

## 最終報告書

表　題： $\alpha$ -ヒドロキシイソラク酸メチル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：SR17144

株式会社化合物安全性研究所

試験責任者の署名

表題：α-ヒドロキシイソラク酸メチル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：SR17144

株式会社化合物安全性研究所

試験責任者

2018年3月22日

## 陳述書

表題：α-ヒドロキシイソラク酸メチル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：SR17144

本試験は、GLP基準「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)を遵守して実施した。

本試験に用いた試験方法は、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27年12月21日薬生発1221第1号・20151209製局第1号・環保企発第1512211号 厚生労働省医薬・生活衛生局長・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)に準拠した。

株式会社化合物安全性研究所

試験責任者

2018年3月22日

## 信頼性保証書

表題 : α-ヒドロキシソラク酸メチル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 : SR17144

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 への報告日	運営管理者 への報告日
試験計画書	2017年9月4日	2017年9月4日	2017年9月4日
コンピュータプロトコール	2017年9月25日	2017年9月25日	2017年9月25日
被験物質の管理	2017年10月3日	2017年10月3日	2017年10月3日
投与液の調製	2017年10月3日	2017年10月3日	2017年10月3日
投与	2017年10月10日	2017年10月10日	2017年10月10日
性周期検査	2017年10月10日	2017年10月10日	2017年10月10日
詳細な状態観察	2017年10月16日	2017年10月16日	2017年10月16日
被験物質のサンプリング	2017年10月18日	2017年10月18日	2017年10月18日
生殖能検査(交配)	2017年10月23日 2017年10月24日	2017年10月24日	2017年10月24日
尿検査	2017年10月31日 2017年11月1日	2017年11月1日	2017年11月1日
機能検査	2017年11月2日	2017年11月2日	2017年11月2日
採血	2017年11月7日	2017年11月7日	2017年11月7日
血液学的検査	2017年11月7日	2017年11月7日	2017年11月7日
血液化学的検査	2017年11月7日	2017年11月7日	2017年11月7日
剖検・器官重量測定	2017年11月7日	2017年11月7日	2017年11月7日
分娩および哺育状態観察	2017年11月15日	2017年11月15日	2017年11月15日
新生児の一般状態観察	2017年11月15日	2017年11月15日	2017年11月15日
新生児の体重測定	2017年11月15日	2017年11月15日	2017年11月15日
病理組織学的検査(標本作製)	2017年11月8日 2017年11月10日 2017年11月16日	2017年11月16日	2017年11月16日
新生児の剖検	2017年11月20日	2017年11月20日	2017年11月20日
試験計画書変更書(No.1)	2017年12月13日	2017年12月13日	2017年12月13日
試験計画書変更書(No.1)*	2017年12月14日	2017年12月14日	2017年12月14日
コンピュータプロトコール	2017年12月14日	2017年12月14日	2017年12月14日
試験計画書変更書(No.2)	2018年1月9日	2018年1月9日	2018年1月9日
病理組織学的検査(鏡検)	2018年1月18日	2018年1月18日	2018年1月18日

査察段階	査察日	試験責任者 への報告日	運営管理者 への報告日
生データ	2018年 2月 26 日 2018年 2月 27 日 2018年 2月 28 日 2018年 3月 1 日	2018年 3月 1 日	2018年 3月 1 日
最終報告書(草案)：図表	2018年 2月 26 日 2018年 2月 27 日 2018年 2月 28 日 2018年 3月 1 日	2018年 3月 1 日	2018年 3月 1 日
最終報告書(草案)：本文	2018年 2月 27 日 2018年 2月 28 日 2018年 3月 1 日	2018年 3月 1 日	2018年 3月 1 日
最終報告書	2018年 3月 22 日	2018年 3月 22 日	2018年 3月 22 日

\* : 改善内容の確認

プロセス調査による査察段階	査察日	試験責任者 への報告日	運営管理者 への報告日
動物受入・検疫・馴化	2017年 9月 4 日	2017年 9月 4 日	2017年 9月 4 日
群分け	2017年 9月 4 日	2017年 9月 4 日	2017年 9月 4 日
一般状態観察	2017年 9月 4 日	2017年 9月 4 日	2017年 9月 4 日
体重測定	2017年 9月 4 日	2017年 9月 4 日	2017年 9月 4 日
摂餌量測定	2017年 9月 4 日	2017年 9月 4 日	2017年 9月 4 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

\_\_\_\_\_ [REDACTED] \_\_\_\_\_ 2018年 3月 22日

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## 表題

$\alpha$ -ヒドロキシイソラク酸メチル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

SR17144

## 試験目的

$\alpha$ -ヒドロキシイソラク酸メチル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 27 年 12 月 21 日 薬生発 1221 第 1 号・20151209 製局第 1 号・環保企発第 1512211 号 厚生労働省医薬・生活衛生局長・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、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により審議され、運営管理者の承認を得ており、  
試験施設の動物実験倫理規程に準拠して実施した。

#### 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 : 医薬品審査管理課 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

被験物質の調製 : [REDACTED]  
動物管理 : [REDACTED]  
検疫・馴化 : [REDACTED]  
投与・観察・測定 : [REDACTED]  
臨床検査 : [REDACTED]  
病理検査 : [REDACTED]

## 試験日程

試験開始日 : 2017年 9月 4日  
動物受入 : 2017年 9月 27日  
群分け : 2017年 10月 9日  
実験開始日 : 2017年 10月 10日  
投与開始 : 2017年 10月 10日  
交配開始 : 2017年 10月 23日  
雄動物およびサテライト群雌動物投与終了  
: 2017年 11月 6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  
: 2017年 11月 7日  
新生児剖検開始 : 2017年 11月 19日  
母動物剖検開始 : 2017年 11月 20日  
サテライト群雄および雌動物(回復終了時剖検例)剖検  
: 2017年 11月 21日  
実験終了日 : 2018年 2月 20日  
試験終了日 : 2018年 3月 22日

## 1 要約

$\alpha$ -ヒドロキシイソラク酸メチルの0(溶媒対照, 精製水), 100, 300および1000 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1000 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匹の非交配群を別に設け, 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

100および300 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.

1000 mg/kg群では, 投与期間中に, 雌雄に赤色尿が観察された. 尿検査では, 雄でpHの低値と尿量の高値, 非交配群の雌でpHの低値がみられた. さらに, 泌尿器系の病理組織学的検査では, 雄および主試験群の雌で, 膀胱に炎症性の変化(尿路上皮過形成, 炎症性細胞浸潤, 粘膜固有層の水腫)の発現とそれらの頻度の増加が認められ, いずれも被験物質投与に関連する変化と考えられた. 器官重量では, 主試験群の雌で胸腺の低値がみられたが, 病理組織学的異常は認められなかった.

以上の変化は, 回復2日以降および回復期間終了時の検査では認められず, 回復性を示した. したがって, 本試験条件下における $\alpha$ -ヒドロキシイソラク酸メチル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300 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, 1000 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 $\alpha$ -ヒドロキシイソラク酸メチル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1000 mg/kg/dayと考えられた.

## 2 緒言

$\alpha$ -ヒドロキシイソラク酸メチルの0(溶媒対照, 精製水), 100, 300および1000 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1000 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匹の非交配群を別に設け, 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	: $\alpha$ -ヒドロキシイソラク酸メチル
別名	: 2-ヒドロキシイソ酪酸メチル <sup>1)</sup> Methyl 2-Hydroxyisobutyrate <sup>1),2)</sup> Methyl 2-hydroxy-2-methylpropionate <sup>2)</sup>
略称 <sup>2)</sup>	: HBM
CAS番号	: 2110-78-3
官報公示整理番号(化審法) <sup>1)</sup>	: (2)-1404, (2)-1430
構造式 <sup>3)</sup>	:
化学式 <sup>1)</sup>	: C <sub>5</sub> H <sub>10</sub> O <sub>3</sub>
分子量 <sup>3)</sup>	: 118.13
物理化学的性質 <sup>1)</sup>	: 外観; 透明液体, 無色 ~ ほとんど無色 沸点/沸騰範囲; 137°C 引火点; 45°C 比重; 1.03
ロット番号	: H3XDK
純度	: 99.9% (GC) (Annex 1)
製造業者	: [REDACTED]
被験物質管理責任者からの移管量	: 1000 g
使用量	: 718.2189 g

試験施設受領日	: 2017 年 6 月 26 日
安定性	: 試験操作終了後、株式会社日曹分析センターにて安定性分析を実施した。その結果、投与期間中被験物質は安定であったことが確認された(Annex 2)。
保存条件	: 冷蔵 (実測範囲 5.5 ~ 7.5°C), 気密, 遮光
保存場所および保存期間	: 被験物質保存室 ; 2017 年 6 月 26 日 (試験施設受領) ~ 2017 年 11 月 15 日 (最終調製)
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。被験物質を分取する場合は、ガラス製の器具を用い、ガラス容器に分取した。
サンプリング	: 約 5 g (実測値 5.0098 g) を採取し、試験施設の資料保存室に保存した。

