10)                      | 86.7            | 13                  | 7                       | 6                               | 13    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50155   | 22                     | 12(5/7)                       | 91.7            | 11                  | 5                       | 6                               | 11    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50156   | 22                     | 15(5/10)                      | 93.3            | 14                  | 4                       | 10                              | 14    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50157   | 23                     | 18(10/8)                      | 50.0            | 9                   | 2                       | 7                               | 9     | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50158   | 22                     | 19(11/8)                      | 100.0           | 19                  | 7                       | 12                              | 19    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50159   | 22                     | 16(6/10)                      | 100.0           | 16                  | 8                       | 8                               | 16    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50161   | 22                     | 16(8/8)                       | 100.0           | 16                  | 10                      | 6                               | 16    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| 50162   | 22                     | 16(10/6)                      | 100.0           | 16                  | 6                       | 10                              | 16    | 0                       | 0   | 0             | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |
| n       |                        | 11                            | 11              | 11                  | 11                      | 11                              | 11    | 11                      | 11  | 11            | 11    | 11          | 11  | 11  | 11    | 11    | 11  | 11  | 11    |
| Mean    |                        | 22.09                         | 15.7            | 90.00               | 14.2                    | 6.6                             | 7.5   | 14.1                    | 0.0 | 0.1           | 0.0   | 0.1         | 0.0 | 0.0 | 0.0   | 0.0   | 0.0 | 0.1 | 0.0   |
| S.D.    |                        | 0.30                          | 1.8             | 15.36               | 2.7                     | 2.2                             | 2.3   | 2.8                     | 0.0 | 0.3           | 0.0   | 0.3         | 0.0 | 0.0 | 0.0   | 0.0   | 0.0 | 0.3 | 0.0   |

(/) : Number of implantation Right/Left, M : Male, F : Female, U : Unable to be sexed

| Dam No. | Gestation period (day) | Delivery data Generation : F0 |                 |                     |                         | Dose : PTSA Monohydrate 50 mg/kg |       |      |     |     |       |                         |     |     |       |             |     | Species : Rat |       |       |     |    |       |
|---------|------------------------|-------------------------------|-----------------|---------------------|-------------------------|----------------------------------|-------|------|-----|-----|-------|-------------------------|-----|-----|-------|-------------|-----|---------------|-------|-------|-----|----|-------|
|         |                        | Number of implantation        | Birth index (%) | Number of offspring | Number of live newborns |                                  |       | Dead |     |     |       | Number of dead newborns |     |     |       | Cannibalism |     |               |       | Total |     |    |       |
|         |                        |                               |                 |                     | M                       | F                                | Total | M    | F   | U   | Total | M                       | F   | U   | Total | M           | F   | U             | Total | M     | F   | U  | Total |
| 50251   | 22                     | 17(12/5)                      | 88.2            | 17                  | 8                       | 7                                | 15    | 1    | 1   | 0   | 2     | 0                       | 0   | 0   | 0     | 1           | 1   | 1             | 0     | 2     |     |    |       |
| 50252   | 22                     | 18(9/9)                       | 94.4            | 17                  | 8                       | 9                                | 17    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50253   | 22                     | 15(7/8)                       | 100.0           | 15                  | 5                       | 10                               | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50254   | 23                     | 16(9/7)                       | 93.8            | 15                  | 4                       | 11                               | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50255   | 22                     | 15(8/7)                       | 86.7            | 13                  | 8                       | 5                                | 13    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50256   | 22                     | 16(4/12)                      | 68.8            | 11                  | 6                       | 5                                | 11    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50257   | 22                     | 15(7/8)                       | 100.0           | 15                  | 7                       | 8                                | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50258   | 22                     | 14(5/9)                       | 92.9            | 13                  | 5                       | 8                                | 13    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50259   | 23                     | 14(11/3)                      | 100.0           | 14                  | 4                       | 10                               | 14    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50260   | 22                     | 15(11/4)                      | 100.0           | 15                  | 9                       | 6                                | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50261   | 23                     | 18(10/8)                      | 100.0           | 18                  | 10                      | 8                                | 18    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| 50262   | 22                     | 17(11/6)                      | 88.2            | 15                  | 6                       | 9                                | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0  | 0     |
| n       |                        | 12                            | 12              | 12                  | 12                      | 12                               | 12    | 12   | 12  | 12  | 12    | 12                      | 12  | 12  | 12    | 12          | 12  | 12            | 12    | 12    | 12  | 12 | 12    |
| Mean    |                        | 22.25                         | 15.8            | 92.75               | 14.8                    | 6.7                              | 8.0   | 14.7 | 0.1 | 0.1 | 0.0   | 0.2                     | 0.0 | 0.0 | 0.0   | 0.0         | 0.0 | 0.1           | 0.1   | 0.0   | 0.2 |    |       |
| S.D.    |                        | 0.45                          | 1.4             | 9.14                | 1.9                     | 2.0                              | 2.0   | 1.8  | 0.3 | 0.3 | 0.0   | 0.6                     | 0.0 | 0.0 | 0.0   | 0.0         | 0.0 | 0.3           | 0.3   | 0.0   | 0.6 |    |       |

(/) : Number of implantation Right/Left, M : Male, F : Female, U : Unable to be sexed

| Dam No. | Gestation period (day) | Delivery data Generation : F0 |                 |                     |                         | Dose : PTSA Monohydrate 200 mg/kg |       |      |     |     |       |                         |     |     |       |             |     | Species : Rat |       |       |     |     |       |
|---------|------------------------|-------------------------------|-----------------|---------------------|-------------------------|-----------------------------------|-------|------|-----|-----|-------|-------------------------|-----|-----|-------|-------------|-----|---------------|-------|-------|-----|-----|-------|
|         |                        | Number of implantation        | Birth index (%) | Number of offspring | Number of live newborns |                                   |       | Dead |     |     |       | Number of dead newborns |     |     |       | Cannibalism |     |               |       | Total |     |     |       |
|         |                        |                               |                 |                     | M                       | F                                 | Total | M    | F   | U   | Total | M                       | F   | U   | Total | M           | F   | U             | Total | M     | F   | U   | Total |
| 50351   | 22                     | 14(9/5)                       | 100.0           | 14                  | 6                       | 8                                 | 14    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50352   | 23                     | 15(7/8)                       | 100.0           | 15                  | 4                       | 11                                | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50353   | 22                     | 14(5/9)                       | 100.0           | 14                  | 8                       | 6                                 | 14    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50354   | 22                     | 15(4/11)                      | 86.7            | 13                  | 9                       | 4                                 | 13    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50355   | 22                     | 18(6/12)                      | 94.4            | 17                  | 9                       | 8                                 | 17    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50356   | 22                     | 15(8/7)                       | 93.3            | 14                  | 9                       | 5                                 | 14    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50357   | 22                     | 16(11/5)                      | 93.8            | 15                  | 6                       | 9                                 | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50358   | 22                     | 14(6/8)                       | 92.9            | 13                  | 6                       | 7                                 | 13    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50359   | 22                     | 16(8/8)                       | 100.0           | 16                  | 9                       | 7                                 | 16    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50360   | 22                     | 16(11/5)                      | 93.8            | 15                  | 10                      | 5                                 | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50361   | 22                     | 18(9/9)                       | 83.3            | 15                  | 7                       | 8                                 | 15    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| 50362   | 22                     | 18(6/12)                      | 61.1            | 11                  | 4                       | 7                                 | 11    | 0    | 0   | 0   | 0     | 0                       | 0   | 0   | 0     | 0           | 0   | 0             | 0     | 0     | 0   | 0   | 0     |
| n       |                        | 12                            | 12              | 12                  | 12                      | 12                                | 12    | 12   | 12  | 12  | 12    | 12                      | 12  | 12  | 12    | 12          | 12  | 12            | 12    | 12    | 12  | 12  | 12    |
| Mean    |                        | 22.08                         | 15.8            | 91.61               | 14.3                    | 7.3                               | 7.1   | 14.3 | 0.0 | 0.0 | 0.0   | 0.0                     | 0.0 | 0.0 | 0.0   | 0.0         | 0.0 | 0.0           | 0.0   | 0.0   | 0.0 | 0.0 | 0.0   |
| S.D.    |                        | 0.29                          | 1.5             | 10.99               | 1.6                     | 2.1                               | 1.9   | 1.6  | 0.0 | 0.0 | 0.0   | 0.0                     | 0.0 | 0.0 | 0.0   | 0.0         | 0.0 | 0.0           | 0.0   | 0.0   | 0.0 | 0.0 | 0.0   |

( / ) : Number of implantation Right/Left, M : Male, F : Female, U : Unable to be sexed

| Dam No. | Gestation period (day) | Delivery data          |                 | Number of offspring | Dose : PTSA Monohydrate 800 mg/kg |     |       |                         | Species : Rat |     |       |             |     |     |       |       |     |     |       |  |
|---------|------------------------|------------------------|-----------------|---------------------|-----------------------------------|-----|-------|-------------------------|---------------|-----|-------|-------------|-----|-----|-------|-------|-----|-----|-------|--|
|         |                        | Number of implantation | Birth index (%) |                     | Number of live newborns           |     |       | Number of dead newborns |               |     |       | Cannibalism |     |     |       | Total |     |     |       |  |
|         |                        |                        |                 |                     | M                                 | F   | Total | M                       | F             | U   | Total | M           | F   | U   | Total | M     | F   | U   | Total |  |
| 50451   | 22                     | 18(6/12)               | 100.0           | 18                  | 7                                 | 11  | 18    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50452   | 22                     | 17(9/8)                | 94.1            | 16                  | 8                                 | 8   | 16    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50453   | 23                     | 12(6/6)                | 75.0            | 9                   | 3                                 | 6   | 9     | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50454   | 22                     | 17(8/9)                | 82.4            | 14                  | 9                                 | 5   | 14    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50455   | 22                     | 16(8/8)                | 87.5            | 14                  | 11                                | 3   | 14    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50457   | 22                     | 16(9/7)                | 100.0           | 16                  | 8                                 | 8   | 16    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50458   | 22                     | 15(8/7)                | 100.0           | 15                  | 6                                 | 9   | 15    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50459   | 22                     | 13(6/7)                | 92.3            | 12                  | 8                                 | 4   | 12    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50460   | 23                     | 16(12/4)               | 87.5            | 15                  | 4                                 | 10  | 14    | 1                       | 0             | 0   | 1     | 0           | 0   | 0   | 0     | 0     | 1   | 0   | 0     |  |
| 50461   | 22                     | 18(11/7)               | 88.9            | 16                  | 7                                 | 9   | 16    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| 50462   | 22                     | 13(5/8)                | 100.0           | 13                  | 5                                 | 8   | 13    | 0                       | 0             | 0   | 0     | 0           | 0   | 0   | 0     | 0     | 0   | 0   | 0     |  |
| n       |                        | 11                     | 11              | 11                  | 11                                | 11  | 11    | 11                      | 11            | 11  | 11    | 11          | 11  | 11  | 11    | 11    | 11  | 11  | 11    |  |
| Mean    |                        | 22.18                  | 15.5            | 91.61               | 14.4                              | 6.9 | 7.4   | 14.3                    | 0.1           | 0.0 | 0.0   | 0.1         | 0.0 | 0.0 | 0.0   | 0.0   | 0.1 | 0.0 | 0.0   |  |
| S.D.    |                        | 0.40                   | 2.1             | 8.31                | 2.4                               | 2.3 | 2.5   | 2.4                     | 0.3           | 0.0 | 0.0   | 0.3         | 0.0 | 0.0 | 0.0   | 0.0   | 0.3 | 0.0 | 0.0   |  |