### 3.2 対照物質 (媒体)

名称	: 精製水 (日本薬局方精製水)
ロット番号	: C01700
製造者	: 日医工株式会社
被験物質管理責任者からの移管量	: 20 L
保存場所および保存期間	: 被験物質保存室 ; 2017 年 8 月 24 日 (試験施設受領) ~ 2017 年 11 月 15 日 (最終分注)
保存条件	: 室温 (実測範囲 20.9 ~ 23.2°C) で保存した。ただし、開封後の残余は保存しなかった。 対照群の投与用として分注後は、被験物質調製液と同様に保存した。
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た。所定の濃度となるように媒体(対照物質)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	: 調製液は 5 ~ 9 日の間隔で調製し、9 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 ; 2017 年 10 月 3 日 (初回調製) ~ 2017 年 11 月 24 日 (最終投与)
保存条件	: ガラス製の遮光気密容器に入れ、冷蔵 (実測範囲 5.7 ~ 7.0°C) で保存した。
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、ゴム手袋、保護メガネ等を着用し、吸入、眼、皮膚および衣類等との接触を

- 避けた。調製および分取の際は、ガラス製の器具を使用した。
- 残余投与液の処置 : 焚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 : 10 および 200 mg/mL の濃度の調製液について、冷蔵保存 9 日 + 室温保存 1 日 (調製日を 0 日として起算) の安定性を確認した。調製および安定性の分析は株式会社日曹分析センターが実施し、分析結果を入手した。分析の結果、冷蔵保存 9 日 + 室温保存 1 日の安定性が確認された (Annex 2)。
- 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、初回および雄の最終回投与に使用する調製液について確認した。投与液の濃度分析は株式会社日曹分析センターが実施し、分析結果を入手した。分析の結果、いずれの濃度も適切であることが確認された (Annex 2)。

### 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試験施設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 261 ~ 295 g、雌 175 ~ 215 g
- 投与開始時週齢 : 雌雄とも 9 週齢 (6 項参照)
- 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。  
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、雌の 1 例（受入時動物番号 5036）に体重減少がみられた以外に、異常は認められなかつた。

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、1 例（受入時動物番号 5050）に性周期異常がみられた以外に、異常は認められなかつた。

### 3.6 群分け

馴化期間中に実施した一般状態観察、体重測定および雌の性周期検査の結果を参考にして、動物の使用の適否を決定した。群分けは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、馴化期間中に異常がみられた雌 2 例を除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行った。ただし、雌については主試験群、サテライト群それぞれの平均体重が均一になるようにした。選抜した動物の体重範囲は、雄で 340 ~ 405 g、雌で 206 ~ 272 g であり、平均体重（雄 373.0 g、雌 237.0 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、試験施設の標準操作手順書に従って取り扱つた。

### 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、個体識別を行つた。  
群分け後は耳介に動物番号を入れ墨し、個体識別を行つた。

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。  
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 日の日付ならびに哺育 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 : 302 号室

温度・湿度 : 22 ± 3°C (実測範囲 20 ~ 24°C), 50 ± 20% (実測範囲 43 ~ 56%)

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)

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 (ホワイトフレーク, 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 : 170413, 170623, 170822

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。  
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-17-JP-004218-01-JA, AR-17-JP-004984-01-JA, AR-17-JP-005599-01-JA) および飼料製

造業者（分析試験報告書：No. 17G03-050, 17G03-077, 17G03-101）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試験施設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、2017年7月4日および2018年1月5日に当該飼育室の配管の最末端（301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. A291241, A295124）が行い、分析データを入手した。分析項目と許容値は試験施設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), 100, 300 および 1000 mg/kg/day
設定理由	: 先に実施した予備試験（SR17143） <sup>4)</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 群の用量まで、一般状態、体重、摂餌量、血液学的検査、血液化学的検査、剖検および器官重量のいずれの項目にも、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。以上より、本試験では、1000 mg/kg/day を高用量とし、以下公比約 3 として 300 および 100 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 (mg/kg)	濃度 (mg/mL)	投与容量 (mL/kg)	動物数(動物番号)		識別
				雄	雌	
<主試験群>						
対照	0	0	5.0	12 (10101~10112)	12 (50151~50162)	白
低用量	100	20	5.0	12 (10201~10212)	12 (50251~50262)	緑
中用量	300	60	5.0	12 (10301~10312)	12 (50351~50362)	青

高用量	1000	200	5.0	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	5.0		5 (50551~50555) <sup>b</sup>	白
(回復終了時剖検例)	0	0	5.0	5 (10103, 10104, 10105, 10109, 10111) <sup>a</sup>	5 (50556~50560) <sup>b</sup>	白
高用量 (投与終了時剖検例)	1000	200	5.0		5 (50651~50655) <sup>b</sup>	赤
(回復終了時剖検例)	1000	200	5.0	5 (10403, 10407, 10408, 10411, 10412) <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対照物質（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。

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ガラス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 : 9:00 ~ 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、分娩遅延例（妊娠 25 日まで分娩が認められない交尾成立例）は妊娠 25 日までの期間

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。雌動物の交配後は、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.

#### 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 24 日) に実施した. 投与 4 週の検査の結果, 雄で自発運動量に有意な高値がみられたため, 回復 2 週 (回復 8 日) の検査は雄のみ実施した. 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) にも測定した.
- 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 ;  

$$\text{体重増加量 (g)} = \text{投与 28 日体重 (g)} - \text{投与 1 日体重 (g)}$$
 回復期間 ;  

$$\text{体重増加量 (g)} = \text{回復 14 日体重 (g)} - \text{回復 1 日体重 (g)}$$
<主試験群の雌>  
 妊娠前投与期間 ;  

$$\text{体重増加量 (g)} = \text{妊娠 20 日体重 (g)} - \text{妊娠 0 日体重 (g)}$$
 妊娠期間 ;  

$$\text{体重増加量 (g)} = \text{妊娠 20 日体重 (g)} - \text{妊娠 0 日体重 (g)}$$
 哺育期間 ;  

$$\text{体重増加量 (g)} = \text{哺育 4 日体重 (g)} - \text{哺育 0 日体重 (g)}$$

### 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] の沈渣については、遠心分離 (約  $400 \times g$ , 5 分,  $4^{\circ}\text{C}$ ) した後に検査を行った。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, 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) でラットをイソフルラン麻酔し, 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 1 mL 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 1 mL (3.8% クエン酸ナトリウム溶液 0.1 mL+血液 0.9 mL) を遠心分離 (約 2000 × g, 10 分, 4°C) し, 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 <sup>3</sup> /μL)	
2 好酸球 (Eosinophil, 10 <sup>3</sup> /μL)	
3 好塩基球 (Basophil, 10 <sup>3</sup> /μL)	
4 単球 (Monocyte, 10 <sup>3</sup> /μL)	
5 リンパ球 (Lymphocyte, 10 <sup>3</sup> /μL)	
[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) でラットをイソフルラン麻酔し、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、遠心分離 (約 2000 × g, 10 分, 4°C) して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、遠心分離 (約 2000 × g, 10 分, 4°C) して得られた血清を用いて検査した。主試験群の雌の血清および血漿は、採取後凍結保存 (-80°C 設定) し、測定直前に融解して用いた。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 μL 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つたため、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]	γ-GTP	L-γ-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)	OCPD 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)	アガロースゲル電気泳動法
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] 全自動電気泳動分析装置エパライザ 2 ジュニア, 株式会社ヘレナ研究所

### 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, 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 日に実施した.
検査方法	: 体外表を観察し, イソフルラン麻酔下で, 血液検査実施例については腹部大動脈より採血後, 放血により安楽死させ, 全身の器官・組織を肉眼的に観察した. 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. 眼球およびハーダー腺はデビッドソン液で固定・保存し, 精巣および精巣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. 主試験群の雌では, 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 (大脑, 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, 脾臓, 顎下腺, 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, 精巣, 精巣上体, 前立腺, 精囊 (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 (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 : 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・ディ) を用いて、以下の器官の重量を測定した。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, 精巣, 精巣上体, 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。高用量群の主試験群の雌において、肉眼的病変が胃にみられたため、主試験群の雌の低用量群および中用量群のすべての動物の胃の病理組織学的検査を追加実施した。さらに、病理組織学的検査の結果、雄および主試験群の雌の膀胱に異常がみられたため、雄および主試験群の雌の低用量群および中用量群、ならびに雄の回復群のすべての動物の膀胱の病理組織学的検査を追加実施した。また、中用量群において、剖検時にみられた肉眼的異常部位 (動物番号 10311 の精巣上体、動物番号 50361 の胃) についても鏡検した。
- 検査方法 : パラフィン包埋後薄切り、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. 同居開始後 5 日までに全例の交尾が確認された.
- 交配組み合せ : 同一群の雌雄を, 雌の動物番号末尾 2 桁が雄の動物番号末尾 2 桁に 50 を足したものとなるよう組み合わせた.
- 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. 動物番号 50358 については, 剖検時に子宮内の着床痕が確認されなかっ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.  
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、0.1 g 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。
- 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の過剰投与 (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。黄体数, 着床率ならびに生後 0 日および 4 日の生存率については, 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については, Fisher の正確確率検定法を用いた。哺育率および病理組織学的

検査（主試験群およびサテライト群）については、別途 SAS システムを用いて上記と同様の検定を実施した。なお、雄の中用量群における肉眼的異常がみられた精巣上体の病理組織学的所見については、検査例数が 1 例のみであることから、検定は実施しなかった。

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 検定による等分散性の解析を行った。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。

主試験群の雌で不妊が確認された動物については、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。

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（A/G 比、蛋白分画を除く）、器官重量、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）、血液化学的検査（A/G 比、蛋白分画）、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。

## 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 ~ 1-7, Appendix 1-1 ~ 1-28 に示す。

[投与期間]

(1) 雄：主試験群

対照群、100 および 300 mg/kg 群では、いずれの動物にも異常は認められなかった。1000 mg/kg

群では、投与 22, 23 および 24 日に同一の 1 例に赤色尿がみられた。その他の動物では、異常は認められなかった。

(2) 雌：主試験群

対照群、100 および 300 mg/kg 群では、いずれの動物にも異常は認められなかった。1000 mg/kg 群では、投与 2, 3 および 4 日に同一の 1 例に赤色尿がみられた。その他の動物では、異常は認められなかった。

(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。1000 mg/kg 群では、投与 28 日に 1 例に赤色尿がみられた。

[回復期間]

(1) 雄：サテライト群

対照群および 1000 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）

対照群の動物には異常は認められなかった。1000 mg/kg 群では、回復 1 日（投与 28 日の翌日）に、投与 28 日に赤色尿がみられた動物と同じ動物に赤色尿がみられた。回復 2 日以降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

100 および 1000 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。300 mg/kg 群では、投与 21 日の検査での排糞に有意な高値がみられたが、高用量群では変化がみられないことから、被験物質投与との関連はないと考えられた。

(2) 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。

(3) 雌：サテライト群（非交配群）

1000 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

1000 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）

1000 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 ~ 5-4, Appendix 5-1 ~ 5-12, 握力の成績を Table 6-1 ~ 6-4, Appendix 6-1 ~ 6-12, 自発運動量の成績を Table 7-1 ~ 7-4, Appendix 7-1 ~ 7-12 に示す。

##### [投与期間]

###### (1) 雄：主試験群（投与 4 週）

100 および 300 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。1000 mg/kg 群では、自発運動量の 0-10 分の間に有意な高値がみられたが、0-60 分には有意な差は認められなかつたことから偶発的な変動と考えられた。同群のその他の項目には変化は認められなかつた。

###### (2) 雌：主試験群（哺育 4 日）

いずれの検査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つた。

###### (3) 雌：サテライト群（非交配群、投与 4 週）

1000 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。

##### [回復期間]

###### (1) 雄：サテライト群

1000 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。

#### 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

いずれの被験物質投与群においても、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つた。

###### (2) 雌：主試験群

いずれの被験物質投与群においても、交配前期間、妊娠期間および哺育期間の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つた。

###### (3) 雌：サテライト群（非交配群）

1000 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つた。

##### [回復期間]

###### (1) 雄：サテライト群

1000 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つた。

###### (2) 雌：サテライト群（非交配群）

1000 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

いずれの被験物質投与群においても、摂餌量に対照群と比較して有意な差は認められなかつた。

(2) 雌：主試験群

いずれの被験物質投与群においても、交配前期間、妊娠期間および哺育期間の摂餌量に、対照群と比較して有意な差は認められなかつた。

(3) 雌：サテライト群（非交配群）

1000 mg/kg 群では、摂餌量に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]

(1) 雄：サテライト群

1000 mg/kg 群では、摂餌量に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）

1000 mg/kg 群では、摂餌量に対照群と比較して有意な差は認められなかつた。

#### 4.1.6 尿検査

尿検査の成績を Table 10-1 ~ 10-21, Appendix 10-1 ~ 10-30 に示す。

##### [投与 4 週]

(1) 雄：主試験群

100 および 300 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。1000 mg/kg 群では、pH に有意な低値、尿量に有意な高値がみられた。

(2) 雌：サテライト群（非交配群）

1000 mg/kg 群では、pH に对照群と比較して有意な低値がみられた。

##### [回復 2 週]

(1) 雄：サテライト群

1000 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。

(2) 雌：サテライト群（非交配群）

1000 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。

#### 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

100 および 1000 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。300 mg/kg 群では、網赤血球数に有意な高値がみられたが、高用量群では変化がみられないことから、被験物質投与との関連はないと考えられた。

###### (2) 雌：主試験群

100 mg/kg 群では、MCV に対照群と比較して有意な低値がみられたが、300 mg/kg 群では差はみられないことから、被験物質投与との関連はないと考えられた。300 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。1000 mg/kg 群では、MCV に有意な低値がみられたが、他の関連する項目 (RBC, HGB, HCT, MCH および MCHC) に変化が認められないことから、毒性学的意義のない変化と考えられた。

###### (3) 雌：サテライト群 (非交配群)

1000 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。

##### [回復期間終了時]

###### (1) 雄：サテライト群

1000 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)

1000 mg/kg 群では、MCV, MCH および MCHC に対照群と比較して有意な高値がみられた。しかし、投与期間終了時にはみられない変化であり、いずれの項目も、個々の値は試験施設の背景データ (平均値  $\pm$  2SD: MCV, MCH および MCHC でそれぞれ 47.12 ~ 56.00 fL, 17.11 ~ 19.67 pg, 34.57 ~ 36.81 g/dL, 例数 : 40, 試験期間 : 2013 ~ 2017 年)<sup>5)</sup> の範囲内であることから、被験物質投与との関連はないと考えられた。

#### 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

100 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。300 および 1000 mg/kg 群では、 $\alpha$ 1-グロブリン分画に有意な低値がみられたが、個々の値は試験施設の背景データ (平均値  $\pm$  2SD : 16.75 ~ 26.11%, 例数 : 20, 試験期間 : 2013 ~ 2017 年)<sup>5)</sup> の範囲内であり、他の蛋白分画あるいは AG 比に変化がみられないことから、毒性学的意義はない

と考えられた。

(2) 雌：主試験群

100 および 1000 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。300 mg/kg 群では、 $\gamma$ -GTP に有意な高値がみられたが、高用量群では変化がみられないことから、被験物質投与との関連はないと考えられた。

(3) 雌：サテライト群（非交配群）

1000 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。

[回復期間終了時]

(1) 雄：サテライト群

1000 mg/kg 群では、対照群と比較してナトリウムに有意な高値がみられたが、個々の値は試験施設の背景データ（平均値  $\pm$  2SD : 141.6 ~ 147.6 mEq/L, 例数 : 45, 試験期間 : 2013 ~ 2017 年）<sup>5)</sup> の範囲内であることから、被験物質投与と関連しない変化と考えられた。その他の検査項目には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）

1000 mg/kg 群では、対照群と比較して  $\gamma$ -GTP に有意な高値がみられたが、個々の値は試験施設の背景データ（平均値  $\pm$  2SD : 0.04 ~ 1.24 IU/L, 例数 : 40, 試験期間 : 2013 ~ 2017 年）<sup>5)</sup> の範囲内であることから、被験物質投与と関連しない変化と考えられた。その他の検査項目には有意な差は認められなかった。

#### 4.1.9 病理検査

##### 4.1.9.1 剖検

剖検所見を Table 13-1 ~ 13-6, Appendix 13-1 ~ 13-14 に示す。

[投与期間終了時]

(1) 雄：主試験群

対照群、100 および 1000 mg/kg 群では、異常所見は認められなかった。300 mg/kg 群では、精巣上体尾部黄白色巣が 1 例に認められた。

(2) 雌：主試験群

対照群および 100 mg/kg 群では、異常所見は認められなかった。300 および 1000 mg/kg 群では、腺胃粘膜の黒色巣が、それぞれ 1 例および 2 例に認められた。

(3) 雌：サテライト群（非交配群）

対照群および 1000 mg/kg 群ともに異常所見は認められなかった。

[回復期間終了時]

(1) 雄：サテライト群

対照群および 1000 mg/kg 群と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 1000 mg/kg 群と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

100 および 300 mg/kg 群では、測定したいずれの器官にも対照群と比較して有意な差は認められなかった。1000 mg/kg 群では、腎臓の相対重量の有意な高値、胸腺の絶対および相対重量に有意な低値がみられた。その他の器官には、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）

1000 mg/kg 群では、下垂体の絶対および相対重量に对照群と比較して有意な低値がみられた。

##### [回復期間終了時]

(1) 雄：サテライト群

1000 mg/kg 群では、心臓の相対重量ならびに脳の絶対および相対重量に对照群と比較して高値がみられ、脾臓の相対重量に低値がみられた。しかし、これらは投与期間終了時には認められない変化であることと、個々の値はいずれも試験施設の背景データ（平均値 ± 2SD：脳の絶対および相対重量ならびに脾臓の相対重量でそれぞれ 2.030 ~ 2.366 g および 0.393 ~ 0.509 g/100gBW ならびに 116.874 ~ 193.970 mg/100gBW, 例数：56, 試験期間：2013 ~ 2017 年)<sup>6)</sup> の範囲内であることから、被験物質投与と関連しない変化と考えられた。