(/) : Number of implantation Right/Left, M : Male, F : Female, U : Unable to be sexed

| Delivery data |                         |                        | Dose : PTSA Monohydrate 0 mg/kg | Species : Rat |
|---------------|-------------------------|------------------------|---------------------------------|---------------|
| Dam No.       | Generation : F0         |                        |                                 |               |
|               | Number of corpora lutea | Implantation index (%) |                                 |               |
| 50151         | 16(10/6)                | 100.0                  |                                 |               |
| 50152         | 15(8/7)                 | 100.0                  |                                 |               |
| 50153         | 15(7/8)                 | 100.0                  |                                 |               |
| 50154         | 16(6/10)                | 93.8                   |                                 |               |
| 50155         | 12(5/7)                 | 100.0                  |                                 |               |
| 50156         | 15(5/10)                | 100.0                  |                                 |               |
| 50157         | 18(10/8)                | 100.0                  |                                 |               |
| 50158         | 19(11/8)                | 100.0                  |                                 |               |
| 50159         | 16(6/10)                | 100.0                  |                                 |               |
| 50161         | 16(8/8)                 | 100.0                  |                                 |               |
| 50162         | 16(10/6)                | 100.0                  |                                 |               |
| n             | 11                      | 11                     |                                 |               |
| Mean          | 15.8                    | 99.44                  |                                 |               |
| S.D.          | 1.8                     | 1.87                   |                                 |               |

( / ) : Right/Left

| Delivery data   |                         |                                  |               |
|-----------------|-------------------------|----------------------------------|---------------|
| Generation : F0 |                         | Dose : PTSA Monohydrate 50 mg/kg | Species : Rat |
| Dam No.         | Number of corpora lutea | Implantation index (%)           |               |
| 50251           | 17(12/5)                | 100.0                            |               |
| 50252           | 18(9/9)                 | 100.0                            |               |
| 50253           | 15(7/8)                 | 100.0                            |               |
| 50254           | 16(9/7)                 | 100.0                            |               |
| 50255           | 16(8/8)                 | 93.8                             |               |
| 50256           | 16(4/12)                | 100.0                            |               |
| 50257           | 15(7/8)                 | 100.0                            |               |
| 50258           | 14(5/9)                 | 100.0                            |               |
| 50259           | 15(11/4)                | 93.3                             |               |
| 50260           | 17(11/6)                | 88.2                             |               |
| 50261           | 18(10/8)                | 100.0                            |               |
| 50262           | 17(11/6)                | 100.0                            |               |
| n               | 12                      | 12                               |               |
| Mean            | 16.2                    | 97.94                            |               |
| S.D.            | 1.3                     | 3.95                             |               |

( / ) : Right/Left

| Delivery data   |                         |                                   |  |               |
|-----------------|-------------------------|-----------------------------------|--|---------------|
| Generation : F0 |                         | Dose : PTSA Monohydrate 200 mg/kg |  | Species : Rat |
| Dam No.         | Number of corpora lutea | Implantation index (%)            |  |               |
| 50351           | 14(9/5)                 | 100.0                             |  |               |
| 50352           | 15(7/8)                 | 100.0                             |  |               |
| 50353           | 14(5/9)                 | 100.0                             |  |               |
| 50354           | 15(4/11)                | 100.0                             |  |               |
| 50355           | 18(6/12)                | 100.0                             |  |               |
| 50356           | 15(8/7)                 | 100.0                             |  |               |
| 50357           | 16(11/5)                | 100.0                             |  |               |
| 50358           | 14(6/8)                 | 100.0                             |  |               |
| 50359           | 16(8/8)                 | 100.0                             |  |               |
| 50360           | 16(11/5)                | 100.0                             |  |               |
| 50361           | 18(9/9)                 | 100.0                             |  |               |
| 50362           | 18(6/12)                | 100.0                             |  |               |
| n               | 12                      | 12                                |  |               |
| Mean            | 15.8                    | 100.00                            |  |               |
| S.D.            | 1.5                     | 0.00                              |  |               |

( / ) : Right/Left

| Delivery data   |                         | Dose : PTSA Monohydrate 800 mg/kg | Species : Rat |
|-----------------|-------------------------|-----------------------------------|---------------|
| Generation : F0 | Number of corpora lutea | Implantation index (%)            |               |
| Dam No.         |                         |                                   |               |
| 50451           | 18(6/12)                | 100.0                             |               |
| 50452           | 17(9/8)                 | 100.0                             |               |
| 50453           | 12(6/6)                 | 100.0                             |               |
| 50454           | 17(8/9)                 | 100.0                             |               |
| 50455           | 16(8/8)                 | 100.0                             |               |
| 50457           | 16(9/7)                 | 100.0                             |               |
| 50458           | 15(8/7)                 | 100.0                             |               |
| 50459           | 14(7/7)                 | 92.9                              |               |
| 50460           | 16(12/4)                | 100.0                             |               |
| 50461           | 18(11/7)                | 100.0                             |               |
| 50462           | 15(6/9)                 | 86.7                              |               |
| n               | 11                      | 11                                |               |
| Mean            | 15.8                    | 98.15                             |               |
| S.D.            | 1.8                     | 4.35                              |               |

( / ) : Right/Left

| Delivery data (external examination of offspring) |                              | Unit : Number of anomalous offspring (incidence %) | Day after birth : 0 |
|---|------------------------------|--|---------------------|
| Generation : F0                                   |                              | Dose : PTSA Monohydrate 0 mg/kg                    | Species : Rat       |
| Dam No.   | Number of offspring examined | /Findings  |                     |
| 50151   | 12                           | No anomaly   |                     |
| 50152   | 15                           | No anomaly   |                     |
| 50153   | 14                           | No anomaly   |                     |
| 50154   | 13                           | No anomaly   |                     |
| 50155   | 11                           | No anomaly   |                     |
| 50156   | 14                           | No anomaly   |                     |
| 50157   | 9                            | No anomaly   |                     |
| 50158   | 19                           | No anomaly   |                     |
| 50159   | 16                           | No anomaly   |                     |
| 50161   | 16                           | No anomaly   |                     |
| 50162   | 16                           | No anomaly   |                     |
| Total   | 155                          |  |                     |
| n   | 11                           |  |                     |
| Mean  |                              |  |                     |
| S.D.  |                              |  |                     |

Mean : Average of incidence (%)

| Delivery data (external examination of offspring) |                              |            | Unit : Number of anomalous offspring (incidence %) | Day after birth : 0 |
|---|------------------------------|------------|--|---------------------|
| Generation : F0                                   |                              |            | Dose : PTSA Monohydrate 50 mg/kg                   | Species : Rat       |
| Dam No.   | Number of offspring examined | /Findings  |  |                     |
| 50251   | 15                           | No anomaly |  |                     |
| 50252   | 17                           | No anomaly |  |                     |
| 50253   | 15                           | No anomaly |  |                     |
| 50254   | 15                           | No anomaly |  |                     |
| 50255   | 13                           | No anomaly |  |                     |
| 50256   | 11                           | No anomaly |  |                     |
| 50257   | 15                           | No anomaly |  |                     |
| 50258   | 13                           | No anomaly |  |                     |
| 50259   | 14                           | No anomaly |  |                     |
| 50260   | 15                           | No anomaly |  |                     |
| 50261   | 18                           | No anomaly |  |                     |
| 50262   | 15                           | No anomaly |  |                     |
| Total   | 176                          |            |  |                     |
| n   | 12                           |            |  |                     |
| Mean  |                              |            |  |                     |
| S.D.  |                              |            |  |                     |

Mean : Average of incidence (%)

| Delivery data (external examination of offspring) |                              |            | Unit : Number of anomalous offspring (incidence %) | Day after birth : 0 |
|---|------------------------------|------------|--|---------------------|
| Generation : F0                                   |                              |            | Dose : PTSA Monohydrate 200 mg/kg                  | Species : Rat       |
| Dam No.   | Number of offspring examined | /Findings  |  |                     |
| 50351   | 14                           | No anomaly |  |                     |
| 50352   | 15                           | No anomaly |  |                     |
| 50353   | 14                           | No anomaly |  |                     |
| 50354   | 13                           | No anomaly |  |                     |
| 50355   | 17                           | No anomaly |  |                     |
| 50356   | 14                           | No anomaly |  |                     |
| 50357   | 15                           | No anomaly |  |                     |
| 50358   | 13                           | No anomaly |  |                     |
| 50359   | 16                           | No anomaly |  |                     |
| 50360   | 15                           | No anomaly |  |                     |
| 50361   | 15                           | No anomaly |  |                     |
| 50362   | 11                           | No anomaly |  |                     |
| Total   | 172                          |            |  |                     |
| n   | 12                           |            |  |                     |
| Mean  |                              |            |  |                     |
| S.D.  |                              |            |  |                     |

Mean : Average of incidence (%)

| Delivery data (external examination of offspring) |                              | Unit : Number of anomalous offspring (incidence %) | Day after birth : 0 |
|---|------------------------------|--|---------------------|
| Generation : F0                                   |                              | Dose : PTSA Monohydrate 800 mg/kg                  | Species : Rat       |
| Dam No.   | Number of offspring examined | /Findings  |                     |
| 50451   | 18                           | No anomaly   |                     |
| 50452   | 16                           | No anomaly   |                     |
| 50453   | 9                            | No anomaly   |                     |
| 50454   | 14                           | No anomaly   |                     |
| 50455   | 14                           | No anomaly   |                     |
| 50457   | 16                           | No anomaly   |                     |
| 50458   | 15                           | No anomaly   |                     |
| 50459   | 12                           | No anomaly   |                     |
| 50460   | 14                           | No anomaly   |                     |
| 50461   | 16                           | No anomaly   |                     |
| 50462   | 13                           | No anomaly   |                     |
| Total   | 157                          |  |                     |
| n   | 11                           |  |                     |
| Mean  |                              |  |                     |
| S.D.  |                              |  |                     |