(2) 雌：サテライト群（非交配群）

1000 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 ~ 15-14, Appendix 15-1 ~ 15-22 に示す。

##### [投与期間終了時]

(1) 雄：主試験群

100 および 300 mg/kg 群の膀胱では、異常は認められなかった。300 mg/kg 群において肉眼的異常がみられた 1 例の精巣上体では、その所見に対応して精子肉芽腫（軽微）がみられた。

1000 mg/kg 群では、膀胱に尿路上皮過形成（軽微）が 3 例にみられ、統計学的に有意な差ではなかったが発現頻度の増加が認められた。

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萎縮（軽微）、肝臓に小肉芽腫（軽微）、心臓に限局性炎症（軽微）、前立腺に間質の炎症（軽微）、下垂体に頭蓋咽頭管遺残（軽微）、眼球に限局性網膜異形成（軽微）が散見された。しかし、これらは 1 例のみの発現あるいは対照群または試験施設の背景データ<sup>7)</sup>に認められる所見であり、発現頻度の増加も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。

対照群のみの所見として、肺に肺動脈限局性鉱質沈着（軽微）、腎臓に尿細管の好塩基性化（軽微）、下垂体に前葉囊胞（軽微）、甲状腺に鰓後体遺残（軽微）が 1 または 2 例にみられた。

#### (2) 雌：主試験群

100 mg/kg 群の胃および膀胱では、異常は認められなかった。

300 mg/kg 群の胃では、腺胃に肉眼所見に対応して、限局性びらん（軽微）が 1 例にみられた。膀胱では、異常は認められなかった。

1000 mg/kg 群では、膀胱に尿路上皮過形成（軽微）および炎症性細胞浸潤（軽微）が各 6 例に認められ、それらの発現頻度は統計学的に有意に高かった。これらに関連する所見として粘膜固有層の水腫（軽微）が 4 例にみられた。腺胃では肉眼所見に対応して、限局性びらん（軽微）が 2 例にみられた以外に異常は認められなかった。

その他に、肺に肺胞内マクロファージ集簇（軽微）、心臓に限局性炎症（軽微）、腎臓に鉱質沈着（軽微）、大脳に鉱質沈着（軽微）、脾臓に髓外造血（軽微）、パインエル板に鉱質沈着（軽微）、下垂体に前葉囊胞（軽微）、甲状腺に鰓後体遺残（軽微）、眼球に限局性網膜異形成（軽微）が散見された。しかし、これらは 1 例のみの発現あるいは対照群または試験施設の背景データ<sup>7)</sup>に認められる所見であり、発現頻度の増加も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。

対照群のみの所見として、脾臓に限局性腺房細胞萎縮（軽微）、腎臓に尿細管の好塩基性化（軽微）、炎症性細胞浸潤（軽微）、胸腺に上皮過形成（軽微）が各 1 例にみられた。

#### (3) 雌：サテライト群（非交配群）

1000 mg/kg 群では、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）、甲状腺に鰓後体遺残（軽微）が散見された。しかし、これらは対照群あるいは試験施設の背景データ<sup>7)</sup>に認められる所見であり、発現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。

#### [回復期間終了時]

##### (1) 雄：サテライト群

1000 mg/kg 群の膀胱には、異常は観察されなかった。

## 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った. また、いずれの出産生児にも外表異常は認められなかった.

### 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.

生後 0 日から 4 日の一般状態に、対照群を含むいずれの試験群においても、異常は認められなかった.

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った.

### 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 日に、300 mg/kg 群における雌の体重に対照群と比較して有意な高値がみられたが、1000 mg/kg 群では有意な差はなかったことから、被験物質投与と関連のない変化と考えられた.

生後 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った.

#### 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、1000 mg/kg 群で異常は認められず、対照群で雌の 1 例の肝臓に多巣性黄白色巣がみられたのみであった.

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った.

### 5 考察

#### 5.1 反復投与毒性

100 および 300 mg/kg 群では、投与期間中の一般状態、体重、体重増加量および摂餌量、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.

投与期間終了時の主試験群の雌の剖検で、300 および 1000 mg/kg 群において、腺胃粘膜黒色巣が 1 または 2 例にみられ、病理組織学的検査ではこれに対応して限局性びらんがみられた。しかし、この変化は試験施設の背景データ<sup>7)</sup>に認められる所見であり、主試験群の雌は投与期間が長いことと、病変も限局性で表層のみに限られることから、経口投与操作の際の物理的な刺激で粘膜が欠損したものと推察され、被験物質投与による特異的変化とは考えられなかった。

1000 mg/kg 群では、投与期間中の一般状態の変化として、雄 1 例、主試験群の雌 1 例、非交配群の雌 1 例に赤色尿が観察された。尿検査では、雄で pH の低値と尿量の高値、非交配群の雌で pH の低値がみられ、いずれも被験物質投与に関連する変化と考えられた。泌尿器系の組織の病理組織学的検査では、雄および主試験群の雌において、膀胱に一連の炎症性の変化(尿路上皮過形成、炎症性細胞浸潤、粘膜固有層の水腫)がみられ、対照の動物ではみられない異常であり、発現頻度も統計学的に有意に高かった。これらの変化は、泌尿器系の上位の器官に異常は認められないことから、尿中に排泄された代謝物あるいは親化合物による、膀胱粘膜への刺激性に起因する可能性が考えられた。

器官重量では、主試験群の雌で腎臓の相対重量に高値、非交配群の雌で下垂体の絶対および相対重量に低値がみられたが、病理組織学的異常は認めらなかつたことから、これらは毒性学的意義のない変化と考えられた。また、主試験群の雌で胸腺の絶対および相対重量に低値がみられ、投与に加えて妊娠・哺育のストレスによる可能性が考えられたが、病理組織学的異常は認めらなかつた。

以上の変化は、回復 2 日以降および回復期間終了時の検査では認められず、回復性を示した。

同群のその他の項目(体重、体重増加量および摂餌量、詳細な状態観察、機能検査、血液学的検査、血液化学的検査)には、投与期間中／終了時および回復期間／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、100 および 300 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。1000 mg/kg 群では、雌雄で一般状態の変化（赤色尿）、尿 pH 低値、膀胱に病理組織学的変化が認められ、さらに雄では尿量増加も認められた。したがって、本試験条件下における  $\alpha$ -ヒドロキシイソラク酸メチル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 300 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、1000 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、外表異常児出現率および剖検では、1000 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、1000 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  $\alpha$ -ヒドロキシイソラク酸メチル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 1000 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

分娩（哺育 0 日/生後 0 日）観察において、母動物番号 50251 の哺育児雄 1 例が、一般状態および体重測定後に、ケージに戻す際に事故による外傷により死亡した。当該哺育児のデータは、生後 1-4 日の一般状態および生後 4 日の体重が欠測値となつたが、哺育児 1 例のみの欠測値であることから、その腹全体への影響はほとんどなく、試験成績の信頼性に影響はないと考えられた。

試験計画書では、投与開始時週齢が 10 週齢と規定されていたが、実際は 9 週齢であった。試験計画書の誤記であることと、翌日には 10 週齢になり、わずか 1 日の差であることから、この逸脱による試験成績の信頼性に影響はないと考えられた。

尿検査の SOP では試験紙の精度管理は 2 週間を限度に実施すると規定されているが、回復群の尿検査において精度管理を実施していなかつた（前回の精度管理から 15 日後に実施）。使用した試験紙は使用期限内のものであつたことから、試験成績の信頼性に影響はないと考えら

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 Methyl 2-Hydroxyisobutyrate. 東京化成工業株式会社
- 2) Chemical Book: 2110-78-3 (CAS Data Base Reference)
- 3) 東京化成工業株式会社ホームページ. オンラインカタログ Methyl 2-Hydroxyisobutyrate.
- 4) 最終報告書 :  $\alpha$ -ヒドロキシイソラク酸メチル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 (SR17143), 株式会社化合物安全性研究所 2017 年
- 5) 血液学的検査/血液化学的検査/蛋白分画 背景データ Crl:CD(SD) ラット(雌雄 : 13 ~ 16 週齢) (2013-2017) 株式会社化合物安全性研究所 社内資料
- 6) 器官重量 背景データ Crl:CD(SD) ラット(雄 : 15 ~ 16 週齢) (2013-2017) 株式会社化合物安全性研究所 社内資料
- 7) Historical data of Crl:CD(SD) male and female rats: Histopathological findings (2006-2011) 株式会社化合物安全性研究所 社内資料

Figure 1 - 1

Study No. : SR17144

Body weight, Male

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

Species : Rat

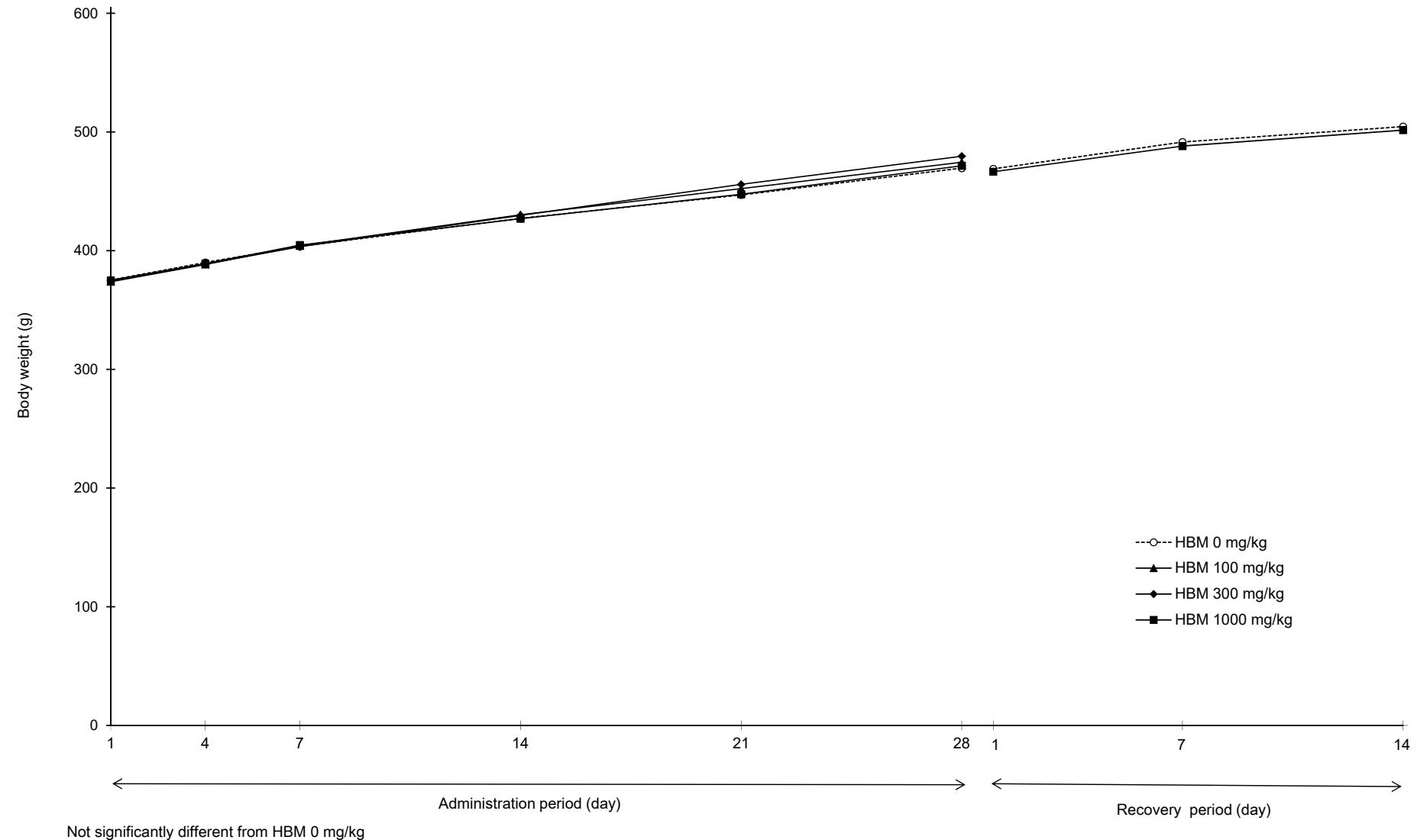


Figure 1 - 2

Study No. : SR17144

Body weight, Female

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

Species : Rat

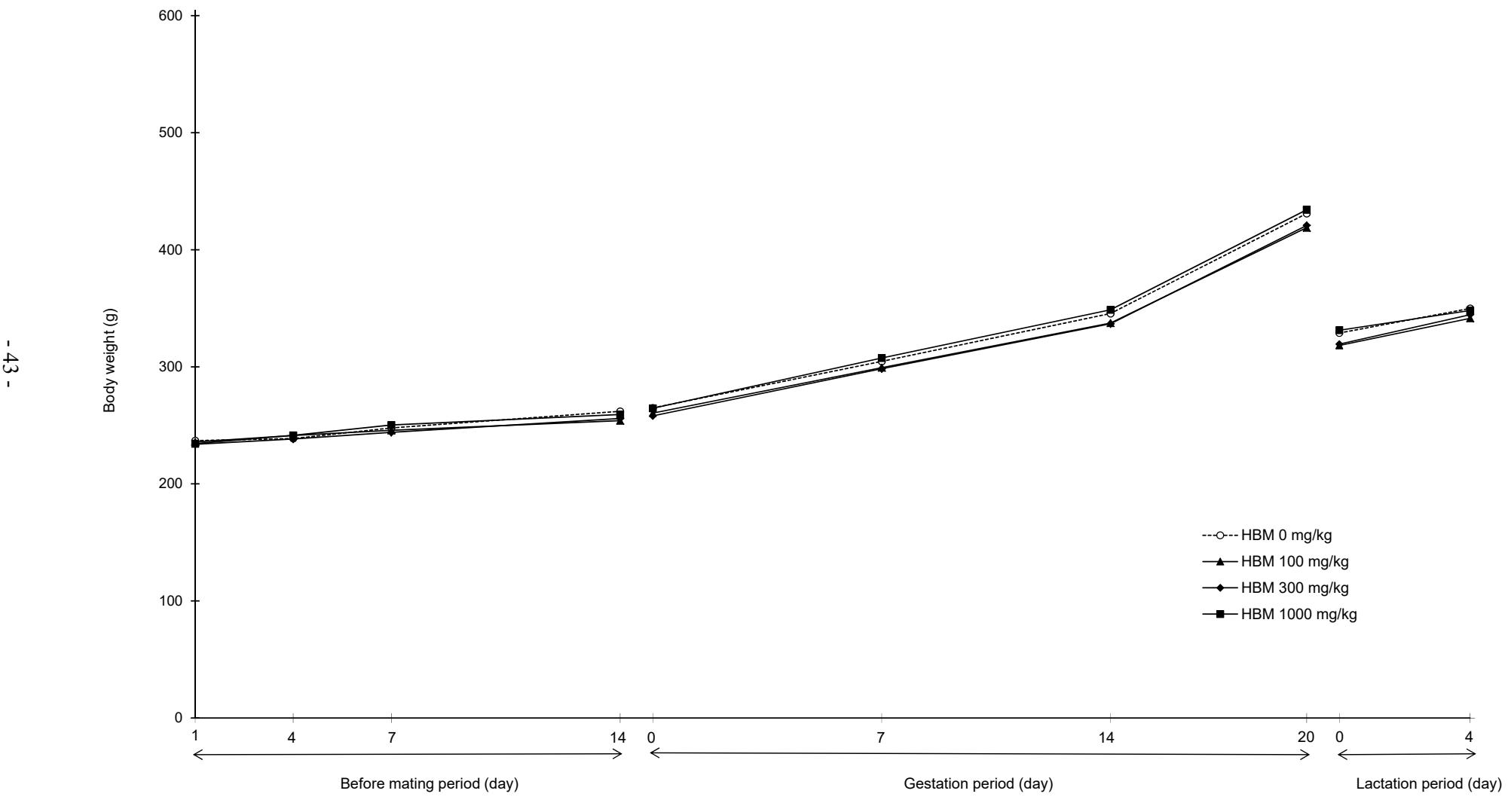


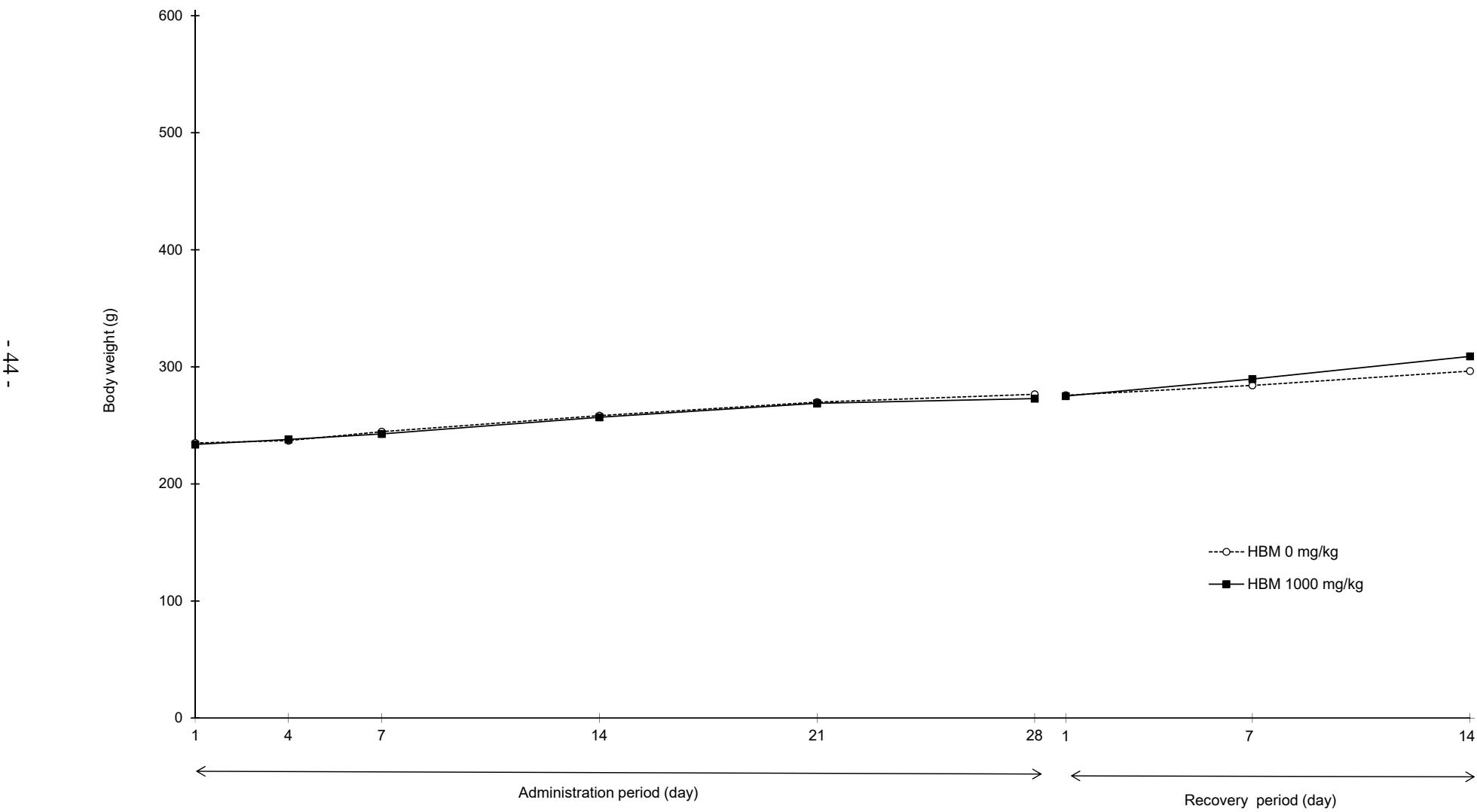
Figure 1 - 3

Study No. : SR17144

Body weight, Female (satellite)