Mean : Average of incidence (%)

|         |  | Clinical sign of offspring<br>Generation : F0 |       |       |       |       | Species : Rat |
|---------|--|---|-------|-------|-------|-------|---------------|
| Dam No. | Number of offspring                                      | Dose : PTSA Monohydrate 0 mg/kg               |       |       |       |       |               |
|         |  | /Day after birth                              | 0     | 1     | 2     | 3     | 4             |
| 50151   | Alive : Male   |   | 8     | 8     | 8     | 8     | 8             |
|         | Female   |   | 4     | 4     | 4     | 4     | 4             |
|         | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs  |   |       |       |       |       |               |
|         | No abnormality   |   | 8/4   | 8/4   | 8/4   | 8/4   | 8/4           |
|         | Alive : Male   |   | 8     | 8     | 8     | 8     | 8             |
|         | Female   |   | 7     | 7     | 7     | 7     | 7             |
|         | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
| 50152   | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs  |   |       |       |       |       |               |
|         | No abnormality   |   | 8/7   | 8/7   | 8/7   | 8/7   | 8/7           |
|         | Alive : Male   |   | 8     | 8     | 8     | 8     | 8             |
|         | Female   |   | 6     | 6     | 6     | 6     | 6             |
|         | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs  |   |       |       |       |       |               |
| 50153   | No abnormality   |   | 8/6   | 8/6   | 8/6   | 8/6   | 8/6           |
|         | Alive : Male   |   | 7     | 7     | 7     | 7     | 7             |
|         | Female   |   | 6     | 6     | 6     | 6     | 6             |
|         | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs  |   |       |       |       |       |               |
|         | No abnormality   |   | 7/6   | 7/6   | 7/6   | 7/6   | 7/6           |
|         | Alive : Male   |   | 5     | 5     | 5     | 5     | 5             |
|         | Female   |   | 6     | 6     | 6     | 6     | 6             |
| 50154   | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs  |   |       |       |       |       |               |
|         | No abnormality   |   | 7/6   | 7/6   | 7/6   | 7/6   | 7/6           |
|         | Alive : Male   |   | 5     | 5     | 5     | 5     | 5             |
|         | Female   |   | 6     | 6     | 6     | 6     | 6             |
|         | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
| 50155   | Signs  |   |       |       |       |       |               |
|         | No abnormality   |   | 5/6   | 5/6   | 5/6   | 5/6   | 5/6           |
|         | Alive : Male   |   | 4     | 4     | 4     | 4     | 4             |
|         | Female   |   | 10    | 10    | 10    | 10    | 10            |
|         | Dead : Dead  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism  |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs  |   |       |       |       |       |               |
|         | No abnormality   |   | 4/10  | 4/10  | 4/10  | 4/10  | 4/10          |
|         | (/) : Number of offspring Male/Female/Unable to be sexed |   |       |       |       |       |               |

|         |                     | Clinical sign of offspring      |       |       |       |       | Species : Rat |  |
|---------|---------------------|---------------------------------|-------|-------|-------|-------|---------------|--|
|         |                     | Generation : F0                 |       |       |       |       |               |  |
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 0 mg/kg |       |       |       |       |               |  |
|         |                     | 0                               | 1     | 2     | 3     | 4     |               |  |
| 50157   | Alive : Male        | 2                               | 2     | 2     | 2     | 2     |               |  |
|         | Female              | 7                               | 7     | 7     | 7     | 7     |               |  |
|         | Dead : Dead         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Unknown             | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Signs               |                                 |       |       |       |       |               |  |
|         | No abnormality      | 2/7                             | 2/7   | 2/7   | 2/7   | 2/7   |               |  |
| 50158   | Alive : Male        | 7                               | 7     | 7     | 7     | 7     |               |  |
|         | Female              | 12                              | 12    | 12    | 12    | 11    |               |  |
|         | Dead : Dead         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Unknown             | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/1/0 |               |  |
|         | Cannibalism         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Signs               |                                 |       |       |       |       |               |  |
|         | No abnormality      | 7/12                            | 7/12  | 7/12  | 7/12  | 7/11  |               |  |
| 50159   | Alive : Male        | 8                               | 8     | 8     | 8     | 8     |               |  |
|         | Female              | 8                               | 8     | 8     | 8     | 8     |               |  |
|         | Dead : Dead         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Unknown             | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Signs               |                                 |       |       |       |       |               |  |
|         | No abnormality      | 8/8                             | 8/8   | 8/8   | 8/8   | 8/8   |               |  |
| 50161   | Alive : Male        | 10                              | 10    | 10    | 10    | 10    |               |  |
|         | Female              | 6                               | 6     | 6     | 6     | 6     |               |  |
|         | Dead : Dead         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Unknown             | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Signs               |                                 |       |       |       |       |               |  |
|         | No abnormality      | 10/6                            | 10/6  | 10/6  | 10/6  | 10/6  |               |  |
| 50162   | Alive : Male        | 6                               | 6     | 6     | 6     | 6     |               |  |
|         | Female              | 10                              | 10    | 10    | 10    | 10    |               |  |
|         | Dead : Dead         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Unknown             | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0                           | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |  |
|         | Signs               |                                 |       |       |       |       |               |  |
|         | No abnormality      | 6/10                            | 6/10  | 6/10  | 6/10  | 6/10  |               |  |

( / ) : Number of offspring Male/Female/Unable to be sexed

|         |                     | Clinical sign of offspring<br>Generation : F0 |       |       |       |       | Species : Rat |
|---------|---------------------|---|-------|-------|-------|-------|---------------|
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 50 mg/kg              |       |       |       |       |               |
|         |                     | /Day after birth                              | 0     | 1     | 2     | 3     | 4             |
| 50251   | Alive : Male        |   | 8     | 8     | 8     | 8     | 8             |
|         | Female              |   | 7     | 7     | 7     | 7     | 7             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 8/7   | 8/7   | 8/7   | 8/7   | 8/7           |
|         | Alive : Male        |   | 8     | 8     | 8     | 8     | 8             |
|         | Female              |   | 9     | 9     | 9     | 9     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50252   | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/1/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 8/9   | 8/9   | 8/9   | 8/9   | 8/8           |
|         | Alive : Male        |   | 5     | 5     | 5     | 5     | 5             |
|         | Female              |   | 10    | 10    | 10    | 10    | 10            |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
| 50253   | No abnormality      |   | 5/10  | 5/10  | 5/10  | 5/10  | 5/10          |
|         | Alive : Male        |   | 4     | 4     | 4     | 4     | 4             |
|         | Female              |   | 11    | 11    | 11    | 11    | 11            |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 4/11  | 4/11  | 4/11  | 4/11  | 4/11          |
|         | Alive : Male        |   | 8     | 8     | 8     | 8     | 8             |
|         | Female              |   | 5     | 5     | 5     | 5     | 4             |
| 50254   | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 4/11  | 4/11  | 4/11  | 4/11  | 4/11          |
|         | Alive : Male        |   | 8     | 8     | 8     | 8     | 8             |
|         | Female              |   | 5     | 5     | 5     | 5     | 4             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/1/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50255   | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 8/5   | 8/5   | 8/5   | 8/5   | 8/4           |
|         | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
|         | Female              |   | 5     | 5     | 5     | 5     | 5             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 6/5   | 6/5   | 6/5   | 6/5   | 6/5           |
|         | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
| 50256   | Female              |   | 5     | 5     | 5     | 5     | 5             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 6/5   | 6/5   | 6/5   | 6/5   | 6/5           |
|         | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
|         | Female              |   | 5     | 5     | 5     | 5     | 5             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |

( / ) : Number of offspring Male/Female/Unable to be sexed

|         |                     | Clinical sign of offspring<br>Generation : F0 |       |       |       |       | Species : Rat |
|---------|---------------------|---|-------|-------|-------|-------|---------------|
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 50 mg/kg              |       |       |       |       |               |
|         |                     | /Day after birth                              | 0     | 1     | 2     | 3     | 4             |
| 50257   | Alive : Male        |   | 7     | 7     | 7     | 7     | 6             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 1/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 7/8   | 7/8   | 7/8   | 7/8   | 6/8   |               |
|         | Alive : Male        |   | 5     | 5     | 5     | 5     | 5             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50258   | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 5/8   | 5/8   | 5/8   | 5/8   | 5/8   |               |
|         | Alive : Male        |   | 4     | 4     | 4     | 4     | 4             |
|         | Female              |   | 10    | 10    | 10    | 10    | 10            |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
| 50259   | No abnormality      | 4/10  | 4/10  | 4/10  | 4/10  | 4/10  |               |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 6     | 6     | 6     | 6     | 6             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 9/6   | 9/6   | 9/6   | 9/6   | 9/6   |               |
|         | Alive : Male        |   | 10    | 10    | 10    | 10    | 10            |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
| 50260   | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 9/6   | 9/6   | 9/6   | 9/6   | 9/6   |               |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 6     | 6     | 6     | 6     | 6             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50261   | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 10/8  | 10/8  | 10/8  | 10/8  | 10/8  |               |
|         | Alive : Male        |   | 10    | 10    | 10    | 10    | 10            |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 10/8  | 10/8  | 10/8  | 10/8  | 10/8  |               |
|         | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
| 50262   | Female              |   | 9     | 9     | 9     | 9     | 9             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      | 6/9   | 6/9   | 6/9   | 6/9   | 6/9   |               |
|         | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
|         | Female              |   | 9     | 9     | 9     | 9     | 9             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |

( / ) : Number of offspring Male/Female/Unable to be sexed

|         |                     | Clinical sign of offspring<br>Generation : F0 |       |       |       |       | Species : Rat |
|---------|---------------------|---|-------|-------|-------|-------|---------------|
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 200 mg/kg             |       |       |       |       |               |
|         |                     | /Day after birth                              | 0     | 1     | 2     | 3     | 4             |
| 50351   | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 6/8   | 6/8   | 6/8   | 6/8   | 6/8           |
|         | Alive : Male        |   | 4     | 4     | 4     | 4     | 4             |
|         | Female              |   | 11    | 11    | 11    | 11    | 11            |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50352   | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 4/11  | 4/11  | 4/11  | 4/11  | 4/11          |
|         | Alive : Male        |   | 8     | 8     | 8     | 8     | 8             |
|         | Female              |   | 6     | 6     | 6     | 6     | 6             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
| 50353   | No abnormality      |   | 8/6   | 8/6   | 8/6   | 8/6   | 8/6           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 4     | 4     | 4     | 4     | 4             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 9/4   | 9/4   | 9/4   | 9/4   | 9/4           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
| 50354   | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 9/4   | 9/4   | 9/4   | 9/4   | 9/4           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 4     | 4     | 4     | 4     | 4             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50355   | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 9/8   | 9/8   | 9/8   | 9/8   | 9/8           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 9/8   | 9/8   | 9/8   | 9/8   | 9/8           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
| 50356   | Female              |   | 5     | 5     | 5     | 5     | 5             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 9/5   | 9/5   | 9/5   | 9/5   | 9/5           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 5     | 5     | 5     | 5     | 5             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |

( / ) : Number of offspring Male/Female/Unable to be sexed

|         |                     | Clinical sign of offspring<br>Generation : F0 |       |       |       |       | Species : Rat |
|---------|---------------------|---|-------|-------|-------|-------|---------------|
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 200 mg/kg             |       |       |       |       |               |
|         |                     | /Day after birth                              | 0     | 1     | 2     | 3     | 4             |
| 50357   | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
|         | Female              |   | 9     | 9     | 9     | 9     | 9             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 6/9   | 6/9   | 6/9   | 6/9   | 6/9           |
|         | Alive : Male        |   | 6     | 6     | 6     | 6     | 6             |
|         | Female              |   | 7     | 7     | 7     | 7     | 7             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50358   | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 6/7   | 6/7   | 6/7   | 6/7   | 6/7           |
|         | Alive : Male        |   | 9     | 9     | 9     | 9     | 9             |
|         | Female              |   | 7     | 7     | 7     | 7     | 7             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
| 50359   | No abnormality      |   | 9/7   | 9/7   | 9/7   | 9/7   | 9/7           |
|         | Alive : Male        |   | 10    | 10    | 10    | 10    | 10            |
|         | Female              |   | 5     | 5     | 5     | 5     | 5             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 10/5  | 10/5  | 10/5  | 10/5  | 10/5          |
|         | Alive : Male        |   | 7     | 7     | 7     | 7     | 7             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
| 50360   | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 7/8   | 7/8   | 7/8   | 7/8   | 7/8           |
|         | Alive : Male        |   | 4     | 4     | 4     | 4     | 4             |
|         | Female              |   | 7     | 7     | 7     | 7     | 7             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
| 50361   | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 7/8   | 7/8   | 7/8   | 7/8   | 7/8           |
|         | Alive : Male        |   | 7     | 7     | 7     | 7     | 7             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 7/8   | 7/8   | 7/8   | 7/8   | 7/8           |
|         | Alive : Male        |   | 4     | 4     | 4     | 4     | 4             |
| 50362   | Female              |   | 7     | 7     | 7     | 7     | 7             |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 |               |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 4/7   | 4/7   | 4/7   | 4/7   | 4/7           |

( / ) : Number of offspring Male/Female/Unable to be sexed

|         |                     | Clinical sign of offspring<br>Generation : F0 |       |       |        |       | Species : Rat |  |
|---------|---------------------|---|-------|-------|--------|-------|---------------|--|
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 800 mg/kg             |       |       |        |       |               |  |
|         |                     | 0   | 1     | 2     | 3      | 4     |               |  |
| 50451   | Alive : Male        | 7   | 7     | 7     | 7      | 7     |               |  |
|         | Female              | 11  | 11    | 11    | 11     | 11    |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 7/11  | 7/11  | 7/11  | 7/11   | 7/11  |               |  |
|         | Alive : Male        | 8   | 8     | 8     | 8      | 7     |               |  |
|         | Female              | 8   | 8     | 8     | 8      | 8     |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
| 50452   | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 1/0/0 |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 8/8   | 8/8   | 8/8   | 8/8    | 7/8   |               |  |
|         | Alive : Male        | 3   | 3     | 3     | 3      | 3     |               |  |
|         | Female              | 6   | 6     | 6     | 6      | 6     |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Signs               |   |       |       |        |       |               |  |
| 50453   | No abnormality      | 3/6   | 3/6   | 3/6   | 3/6    | 3/6   |               |  |
|         | Alive : Male        | 9   | 9     | 9     | 9      | 9     |               |  |
|         | Female              | 5   | 5     | 5     | 5      | 5     |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 9/5   | 9/5   | 9/5   | 9/5    | 9/5   |               |  |
|         | Alive : Male        | 11  | 11    | 11    | 0      | -     |               |  |
|         | Female              | 3   | 3     | 3     | 0      | -     |               |  |
| 50454   | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 11/3/0 | -     |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | -     |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | -     |               |  |
|         | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 11/3  | 11/3  | 11/3  | 0/0    | -     |               |  |
|         | Alive : Male        | 8   | 8     | 8     | 8      | 7     |               |  |
|         | Female              | 8   | 8     | 8     | 8      | 8     |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 1/0/0 |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
| 50455   | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 8/8   | 8/8   | 8/8   | 8/8    | 7/8   |               |  |
|         | Alive : Male        | 11/3  | 11/3  | 11/3  | 0/0    | -     |               |  |
|         | Female              | 3   | 3     | 3     | 0      | -     |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 11/3/0 | -     |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | -     |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | -     |               |  |
|         | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 11/3  | 11/3  | 11/3  | 0/0    | -     |               |  |
|         | Alive : Male        | 8   | 8     | 8     | 8      | 7     |               |  |
| 50457   | Female              | 8   | 8     | 8     | 8      | 8     |               |  |
|         | Dead : Dead         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Unknown             | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 1/0/0 |               |  |
|         | Cannibalism         | 0/0/0   | 0/0/0 | 0/0/0 | 0/0/0  | 0/0/0 |               |  |
|         | Signs               |   |       |       |        |       |               |  |
|         | No abnormality      | 8/8   | 8/8   | 8/8   | 8/8    | 7/8   |               |  |

( / ) : Number of offspring Male/Female/Unable to be sexed

Dam No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

- : Not applicable

|         |                     | Clinical sign of offspring<br>Generation : F0 |       |       |       |       | Species : Rat |
|---------|---------------------|---|-------|-------|-------|-------|---------------|
| Dam No. | Number of offspring | Dose : PTSA Monohydrate 800 mg/kg             |       |       |       |       |               |
|         |                     | /Day after birth                              | 0     | 1     | 2     | 3     | 4             |
| 50458   | Alive : Male        |   | 6     | -     | -     | -     | -             |
|         | Female              |   | 9     | -     | -     | -     | -             |
|         | Dead : Dead         |   | 0/0/0 | -     | -     | -     | -             |
|         | Unknown             |   | 0/0/0 | -     | -     | -     | -             |
|         | Cannibalism         |   | 0/0/0 | -     | -     | -     | -             |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 6/9   | -     | -     | -     | -             |
|         |                     |   |       |       |       |       |               |
| 50459   | Alive : Male        |   | 8     | 8     | 8     | 8     | 8             |
|         | Female              |   | 4     | 4     | 4     | 4     | 4             |
|         | Dead : Dead         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown             |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 8/4   | 8/4   | 8/4   | 8/4   | 8/4           |
|         |                     |   |       |       |       |       |               |
| 50460   | Alive : Male        |   | 4     | 4     | 4     | 4     | 4             |
|         | Female              |   | 10    | 10    | 10    | 10    | 10            |
|         | Dead : Dead         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown             |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 4/10  | 4/10  | 4/10  | 4/10  | 4/10          |
|         |                     |   |       |       |       |       |               |
| 50461   | Alive : Male        |   | 7     | 7     | 7     | 7     | 7             |
|         | Female              |   | 9     | 9     | 9     | 9     | 9             |
|         | Dead : Dead         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown             |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 7/9   | 7/9   | 7/9   | 7/9   | 7/9           |
|         |                     |   |       |       |       |       |               |
| 50462   | Alive : Male        |   | 5     | 5     | 5     | 5     | 5             |
|         | Female              |   | 8     | 8     | 8     | 8     | 8             |
|         | Dead : Dead         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Unknown             |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Cannibalism         |   | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0 | 0/0/0         |
|         | Signs               |   |       |       |       |       |               |
|         | No abnormality      |   | 5/8   | 5/8   | 5/8   | 5/8   | 5/8           |
|         |                     |   |       |       |       |       |               |

( / ) : Number of offspring Male/Female/Unable to be sexed

Dam No. 50458 : Died on lactation day 0 and the live pups were euthanized on that day

- : Not applicable

Litter size and viability index of offspring  
Generation : F0  
/Day after birth

| Dam No.     | Sex   | 0                       |                          | 0                      |                          | 4                      |  | Species : Rat |
|-------------|-------|-------------------------|--------------------------|------------------------|--------------------------|------------------------|--|---------------|
|             |       | All pups<br>Male/Female | Live pups<br>Male/Female | Viability<br>index (%) | Live pups<br>Male/Female | Viability<br>index (%) |  |               |
| 50151       | Total | 13<br>(8/5)             | 12<br>(8/4)              | 92.3                   | 12<br>(8/4)              | 100.0                  |  |               |
| 50152       | Total | 15<br>(8/7)             | 15<br>(8/7)              | 100.0                  | 15<br>(8/7)              | 100.0                  |  |               |
| 50153       | Total | 14<br>(8/6)             | 14<br>(8/6)              | 100.0                  | 14<br>(8/6)              | 100.0                  |  |               |
| 50154       | Total | 13<br>(7/6)             | 13<br>(7/6)              | 100.0                  | 13<br>(7/6)              | 100.0                  |  |               |
| 50155       | Total | 11<br>(5/6)             | 11<br>(5/6)              | 100.0                  | 11<br>(5/6)              | 100.0                  |  |               |
| 50156       | Total | 14<br>(4/10)            | 14<br>(4/10)             | 100.0                  | 14<br>(4/10)             | 100.0                  |  |               |
| 50157       | Total | 9<br>(2/7)              | 9<br>(2/7)               | 100.0                  | 9<br>(2/7)               | 100.0                  |  |               |
| 50158       | Total | 19<br>(7/12)            | 19<br>(7/12)             | 100.0                  | 18<br>(7/11)             | 94.7                   |  |               |
| 50159       | Total | 16<br>(8/8)             | 16<br>(8/8)              | 100.0                  | 16<br>(8/8)              | 100.0                  |  |               |
| 50161       | Total | 16<br>(10/6)            | 16<br>(10/6)             | 100.0                  | 16<br>(10/6)             | 100.0                  |  |               |
| 50162       | Total | 16<br>(6/10)            | 16<br>(6/10)             | 100.0                  | 16<br>(6/10)             | 100.0                  |  |               |
| Total       |       | 156                     | 155                      | 154                    |                          |                        |  |               |
| Male/Female |       | 73/83                   | 73/82                    | 73/81                  |                          |                        |  |               |
| n           |       | 11                      | 11                       | 11                     |                          |                        |  |               |
| Mean        |       |                         |                          | 99.30                  |                          |                        |  |               |
| S.D.        |       |                         |                          | 2.32                   |                          |                        |  |               |
|             |       |                         |                          | 99.52                  |                          |                        |  |               |
|             |       |                         |                          | 1.60                   |                          |                        |  |               |