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

Species : Rat



Not significantly different from HBM 0 mg/kg

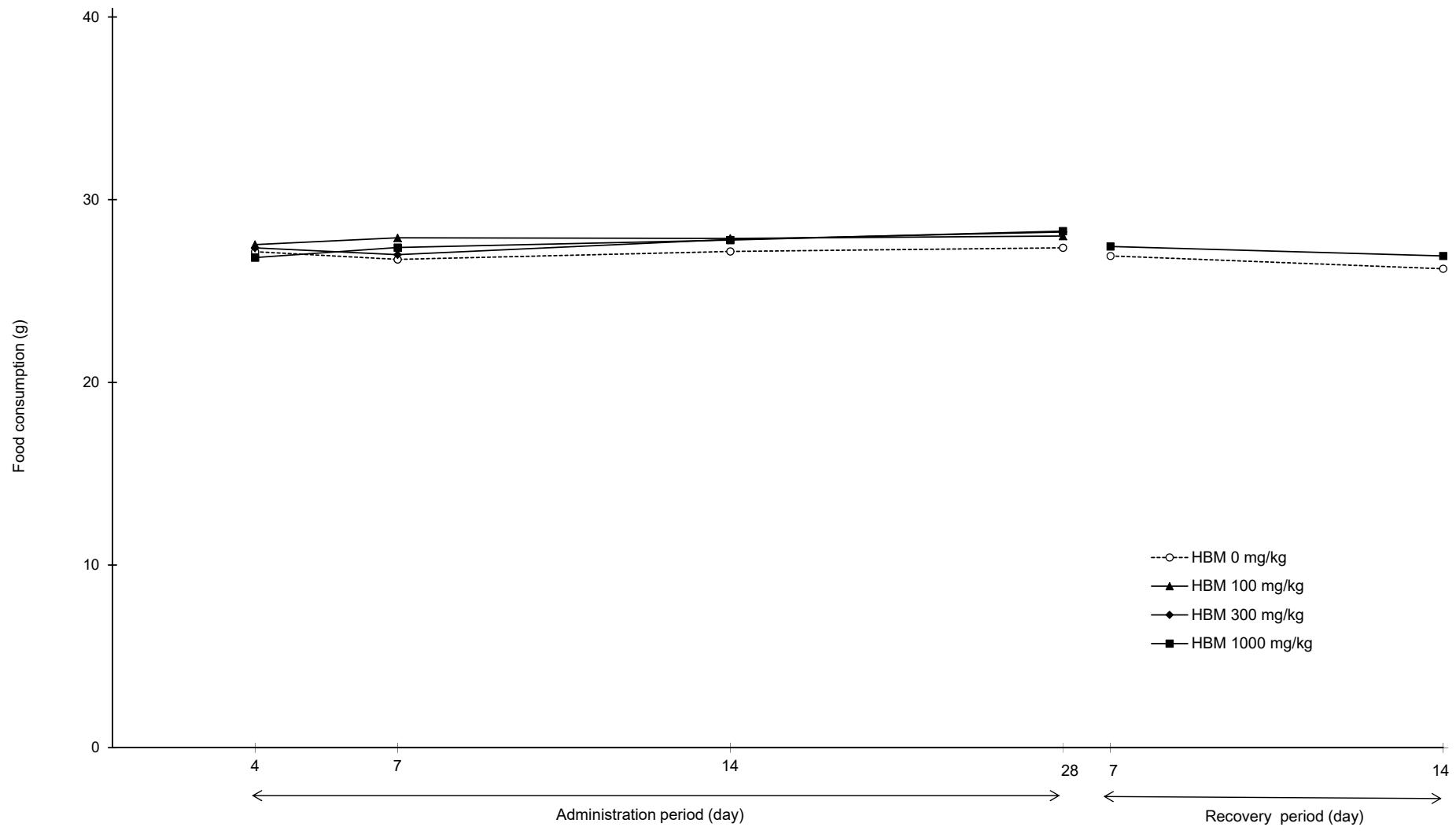
Figure 2 - 1

Study No. : SR17144

Food consumption, Male

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

Species : Rat



Not significantly different from HBM 0 mg/kg

Figure 2 - 2

Study No. : SR17144

Food consumption, Female

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

Species : Rat