| Litter size and viability index of offspring |       |                  |                                  |                               |                             | Species : Rat         |  |
|--|-------|------------------|----------------------------------|-------------------------------|-----------------------------|-----------------------|--|
| Generation : F0                              |       |                  | Dose : PTSA Monohydrate 50 mg/kg |                               |                             |                       |  |
| Dam No.                                      | Sex   | /Day after birth | 0<br>All pups<br>Male/Female     | 0<br>Live pups<br>Male/Female | 0<br>Viability<br>index (%) |                       |  |
| 50251  | Total |                  | 17<br>(9/8)                      | 15<br>(8/7)                   | 88.2                        | 15<br>(8/7)<br>100.0  |  |
| 50252  | Total |                  | 17<br>(8/9)                      | 17<br>(8/9)                   | 100.0                       | 16<br>(8/8)<br>94.1   |  |
| 50253  | Total |                  | 15<br>(5/10)                     | 15<br>(5/10)                  | 100.0                       | 15<br>(5/10)<br>100.0 |  |
| 50254  | Total |                  | 15<br>(4/11)                     | 15<br>(4/11)                  | 100.0                       | 15<br>(4/11)<br>100.0 |  |
| 50255  | Total |                  | 13<br>(8/5)                      | 13<br>(8/5)                   | 100.0                       | 12<br>(8/4)<br>92.3   |  |
| 50256  | Total |                  | 11<br>(6/5)                      | 11<br>(6/5)                   | 100.0                       | 11<br>(6/5)<br>100.0  |  |
| 50257  | Total |                  | 15<br>(7/8)                      | 15<br>(7/8)                   | 100.0                       | 14<br>(6/8)<br>93.3   |  |
| 50258  | Total |                  | 13<br>(5/8)                      | 13<br>(5/8)                   | 100.0                       | 13<br>(5/8)<br>100.0  |  |
| 50259  | Total |                  | 14<br>(4/10)                     | 14<br>(4/10)                  | 100.0                       | 14<br>(4/10)<br>100.0 |  |
| 50260  | Total |                  | 15<br>(9/6)                      | 15<br>(9/6)                   | 100.0                       | 15<br>(9/6)<br>100.0  |  |
| 50261  | Total |                  | 18<br>(10/8)                     | 18<br>(10/8)                  | 100.0                       | 18<br>(10/8)<br>100.0 |  |
| 50262  | Total |                  | 15<br>(6/9)                      | 15<br>(6/9)                   | 100.0                       | 15<br>(6/9)<br>100.0  |  |
| Total  |       |                  | 178                              | 176                           | 173                         |                       |  |
| Male/Female                                  |       |                  | 81/97                            | 80/96                         | 79/94                       |                       |  |
| n  |       |                  | 12                               | 12                            | 12                          |                       |  |
| Mean   |       |                  |                                  | 99.02                         | 98.31                       |                       |  |
| S.D.   |       |                  |                                  | 3.41                          | 3.08                        |                       |  |

| Litter size and viability index of offspring |       |                  |                                   |                               |                             | Species : Rat |  |
|--|-------|------------------|-----------------------------------|-------------------------------|-----------------------------|---------------|--|
| Generation : F0                              |       |                  | Dose : PTSA Monohydrate 200 mg/kg |                               |                             |               |  |
| Dam No.                                      | Sex   | /Day after birth | 0<br>All pups<br>Male/Female      | 0<br>Live pups<br>Male/Female | 0<br>Viability<br>index (%) |               |  |
| 50351  | Total |                  | 14<br>(6/8)                       | 14<br>(6/8)                   | 100.0                       | 14<br>(6/8)   |  |
| 50352  | Total |                  | 15<br>(4/11)                      | 15<br>(4/11)                  | 100.0                       | 15<br>(4/11)  |  |
| 50353  | Total |                  | 14<br>(8/6)                       | 14<br>(8/6)                   | 100.0                       | 14<br>(8/6)   |  |
| 50354  | Total |                  | 13<br>(9/4)                       | 13<br>(9/4)                   | 100.0                       | 13<br>(9/4)   |  |
| 50355  | Total |                  | 17<br>(9/8)                       | 17<br>(9/8)                   | 100.0                       | 17<br>(9/8)   |  |
| 50356  | Total |                  | 14<br>(9/5)                       | 14<br>(9/5)                   | 100.0                       | 14<br>(9/5)   |  |
| 50357  | Total |                  | 15<br>(6/9)                       | 15<br>(6/9)                   | 100.0                       | 15<br>(6/9)   |  |
| 50358  | Total |                  | 13<br>(6/7)                       | 13<br>(6/7)                   | 100.0                       | 13<br>(6/7)   |  |
| 50359  | Total |                  | 16<br>(9/7)                       | 16<br>(9/7)                   | 100.0                       | 16<br>(9/7)   |  |
| 50360  | Total |                  | 15<br>(10/5)                      | 15<br>(10/5)                  | 100.0                       | 15<br>(10/5)  |  |
| 50361  | Total |                  | 15<br>(7/8)                       | 15<br>(7/8)                   | 100.0                       | 15<br>(7/8)   |  |
| 50362  | Total |                  | 11<br>(4/7)                       | 11<br>(4/7)                   | 100.0                       | 11<br>(4/7)   |  |
| Total  |       |                  | 172                               | 172                           | 172                         |               |  |
| Male/Female                                  |       |                  | 87/85                             | 87/85                         | 87/85                       |               |  |
| n  |       |                  | 12                                | 12                            | 12                          |               |  |
| Mean   |       |                  |                                   | 100.00                        |                             | 100.00        |  |
| S.D.   |       |                  |                                   | 0.00                          |                             | 0.00          |  |

| Litter size and viability index of offspring |       |                  |                                   |                               |                             | Species : Rat |
|--|-------|------------------|-----------------------------------|-------------------------------|-----------------------------|---------------|
| Generation : F0                              |       |                  | Dose : PTSA Monohydrate 800 mg/kg |                               |                             |               |
| Dam No.                                      | Sex   | /Day after birth | 0<br>All pups<br>Male/Female      | 0<br>Live pups<br>Male/Female | 0<br>Viability<br>index (%) |               |
| 50451  | Total |                  | 18<br>(7/11)                      | 18<br>(7/11)                  | 100.0                       | 18<br>(7/11)  |
| 50452  | Total |                  | 16<br>(8/8)                       | 16<br>(8/8)                   | 100.0                       | 15<br>(7/8)   |
| 50453  | Total |                  | 9<br>(3/6)                        | 9<br>(3/6)                    | 100.0                       | 9<br>(3/6)    |
| 50454  | Total |                  | 14<br>(9/5)                       | 14<br>(9/5)                   | 100.0                       | 14<br>(9/5)   |
| 50455  | Total |                  | 14<br>(11/3)                      | 14<br>(11/3)                  | 100.0                       | \$<br>(0/0)   |
| 50457  | Total |                  | 16<br>(8/8)                       | 16<br>(8/8)                   | 100.0                       | 15<br>(7/8)   |
| 50458  | Total |                  | 15<br>(6/9)                       | 15<br>(6/9)                   | 100.0                       | \$<br>(0/0)   |
| 50459  | Total |                  | 12<br>(8/4)                       | 12<br>(8/4)                   | 100.0                       | 12<br>(8/4)   |
| 50460  | Total |                  | 15<br>(5/10)                      | 14<br>(4/10)                  | 93.3                        | 14<br>(4/10)  |
| 50461  | Total |                  | 16<br>(7/9)                       | 16<br>(7/9)                   | 100.0                       | 16<br>(7/9)   |
| 50462  | Total |                  | 13<br>(5/8)                       | 13<br>(5/8)                   | 100.0                       | 13<br>(5/8)   |
| Total  |       |                  | 158                               | 157                           | 126                         |               |
| Male/Female                                  |       |                  | 77/81                             | 76/81                         | 57/69                       |               |
| n  |       |                  | 11                                | 11                            | 9                           |               |
| Mean   |       |                  |                                   | 99.39                         | 98.62                       |               |
| S.D.   |       |                  |                                   | 2.02                          | 2.73                        |               |

Dam No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

Dam No. 50458 : Died on lactation day 0 and the live pups were euthanized on that day

\$ : Excepted data from calculation

Body weight of offspring  
Generation : F0  
/Day after birth

| Dam No. | Sex    | 0  |       | 4  |        | Dose : PTSA Monohydrate 0 mg/kg | Unit : g | Species : Rat |
|---------|--------|----|-------|----|--------|---------------------------------|----------|---------------|
|         |        | n  | B.W.  | n  | B.W.   |                                 |          |               |
| 50151   | Male   | 8  | 6.56  | 8  | 11.80  |                                 |          |               |
|         | Female | 4  | 6.28  | 4  | 11.20  |                                 |          |               |
| 50152   | Male   | 8  | 6.61  | 8  | 10.26  |                                 |          |               |
|         | Female | 7  | 6.16  | 7  | 9.69   |                                 |          |               |
| 50153   | Male   | 8  | 6.39  | 8  | 11.00  |                                 |          |               |
|         | Female | 6  | 6.00  | 6  | 10.37  |                                 |          |               |
| 50154   | Male   | 7  | 7.20  | 7  | 12.13  |                                 |          |               |
|         | Female | 6  | 6.65  | 6  | 10.88  |                                 |          |               |
| 50155   | Male   | 5  | 6.58  | 5  | 11.38  |                                 |          |               |
|         | Female | 6  | 6.48  | 6  | 11.37  |                                 |          |               |
| 50156   | Male   | 4  | 6.10  | 4  | 10.00  |                                 |          |               |
|         | Female | 10 | 5.73  | 10 | 9.27   |                                 |          |               |
| 50157   | Male   | 2  | 8.45  | 2  | 16.70  |                                 |          |               |
|         | Female | 7  | 8.07  | 7  | 15.56  |                                 |          |               |
| 50158   | Male   | 7  | 6.34  | 7  | 9.04   |                                 |          |               |
|         | Female | 12 | 5.75  | 11 | 8.59   |                                 |          |               |
| 50159   | Male   | 8  | 6.69  | 8  | 10.84  |                                 |          |               |
|         | Female | 8  | 6.44  | 8  | 10.50  |                                 |          |               |
| 50161   | Male   | 10 | 7.11  | 10 | 11.18  |                                 |          |               |
|         | Female | 6  | 6.18  | 6  | 9.85   |                                 |          |               |
| 50162   | Male   | 6  | 6.48  | 6  | 9.85   |                                 |          |               |
|         | Female | 10 | 5.90  | 10 | 9.08   |                                 |          |               |
| n       | Male   | 73 |       | 73 |        |                                 |          |               |
|         | Female | 82 |       | 81 |        |                                 |          |               |
| Mean    | Male   |    | 6.774 |    | 11.289 |                                 |          |               |
|         | Female |    | 6.331 |    | 10.578 |                                 |          |               |
| S.D.    | Male   |    | 0.640 |    | 2.010  |                                 |          |               |
|         | Female |    | 0.649 |    | 1.876  |                                 |          |               |

Body weight of offspring  
Generation : F0  
/Day after birth

| Dam No. | Sex    | 0  |       | 4  |        | Dose : PTSA Monohydrate 50 mg/kg | Unit : g | Species : Rat |
|---------|--------|----|-------|----|--------|----------------------------------|----------|---------------|
|         |        | n  | B.W.  | n  | B.W.   |                                  |          |               |
| 50251   | Male   | 8  | 6.39  | 8  | 10.13  |                                  |          |               |
|         | Female | 7  | 5.93  | 7  | 9.67   |                                  |          |               |
| 50252   | Male   | 8  | 6.09  | 8  | 10.64  |                                  |          |               |
|         | Female | 9  | 5.71  | 8  | 10.03  |                                  |          |               |
| 50253   | Male   | 5  | 7.02  | 5  | 11.06  |                                  |          |               |
|         | Female | 10 | 6.49  | 10 | 10.08  |                                  |          |               |
| 50254   | Male   | 4  | 7.50  | 4  | 12.33  |                                  |          |               |
|         | Female | 11 | 7.20  | 11 | 12.08  |                                  |          |               |
| 50255   | Male   | 8  | 6.14  | 8  | 10.66  |                                  |          |               |
|         | Female | 5  | 5.74  | 4  | 10.05  |                                  |          |               |
| 50256   | Male   | 6  | 7.22  | 6  | 12.80  |                                  |          |               |
|         | Female | 5  | 6.42  | 5  | 11.14  |                                  |          |               |
| 50257   | Male   | 7  | 5.54  | 6  | 8.90   |                                  |          |               |
|         | Female | 8  | 5.21  | 8  | 8.38   |                                  |          |               |
| 50258   | Male   | 5  | 6.80  | 5  | 11.72  |                                  |          |               |
|         | Female | 8  | 6.55  | 8  | 11.33  |                                  |          |               |
| 50259   | Male   | 4  | 7.25  | 4  | 12.13  |                                  |          |               |
|         | Female | 10 | 6.72  | 10 | 11.21  |                                  |          |               |
| 50260   | Male   | 9  | 6.86  | 9  | 10.90  |                                  |          |               |
|         | Female | 6  | 6.27  | 6  | 10.08  |                                  |          |               |
| 50261   | Male   | 10 | 7.05  | 10 | 10.97  |                                  |          |               |
|         | Female | 8  | 6.84  | 8  | 10.88  |                                  |          |               |
| 50262   | Male   | 6  | 6.82  | 6  | 11.98  |                                  |          |               |
|         | Female | 9  | 6.58  | 9  | 11.42  |                                  |          |               |
| n       | Male   | 80 |       | 79 |        |                                  |          |               |
|         | Female | 96 |       | 94 |        |                                  |          |               |
| Mean    | Male   |    | 6.723 |    | 11.185 |                                  |          |               |
|         | Female |    | 6.305 |    | 10.529 |                                  |          |               |
| S.D.    | Male   |    | 0.573 |    | 1.078  |                                  |          |               |
|         | Female |    | 0.561 |    | 1.002  |                                  |          |               |

Body weight of offspring  
Generation : F0  
/Day after birth

| Dam No. | Sex    | 0  |       | 4  |        | Dose : PTSA Monohydrate 200 mg/kg | Unit : g | Species : Rat |
|---------|--------|----|-------|----|--------|-----------------------------------|----------|---------------|
|         |        | n  | B.W.  | n  | B.W.   |                                   |          |               |
| 50351   | Male   | 6  | 6.45  | 6  | 11.38  |                                   |          |               |
|         | Female | 8  | 5.80  | 8  | 10.16  |                                   |          |               |
| 50352   | Male   | 4  | 7.73  | 4  | 11.58  |                                   |          |               |
|         | Female | 11 | 7.53  | 11 | 11.89  |                                   |          |               |
| 50353   | Male   | 8  | 6.39  | 8  | 10.23  |                                   |          |               |
|         | Female | 6  | 5.82  | 6  | 9.92   |                                   |          |               |
| 50354   | Male   | 9  | 6.63  | 9  | 11.96  |                                   |          |               |
|         | Female | 4  | 6.25  | 4  | 11.68  |                                   |          |               |
| 50355   | Male   | 9  | 6.72  | 9  | 10.67  |                                   |          |               |
|         | Female | 8  | 5.88  | 8  | 9.70   |                                   |          |               |
| 50356   | Male   | 9  | 7.43  | 9  | 11.46  |                                   |          |               |
|         | Female | 5  | 7.00  | 5  | 11.76  |                                   |          |               |
| 50357   | Male   | 6  | 6.45  | 6  | 10.97  |                                   |          |               |
|         | Female | 9  | 6.01  | 9  | 10.07  |                                   |          |               |
| 50358   | Male   | 6  | 6.55  | 6  | 10.80  |                                   |          |               |
|         | Female | 7  | 5.97  | 7  | 10.01  |                                   |          |               |
| 50359   | Male   | 9  | 6.93  | 9  | 10.76  |                                   |          |               |
|         | Female | 7  | 6.47  | 7  | 9.54   |                                   |          |               |
| 50360   | Male   | 10 | 6.34  | 10 | 10.14  |                                   |          |               |
|         | Female | 5  | 6.00  | 5  | 9.92   |                                   |          |               |
| 50361   | Male   | 7  | 5.71  | 7  | 10.60  |                                   |          |               |
|         | Female | 8  | 5.68  | 8  | 10.75  |                                   |          |               |
| 50362   | Male   | 4  | 7.15  | 4  | 12.05  |                                   |          |               |
|         | Female | 7  | 6.47  | 7  | 11.44  |                                   |          |               |
| n       | Male   | 87 |       | 87 |        |                                   |          |               |
|         | Female | 85 |       | 85 |        |                                   |          |               |
| Mean    | Male   |    | 6.707 |    | 11.050 |                                   |          |               |
|         | Female |    | 6.240 |    | 10.570 |                                   |          |               |
| S.D.    | Male   |    | 0.540 |    | 0.631  |                                   |          |               |
|         | Female |    | 0.551 |    | 0.883  |                                   |          |               |

| Body weight of offspring<br>Generation : F0<br>/Day after birth |        |       |        | Dose : PTSA Monohydrate 800 mg/kg | Unit : g | Species : Rat |
|---|--------|-------|--------|-----------------------------------|----------|---------------|
| Dam No.   | Sex    | 0     | 4      |                                   |          |               |
|   |        | n     | B.W.   | n                                 | B.W.     |               |
| 50451   | Male   | 7     | 6.20   | 7                                 | 9.67     |               |
|   | Female | 11    | 6.00   | 11                                | 9.10     |               |
| 50452   | Male   | 8     | 6.69   | 7                                 | 11.00    |               |
|   | Female | 8     | 6.54   | 8                                 | 10.20    |               |
| 50453   | Male   | 3     | 8.50   | 3                                 | 15.23    |               |
|   | Female | 6     | 7.95   | 6                                 | 14.25    |               |
| 50454   | Male   | 9     | 6.00   | 9                                 | 9.98     |               |
|   | Female | 5     | 5.70   | 5                                 | 9.16     |               |
| 50455   | Male   | 11    | 6.70   | 0                                 | -        |               |
|   | Female | 3     | 6.37   | 0                                 | -        |               |
| 50457   | Male   | 8     | 6.38   | 7                                 | 10.91    |               |
|   | Female | 8     | 5.98   | 8                                 | 10.24    |               |
| 50458   | Male   | 6     | 6.57   | 0                                 | -        |               |
|   | Female | 9     | 6.24   | 0                                 | -        |               |
| 50459   | Male   | 8     | 7.01   | 8                                 | 11.45    |               |
|   | Female | 4     | 6.70   | 4                                 | 10.68    |               |
| 50460   | Male   | 4     | 7.53   | 4                                 | 14.30    |               |
|   | Female | 10    | 6.97   | 10                                | 12.41    |               |
| 50461   | Male   | 7     | 6.21   | 7                                 | 10.31    |               |
|   | Female | 9     | 5.86   | 9                                 | 9.83     |               |
| 50462   | Male   | 5     | 6.62   | 5                                 | 12.08    |               |
|   | Female | 8     | 5.96   | 8                                 | 10.26    |               |
| n   | Male   | 76    | 57     |                                   |          |               |
|   | Female | 81    | 69     |                                   |          |               |
| Mean  | Male   | 6.765 | 11.659 |                                   |          |               |
|   | Female | 6.388 | 10.681 |                                   |          |               |
| S.D.  | Male   | 0.713 | 1.922  |                                   |          |               |
|   | Female | 0.646 | 1.653  |                                   |          |               |

Dam No. 50455 : All live pups died on lactation day 3 due to an accident of water leakage

Dam No. 50458 : Died on lactation day 0 and the live pups were euthanized on that day