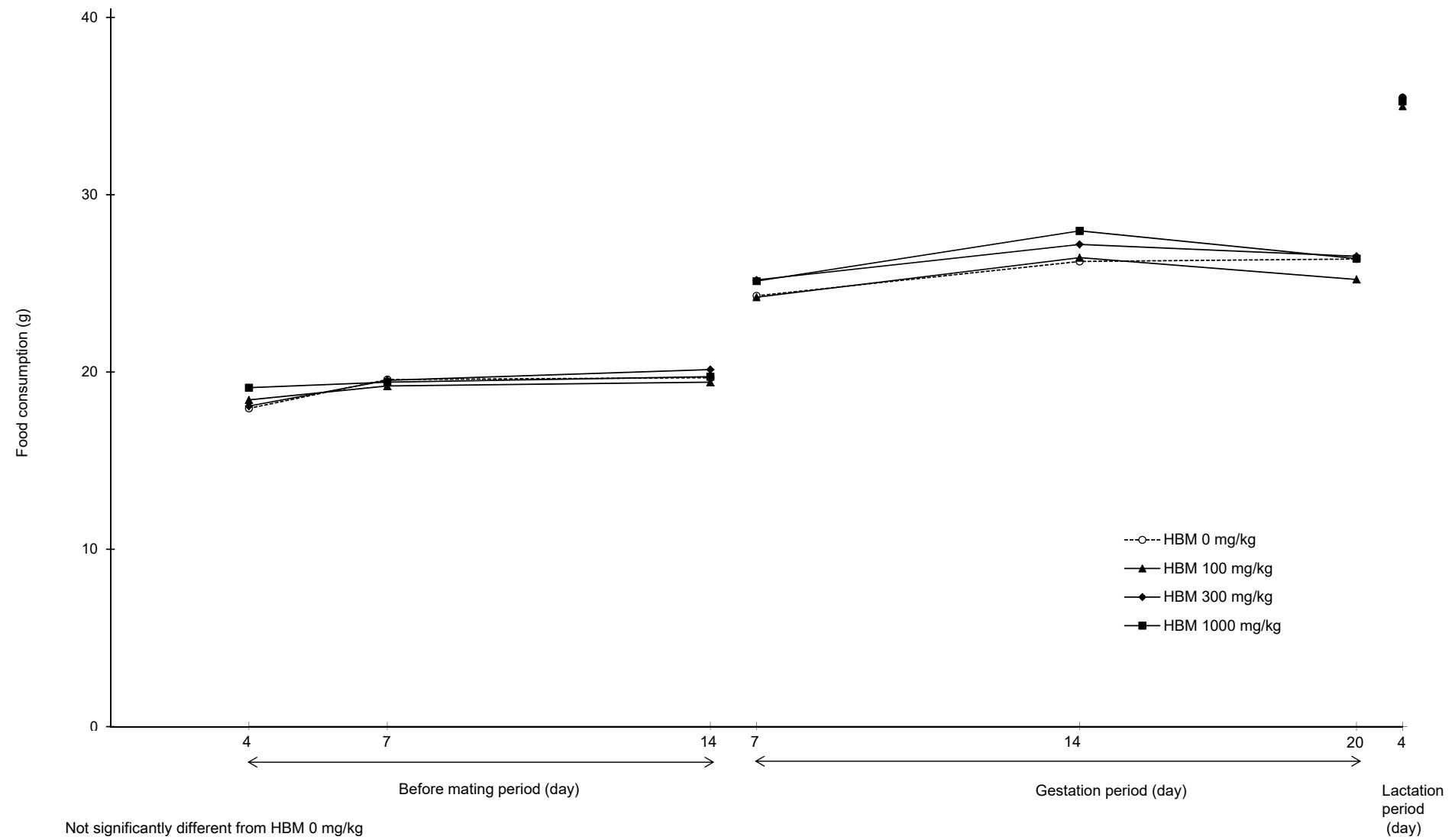
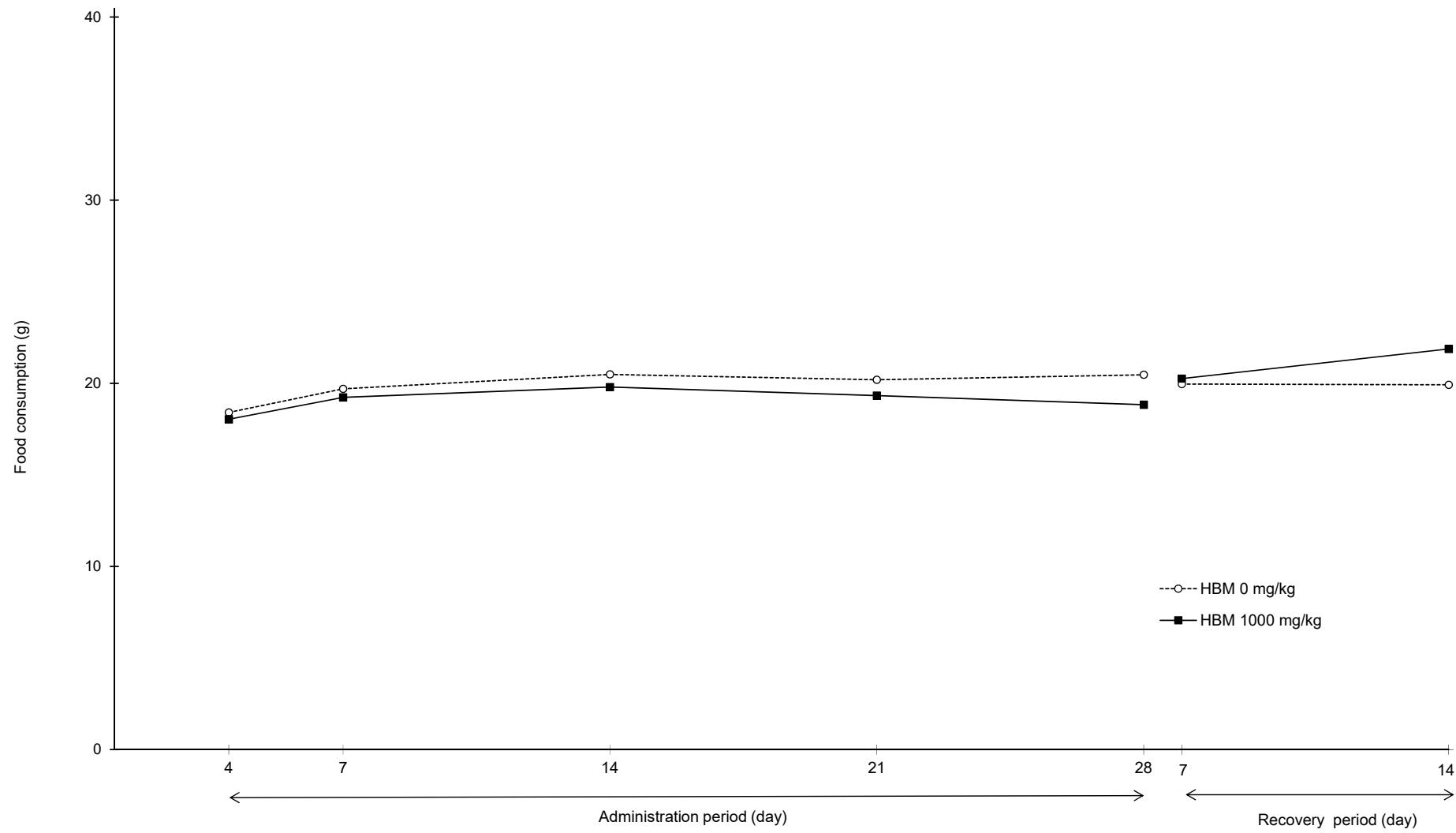


Figure 2 - 3

Study No. : SR17144

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

Species : Rat



Not significantly different from HBM 0 mg/kg

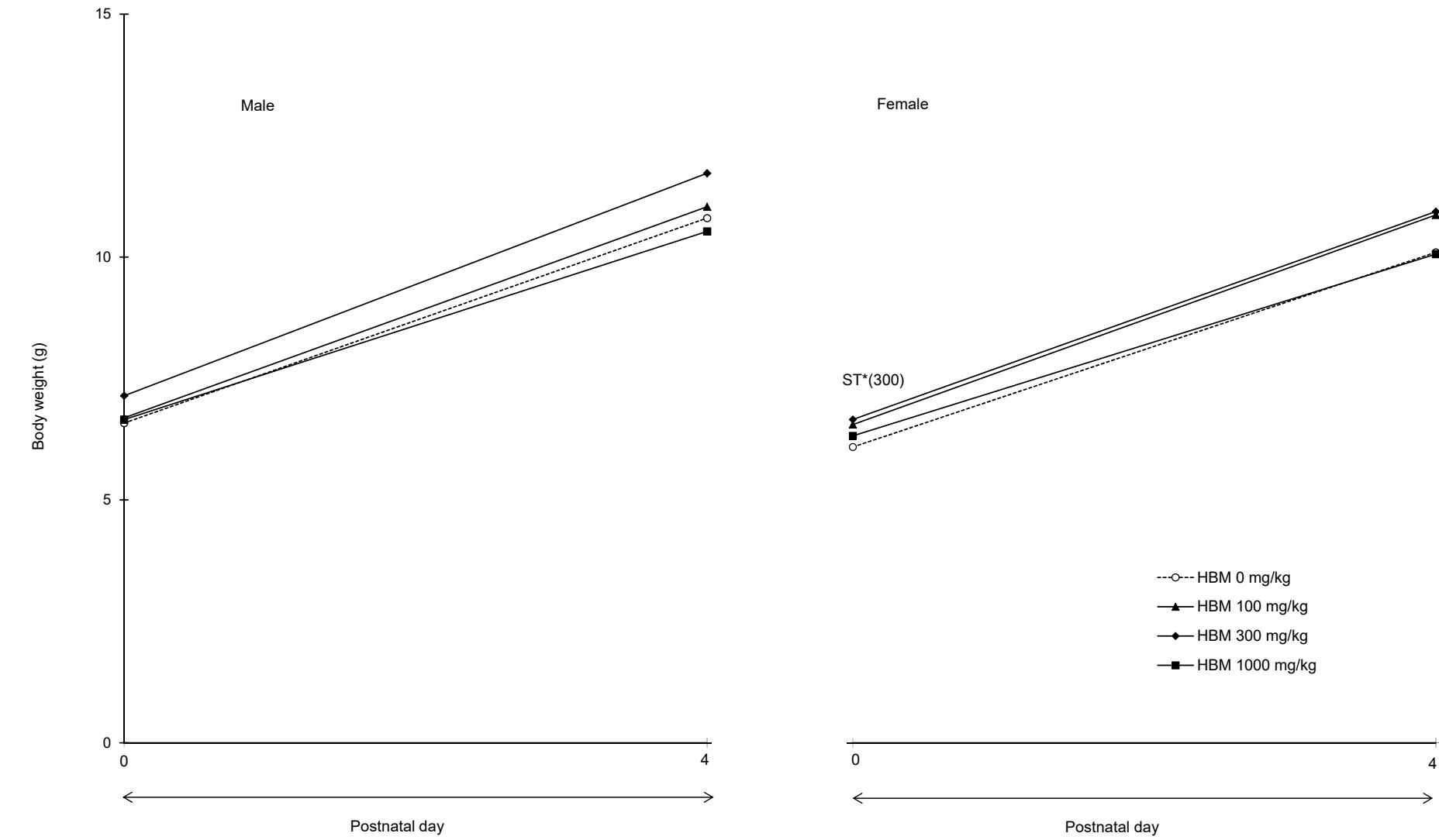
Figure 3

Study No. : SR17144

Body weight of offspring

Period : Postnatal Day 0-4

Species : Rat



Significantly different from HBM 0 mg/kg: \* P<0.05

ST : Steel test (two-side)