- : Not applicable

| Necropsy findings of offspring |  |           | Dose : PTSA Monohydrate 0 mg/kg              | Species : Rat                   |
|--------------------------------|--|-----------|--|---------------------------------|
| Generation : F0                | Number of live offspring examined on Day 4 | /Findings |  |                                 |
| Dam No.                        |  |           | Number of dead offspring examined on Day 0-4 | /Findings                       |
| 50151                          | 12   | Absent    | 1  | 1 <sup>a</sup> , Absent (Day 0) |
| 50152                          | 15   | Absent    | 0  |                                 |
| 50153                          | 14   | Absent    | 0  |                                 |
| 50154                          | 13   | Absent    | 0  |                                 |
| 50155                          | 11   | Absent    | 0  |                                 |
| 50156                          | 14   | Absent    | 0  |                                 |
| 50157                          | 9  | Absent    | 0  |                                 |
| 50158                          | 18   | Absent    | 0  |                                 |
| 50159                          | 16   | Absent    | 0  |                                 |
| 50161                          | 16   | Absent    | 0  |                                 |
| 50162                          | 16   | Absent    | 0  |                                 |
| Total                          | 154  |           | 1  |                                 |
| n                              | 11   |           | 1  |                                 |

a : Showed autolysis in abdominal cavity

| Necropsy findings of offspring<br>Generation : F0 |   |           | Dose : PTSA Monohydrate 50 mg/kg                      | Species : Rat  |
|---|---|-----------|---|----------------|
| Dam No.   | Number of<br>live offspring<br>examined<br>on Day 4 | /Findings | Number of<br>dead offspring<br>examined<br>on Day 0-4 | /Findings      |
| 50251   | 15  | Absent    | 2   | Absent (Day 0) |
| 50252   | 16  | Absent    | 0   |                |
| 50253   | 15  | Absent    | 0   |                |
| 50254   | 15  | Absent    | 0   |                |
| 50255   | 12  | Absent    | 0   |                |
| 50256   | 11  | Absent    | 0   |                |
| 50257   | 14  | Absent    | 0   |                |
| 50258   | 13  | Absent    | 0   |                |
| 50259   | 14  | Absent    | 0   |                |
| 50260   | 15  | Absent    | 0   |                |
| 50261   | 18  | Absent    | 0   |                |
| 50262   | 15  | Absent    | 0   |                |
| Total   | 173   |           | 2   |                |
| n   | 12  |           | 1   |                |

| Necropsy findings of offspring<br>Generation : F0 |   |           | Dose : PTSA Monohydrate 200 mg/kg                     | Species : Rat |
|---|---|-----------|---|---------------|
| Dam No.   | Number of<br>live offspring<br>examined<br>on Day 4 | /Findings | Number of<br>dead offspring<br>examined<br>on Day 0-4 | /Findings     |
| 50351   | 14  | Absent    | 0   |               |
| 50352   | 15  | Absent    | 0   |               |
| 50353   | 14  | Absent    | 0   |               |
| 50354   | 13  | Absent    | 0   |               |
| 50355   | 17  | Absent    | 0   |               |
| 50356   | 14  | Absent    | 0   |               |
| 50357   | 15  | Absent    | 0   |               |
| 50358   | 13  | Absent    | 0   |               |
| 50359   | 16  | Absent    | 0   |               |
| 50360   | 15  | Absent    | 0   |               |
| 50361   | 15  | Absent    | 0   |               |
| 50362   | 11  | Absent    | 0   |               |
| Total   | 172   |           | 0   |               |
| n   | 12  |           | 0   |               |

| Necropsy findings of offspring<br>Generation : F0 |   |  | Dose : PTSA Monohydrate 800 mg/kg                     | Species : Rat                                       |
|---|---|--|---|---|
| Dam No.   | Number of<br>live offspring<br>examined<br>on Day 4 | /Findings  | Number of<br>dead offspring<br>examined<br>on Day 0-4 | /Findings   |
| 50451   | 18  | Absent   | 0   |   |
| 50452   | 15  | Absent   | 0   |   |
| 50453   | 9   | Absent   | 0   |   |
| 50454   | 14  | Absent   | 0   |   |
| 50455   | 0\$   |  | 14\$  | 12; Absent (Day 3), 2 <sup>a</sup> ; Absent (Day 3) |
| 50457   | 15  | Absent   | 0   |   |
| 50458   | 0\$   |  | 15\$  | Absent (Day 0)                                      |
| 50459   | 12  | Absent   | 0   |   |
| 50460   | 14  | Absent   | 1   | Absent (Day 0)                                      |
| 50461   | 16  | 1; Kidney, Dilatation, renal pelvis, bilateral, 15; Absent | 0   |   |
| 50462   | 13  | Absent   | 0   |   |
| Total   | 126   |  | 1   |   |
| n   | 9   |  | 1   |   |

a : Showed partial loss of the body because of maternal cannibalism

Dam No. 50455 : All live pups died on postnatal day 3 due to an accident of water leakage

Dam No. 50458 : Died on lactation day 0 and the live pups were euthanized on that day

\$ : Excepted data from calculation



## 試験成績書

2015年08月24日

東京化成工業株式会社 品質保証  
 T103-0023  
 東京都中央区日本橋本町4丁目10  
 TEL: 03(5640)8860 FAX: 03(56)

|  |         |               |         |
|--|---------|---------------|---------|
| 製品名 : p-Toluenesulfonic Acid Monohydrate |         |               |         |
| 製品コード : T0267<br>CAS番号 : 6192-52-5       | 等級 : EP | 製品ロット : JESNN | 判定 : 合格 |

| 項目       | 結果          | 規格値                 |
|----------|-------------|---------------------|
| 純度(HPLC) | 100.0 area% | 98.0 area%以上        |
| 純度(中和滴定) | 100.2 %     | 98.0 ~ 102.0 %(乾燥後) |
| 融点       | 105.0 deg-C | 104.0 ~ 107.0 deg-C |
| 水溶状      | 澄明          | ほとんど澄明以内            |
| 乾燥減量     | 1.0 %       | 3.0 %以下             |

製品ラベルに記載された弊社のロット番号は、半角のアルファベットと数字の組み合わせで4桁又は5桁です。  
 それ以降は、社内管理用の記号となります。

## 報告書

整理 No.A0032

(株)化合物安全性研究所  
試験管理室  
[REDACTED]

2016年2月19日  
東京化成工業株式会社 深谷工場  
分析センター  
〒366-0816 埼玉県深谷市権合 725 番地  
TEL 048-571-3466  
FAX 048-571-1810  
[REDACTED]

TCI 製品

①T0267 4-メチルベンゼン-1-スルホン酸一水和物  
②B0040 1,2,4,5-ベンゼンテトラカルボン酸無水物  
の分析につきましてご報告致します。

## 分析試料

①4-メチルベンゼン-1-スルホン酸一水和物 Lot. JESNN [東京化成工業(株) 製]

## 1. 純度(HPLC)

## (1) 分析条件

カラム : Kaseisorb LC-ODS-Super 4.6mm × 15cm

検出器 : UV(230nm)

移動相 A : アセトニトリル

B : 1.25% TBA-PO4

グラジエント条件：移動相 A : B の割合を 20 : 80 から 20 分で 70 : 30 にして、  
その後 5 分間保つ。

流量 : 1.0ml/min

カラム温度 : 30°C

試料溶液の調製：試料 10mg + 移動相 B 20mL

注入量 : 試料溶液 10 μL

## (2) 結果 (未補正面積百分率) 添付データ 3 枚

①100.00% ②100.00% 平均 100.0%

## 2. 純度(中和滴定)

### (1)操作

試料 0.25g(0.1mg のけたまではかる) → ビーカー100mL にとる + 水 50ml に溶かす → 0.1mol/L 水酸化ナトリウム溶液で JIS K 0113 の 5 (電位差滴定方法)による。

0.1mol/L 水酸化ナトリウム溶液 1ml は 0.019021g に相当する。

### (2)結果

|     | 試料量(g) | 滴定量(mL) | 純度(%)  |
|-----|--------|---------|--------|
| 1回目 | 0.2593 | 13.6183 | 100.29 |
| 2回目 | 0.2520 | 13.2370 | 100.31 |

ファクター = 1.004

平均 100.3%

分析証明書番号：1781

## 安定性試験 分析証明書

被 験 物 質 名 : 4-メチルベンゼン-1-スルホン酸一水和物  
 ロ ッ ト 番 号 : JESNN  
 媒 体 : 日本薬局方精製水  
 調 製 年 月 日 : 2015年11月30日  
 測 定 年 月 日 : 2015年11月30日(調製時)  
                     2015年12月7日(冷蔵保存7日+室温保存4時間)  
 保 存 条 件 : 冷蔵, 遮光, 気密  
 測 定 方 法 : HPLC法  
 試 験 成 績 :

| 調製液<br>表示濃度 | 測定の<br>繰返し数 | 調製液濃度(mg/mL) |                    |
|-------------|-------------|--------------|--------------------|
|             |             | 調製時          | 冷蔵保存7日<br>+室温保存4時間 |
|             | 1           | 5.14         | 5.11               |
|             | 2           | 5.19         | 5.15               |
|             | 3           | 5.13         | 5.17               |
| 5<br>mg/mL  | 平均値         | 5.15         | 5.14               |
|             | 標準偏差        | 0.032        | 0.031              |
|             | 相対標準偏差(%)   | 0.6          | 0.6                |
|             | 含有率(%)      | 103.0        | -                  |
|             | 残存率(%)      | -            | 99.8               |
|             | 1           | 80.5         | 80.1               |
|             | 2           | 80.8         | 80.6               |
|             | 3           | 80.8         | 80.6               |
| 80<br>mg/mL | 平均値         | 80.7         | 80.4               |
|             | 標準偏差        | 0.17         | 0.29               |
|             | 相対標準偏差(%)   | 0.2          | 0.4                |
|             | 含有率(%)      | 100.9        | -                  |
|             | 残存率(%)      | -            | 99.6               |

判 定 基 準 : 調製時；含有率が  $100 \pm 5.0\%$ 、調製液濃度の相対標準偏差が 5.0%以下の場合を適とする。

保存後；残存率が  $100 \pm 10.0\%$ 、調製液濃度の相対標準偏差が 5.0%以下の場合を適とする。

合 否 判 定 : 5 mg/mL および 80 mg/mL の被験物質調製液について冷蔵保存7日+室温保存4時間までの安定性が認められた。

備 考 :

実施試験名 ; 4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験  
(試験番号 ; SR15146)

試験施設 株式会社化合物安全性研究所

化学分析担当者 :

2015年12月7日

化学分析責任者 :

2015年12月7日

分析証明書番号 : 1782

## 濃度確認試験 分析証明書

試験名 : 4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験

試験番号 : SR15146

被験物質名 : 4-メチルベンゼン-1-スルホン酸一水和物

ロット番号 : JESNN

媒体 : 日本薬局方精製水

調製年月日 : 2015年12月8日

分析試験実施時期 : 初回調製時

測定期年月日 : 2015年12月8日

測定方法 : HPLC法

試験成績 :

| 調製液の表示濃度 | 測定の繰返し数 | 調製液濃度(mg/mL) | 平均値<br>±標準偏差     | 相対標準偏差(%) | 含有率(%) |
|----------|---------|--------------|------------------|-----------|--------|
| 5 mg/mL  | 1       | 4.96         | $5.01 \pm 0.042$ | 0.8       | 100.2  |
|          | 2       | 5.04         |                  |           |        |
|          | 3       | 5.02         |                  |           |        |
| 20 mg/mL | 1       | 20.1         | $20.1 \pm 0.10$  | 0.5       | 100.5  |
|          | 2       | 20.2         |                  |           |        |
|          | 3       | 20.0         |                  |           |        |
| 80 mg/mL | 1       | 77.7         | $78.1 \pm 0.47$  | 0.6       | 97.6   |
|          | 2       | 78.6         |                  |           |        |
|          | 3       | 77.9         |                  |           |        |

判定基準 : 含有率が  $100 \pm 5.0\%$ , 調製液濃度の相対標準偏差が 5.0%以下の場合を適とする。

合否判定 : 適

備考 : -

試験施設 株式会社化合物安全性研究所

化学分析担当者 :

2015年12月8日

化学分析責任者 :

2015年12月8日

分析証明書番号：1790

## 濃度確認試験 分析証明書

試験名 : 4-メチルベンゼン-1-スルホン酸一水和物のラットにおける反復投与毒性・生殖発生毒性併合試験

試験番号 : SR15146

被験物質名 : 4-メチルベンゼン-1-スルホン酸一水和物

ロット番号 : JESNN

媒体 : 日本薬局方精製水

調製年月日 : 2016年1月19日

分析試験実施時期 : 最終回調製時

測定年月日 : 2016年1月19日

測定方法 : HPLC 法

試験成績 :

| 調製液の表示濃度 | 測定の繰返し数 | 調製液濃度 (mg/mL) | 平均値 ± 標準偏差       | 相対標準偏差 (%) | 含有率 (%) |
|----------|---------|---------------|------------------|------------|---------|
| 5 mg/mL  | 1       | 4.89          | $4.96 \pm 0.065$ | 1.3        | 99.2    |
|          | 2       | 5.02          |                  |            |         |
|          | 3       | 4.96          |                  |            |         |
| 20 mg/mL | 1       | 19.8          | $19.7 \pm 0.10$  | 0.5        | 98.5    |
|          | 2       | 19.7          |                  |            |         |
|          | 3       | 19.6          |                  |            |         |
| 80 mg/mL | 1       | 78.5          | $77.9 \pm 0.65$  | 0.8        | 97.4    |
|          | 2       | 77.9          |                  |            |         |
|          | 3       | 77.2          |                  |            |         |

判定基準 : 含有率が  $100 \pm 5.0\%$ , 調製液濃度の相対標準偏差が 5.0%以下の場合を適とする。

合否判定 : 適

備考 : -

試験施設 株式会社化合物安全性研究所

化学分析担当者 :

2016 年 1 月 19 日

化学分析責任者 :

2016 年 1 月 19 日

## 調製液（投与液）の濃度分析方法

## 1 使用機器

高速液体クロマトグラフ装置 (HPLC) Waters システム

Alliance セパレーションモジュール : e2695, 日本ウォーターズ株式会社

UV-VIS 検出器 : 2489, 日本ウォーターズ株式会社

または PDA 検出器 : 2998, 日本ウォーターズ株式会社

HPLC データ処理装置 : Empower 3, 日本ウォーターズ株式会社

電子式上皿天秤 : GH-202, 株式会社エー・アンド・ディ

卓上型超音波洗浄器 : B42JH, 日本エマソン株式会社

超純水製造装置 : Milli-Q Gradient A10, 日本ミリポア株式会社

## 2 標準物質

被験物質を使用した（被験物質と同様に保存）。

## 3 試薬

テトラブチルアンモニウムプロミド : 特級, 和光純薬工業株式会社

アセトニトリル : HPLC 用, 関東化学株式会社

超純水 : 蒸留水を超純水製造装置で精製したもの。

## 4 試薬の調製（以下の割合で調製し, 調製日を 0 日として起算した）

## 4.1 移動相

(1) テトラブチルアンモニウムプロミド 1.61 g に超純水を加えて溶解し, 700 mL とした。

(2) (1)の溶液にアセトニトリル 300 mL を加えて十分に混合した後, 卓上型超音波洗浄器（超音波洗浄機）を用いて約 1 分間脱気した。

(3) 調製後は室温に保存し, 10 日以内に使用した。

## 4.2 オートサンプラ洗浄液, 洗浄用注入液, 希釀液

(1) 超純水 700 mL とアセトニトリル 300 mL を十分に混合した。

(2) 調製後は室温に保存し, 11 日以内に使用した。

## 5 標準溶液の調製および測定 (以下の割合で調製)

- (1) 標準物質約 0.02 g を精密に量り、希釈液を加えて溶解し、正確に 20 mL とした (標準原液 1, SS1, 1000 µg/mL).
- (2) 標準原液 1 の 1 mL を採取し、希釈液を加えて正確に 10 mL とした (標準原液 2, SS2, 100 µg/mL).
- (3) 下表に従い標準溶液 (STD1 ~ STD3) を調製した.

| 調製濃度     | 略号   | 調製方法 (以下の割合で調製) |      |   |           |
|----------|------|-----------------|------|---|-----------|
| 20 µg/mL | STD1 | SS2             | 2 mL | → | 希釈液 10 mL |
| 10 µg/mL | STD2 | SS2             | 1 mL | → | 希釈液 10 mL |
| 1 µg/mL  | STD3 | STD2            | 1 mL | → | 希釈液 10 mL |

- (4) 各標準溶液はオートサンプラー内保存後 4 時間以内に測定した.

## 6 試料溶液の調製および測定 (以下の割合で調製)

調製液の採取は、中層付近から 3 点とした。試料溶液の調製は 1 点につき n=1 で調製し、オートサンプラー内保存後 5 時間以内に測定した。

### 6.1 試料溶液 (5 mg/mL 調製液)

- (1) 5 mg/mL 調製液から 1 mL を採取し、希釈液を加えて正確に 25 mL とした.
- (2) (1)の溶液 1 mL を採取し、希釈液を加えて正確に 20 mL とした (10 µg/mL) .

### 6.2 試料溶液 (20 mg/mL 調製液)

- (1) 20 mg/mL 調製液から 1 mL を採取し、希釈液を加えて正確に 50 mL とした.
- (2) (1)の溶液 1 mL を採取し、希釈液を加えて正確に 40 mL とした (10 µg/mL) .

### 6.3 試料溶液 (80 mg/mL 調製液)

- (1) 80 mg/mL 調製液から 1 mL を採取し、希釈液を加えて正確に 40 mL とした.
- (2) (1)の溶液 1 mL を採取し、希釈液を加えて正確に 20 mL とした.
- (3) (2)の溶液 1 mL を採取し、希釈液を加えて正確に 10 mL とした (10 µg/mL) .

## 7 HPLC 条件

カラム : CAPCELL PAK UG120 phenyl, 5 µm, 4.6 mmID × 250 mm, 株式会社資生堂

移動相 : 5 mmol/L テトラブチルアンモニウム含有 30%アセトニトリル

オートサンプラー洗浄液 : 30%アセトニトリル

洗浄用注入液 : 30%アセトニトリル

流量 : 1.0 mL/min

測定波長 : 222 nm  
 カラム温度 : 30°C  
 注入量 : 10 µL  
 オートサンプラー温度 : 10°C  
 分析時間 : 15 分

#### 8 システム適合性試験

測定日ごとに 10 µg/mL 標準溶液 (STD2) を繰り返し 6 回注入した。4-メチルベンゼン-1-スルホン酸のピーク面積および保持時間について平均値、標準偏差、相対標準偏差を求めた。

#### 9 計算

Microsoft Office Excel を用いて、標準溶液の 4-メチルベンゼン-1-スルホン酸のピーク面積および濃度から検量線 ( $Y = aX + b$ ;  $a$  : 傾き,  $b$  :  $y$ -切片,  $Y$  : ピーク面積,  $X$  : 濃度) を作成し、相関係数を求めた。以下の式より個々の調製液濃度を求め、さらに調製液濃度の平均値、標準偏差、相対標準偏差を求めた。また、濃度確認試験および安定性試験(調製時)では含有率、安定性試験(保存後)では残存率を求めた。

$$\text{調製液濃度 (mg/mL)} = [A_t - (\text{y-切片})] / \text{傾き} \times D / 1000$$

$A_t$  : 試料溶液の 4-メチルベンゼン-1-スルホン酸のピーク面積

$D$  : 希釀倍数

[5 mg/mL 調製液 ; 500, 20 mg/mL 調製液 ; 2000, 80 mg/mL 調製液 ; 8000]

$$\text{含有率 (\%)} = (\text{調製液濃度平均値} / \text{調製液の表示濃度}) \times 100$$

$$\text{残存率 (\%)} = (\text{保存後の調製液濃度平均値} / \text{調製時の調製液濃度平均値}) \times 100$$

$$\text{相対標準偏差 (\%)} = (\text{標準偏差} / \text{平均値}) \times 100$$

#### 10 数値の取扱い

四捨五入して以下の表示値とした。平均値、標準偏差および相対標準偏差を求める場合は四捨五入し、平均値は下記と同じ桁数、標準偏差は平均値の 1 つ下の桁、相対標準偏差は小数点以下第 1 位を表示した。

| 項目 (単位)      | 表示値        |
|--------------|------------|
| 秤量値 (g)      | 小数点以下第 5 位 |
| 保持時間 (分)     | 小数点以下第 3 位 |
| ピーク面積 (µV 秒) | 整数         |
| 検量線 [相関係数]   | 有効数字 6 桁   |

|  |                                   |
|--|-----------------------------------|
| 検量線 [傾き, y-切片]   | 小数点以下第 3 位                        |
| 標準溶液濃度, 試料溶液濃度,<br>調製液濃度 ( $\mu\text{g/mL}$ または $\text{mg/mL}$ ) | 有効数字 3 桁<br>(標準溶液濃度は標準物質の秤量値より算出) |
| 含有率 (%)  | 小数点以下第 1 位                        |
| 残存率 (%)  | 小数点以下第 1 位                        |

## 11 判定基準

- (1) 検量線 : 相関係数が 0.990 以上を採用とした.
- (2) 安定性試験 :
  - 1) 調製時 ; 含有率が  $100 \pm 5.0\%$ , 調製液濃度の相対標準偏差が 5.0%以下の場合を適とした.
  - 2) 保存後 ; 残存率が  $100 \pm 10.0\%$ , 調製液濃度の相対標準偏差が 5.0%以下の場合を適とした.
- (3) 濃度確認試験 : 含有率が  $100 \pm 5.0\%$ , 調製液濃度の相対標準偏差が 5.0%以下の場合を適とした.
- (4) システム適合性試験 : 4-メチルベンゼン-1-スルホン酸のピーク面積と保持時間の相対標準偏差が共に 2.0%以下の場合を適とした. 本試験では, ピーク面積における相対標準偏差が 0.3~0.9%, 保持時間における相対標準偏差が 0.1~0.2%でありいずれも判定基準内であった.