Table 1 - 1

Study No. : SR17144

Clinical sign Sex : Male		Period : Administration Day 1-29																Species : Rat	
		Day 1		2		3		4		5		6		7		8			
Test article	Dose	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	
HBM	n		12	12	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	12	12
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
300 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	Reddish urine		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Test article	Dose	Day	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
HBM	n	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	
0 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
300 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	Reddish urine		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Test article	Dose	Day	17	18	19	20	21	22	23	24	25	26	27	28	29				
HBM	n	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	
0 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
300 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	Reddish urine		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Test article	Dose	Day	25	26	27	28	29												
HBM	n	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	
0 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
300 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	Reddish urine		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

Administration)1 : Before administration, 2 : After administration, 3 : Necropsy day

Table 1 - 2

Study No. : SR17144

Clinical sign Sex : Female		Period : F0 before mating Day 1-14, F0 mating Day 15-18														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			
HBM	n		12	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	12			
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12			
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12			
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12			
300 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12			
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12			
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12			
Test article		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			
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	7	7	1	1		
0 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	7	7	1	1		
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	6	6	4	4		
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	6	6	4	4		
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	5	5	2	2		
300 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	5	5	2	2		
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	8	8	5	5		
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	8	8	5	5		
Test article		Day		17		18															
		Time	1	2	1	2															
HBM	n		0	0	0	0															
0 mg/kg	No abnormality		0	0	0	0															
HBM	n		2	2	0	0															
100 mg/kg	No abnormality		2	2	0	0															
HBM	n		0	0	0	0															
300 mg/kg	No abnormality		0	0	0	0															
HBM	n		1	1	1	1															
1000 mg/kg	No abnormality		1	1	1	1															

F0 before mating; F0 mating)1 : Before administration, 2 : After administration

Table 1 - 3

Study No. : SR17144

Clinical sign 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		
HBM	n		12	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	12
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HBM	n		11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
300 mg/kg	No abnormality		11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
1000 mg/kg	No abnormality		12	12	12	12	11	11	11	12	11	12	12	12	12	12	12	12
	Reddish urine		0	0	0	0	1	1	1	0	1	0	0	0	0	0	0	0
Test article		Day 8		9		10		11		12		13		14		15		
Dose	Clinical signs	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
HBM	n		12	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	12
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
HBM	n		11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
300 mg/kg	No abnormality		11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	Reddish urine		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Test article		Day 16		17		18		19		20		21		22				
Dose	Clinical signs	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2		
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	0	0	
0 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	0	0	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	3	3	
100 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	3	3	
HBM	n		11	11	11	11	11	11	11	11	11	11	11	11	11	2	2	
300 mg/kg	No abnormality		11	11	11	11	11	11	11	11	11	11	11	11	11	2	2	
HBM	n		12	12	12	12	12	12	12	12	12	12	12	12	12	2	2	
1000 mg/kg	No abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	2	2	
	Reddish urine		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

F0 gestation)1 : Before administration, 2 : After administration

Table 1 - 4

Study No. : SR17144

Test article Dose	Clinical sign Sex : Female 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	
HBM 0 mg/kg	n No abnormality		12	12	12	12	12	12	12	12	12	12	
HBM 100 mg/kg	n No abnormality		12	12	12	12	12	12	12	12	12	12	
HBM 300 mg/kg	n No abnormality		11	11	11	11	11	11	11	11	11	11	
HBM 1000 mg/kg	n No abnormality		11	11	11	11	11	11	11	11	11	11	
			12	12	12	12	12	12	12	12	12	12	
			12	12	12	12	12	12	12	12	12	12	

F0 lactation)1 : Before administration, 2 : After administration, 3 : Necropsy day

Table 1 - 5

Study No. : SR17144

Clinical sign Sex : Female (satellite)		Period : Administration Day 1-29														Species : Rat				
		Day		1		2		3		4		5		6		7				
Test article	Dose	Clinical signs		Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2		
		HBM		n	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		
	HBM		n		10	10	10	10	10	10	10	10	10	10	10	10	10	10		
1000 mg/kg	No abnormality				10	10	10	10	10	10	10	10	10	10	10	10	10	10		
	Reddish urine				0	0	0	0	0	0	0	0	0	0	0	0	0	0		
Test article		Day		9		10		11		12		13		14		15		16		
		Clinical signs		Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2		
0 mg/kg	HBM		n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
	No abnormality				10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
1000 mg/kg	HBM		n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
	No abnormality				10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
Reddish urine				0		0	0	0	0	0	0	0	0	0	0	0	0	0		
Test article		Day		17		18		19		20		21		22		23		24		
		Clinical signs		Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2		
0 mg/kg	HBM		n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
	No abnormality				10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
1000 mg/kg	HBM		n		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
	No abnormality				10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
Reddish urine				0		0	0	0	0	0	0	0	0	0	0	0	0	0		
Test article		Day		25		26		27		28		29								
		Clinical signs		Time	1	2	1	2	1	2	1	2	1	2	3					
0 mg/kg	HBM		n		10	10	10	10	10	10	10	10	10	10	10	5				
	No abnormality				10	10	10	10	10	10	10	10	10	10	10	5				
1000 mg/kg	HBM		n		10	10	10	10	10	10	10	10	10	10	10	5				
	No abnormality				10	10	10	10	10	10	10	10	10	10	10	5				
Reddish urine				0		0	0	0	0	0	0	0	0	1	1	0				

Administration)1 : Before administration, 2 : After administration, 3 : Necropsy day

Table 1 - 6

Study No. : SR17144

Test article Dose	Clinical sign Sex : Male	Period : Recovery Day 1-15														Species : Rat							
		Day		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	2			
HBM	n		5	5	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	5	5			
HBM	n		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5			
1000 mg/kg	No abnormality		5	5	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							
Dose		Clinical signs		Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	3				
HBM	n		5	5	5	5	5	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	5	5	5	5	5
HBM	n		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	No abnormality		5	5	5	5	5	5	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 - 7

Study No. : SR17144

Clinical sign Sex : Female (satellite)		Period : Recovery Day 1-15														Species : Rat			
		Day		1		2		3		4		5		6		7		8	
Test article	Dose	Clinical signs	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
HBM	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
HBM	n			5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	No abnormality			4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Reddish urine			1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Test article		Day		9		10		11		12		13		14		15			
		Clinical signs	Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	3	
HBM	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
HBM	n			5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	No abnormality			5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Reddish urine			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

Table 2 - 1

Study No. : SR17144

Detailed clinical observation (in the cage)

Sex : Male

Species : Rat

Stage	Group	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Stereotype		Bizarre behavior Self biting
					1	0	
Pre	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 7	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 14	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 21	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 28	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 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 HBM 0 mg/kg

Table 2 - 2

Study No. : SR17144

Detailed clinical observation (in the cage)

Sex : Female

Species : Rat

Stage	Group	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Stereotype		Bizarre behavior Self biting
					1	0	
Pre	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 7	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 14	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 21	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 28	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 35	0 mg/kg	n	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12
Day 42	0 mg/kg	n	7	7	7	7	7
	100 mg/kg	n	8	8	8	8	8
	300 mg/kg	n	6	6	6	6	6
	1000 mg/kg	n	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.

Not significantly different from HBM 0 mg/kg

Table 2 - 3

Study No. : SR17144

Detailed clinical observation (in the cage)

Sex : Female (satellite)

Species : Rat

Stage	Group	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Stereotype		Bizarre behavior Self biting
					1	0	
Pre	0 mg/kg	n	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10
Day 7	0 mg/kg	n	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10
Day 14	0 mg/kg	n	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10
Day 21	0 mg/kg	n	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10
Day 28	0 mg/kg	n	10	10	10	10	10
	1000 mg/kg	n	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.

Not significantly different from HBM 0 mg/kg

Table 2 - 4

Study No. : SR17144

Detailed clinical observation (in the cage)

Sex : Male

Species : Rat

Stage	Group	Posture	Respiratory pattern	Tremor/Convulsion	Stereotype		Bizarre behavior
					1	1	
Recovery	0 mg/kg	n	5	5	5	5	5
Day 7	1000 mg/kg	n	5	5	5	5	5
Recovery	0 mg/kg	n	5	5	5	5	5
Day 14	1000 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 HBM 0 mg/kg

Table 2 - 5

Study No. : SR17144

Detailed clinical observation (in the cage)

Sex : Female (satellite)

Species : Rat

Stage	Group	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Stereotype		Bizarre behavior Self biting
					1	1	
Recovery	0 mg/kg	n	5	5	5	5	5
Day 7	1000 mg/kg	n	5	5	5	5	5
Recovery	0 mg/kg	n	5	5	5	5	5
Day 14	1000 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 HBM 0 mg/kg

Table 3 - 1

Study No. : SR17144

## Detailed clinical observation (on the hand)

Sex : Male

Species : Rat

Stage	Group	Ease of		Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacration	Salivation	Secretions/Excretions
		Removal	Handling										
1	1	2	1	1	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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 mg/kg	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.

Not significantly different from HBM 0 mg/kg

Table 3 - 2

Study No. : SR17144

Detailed clinical observation (on the hand)

Sex : Female

Species : Rat

Stage	Group	Ease of		Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacration	Salivation	Secretions/Excretions
		Removal	Handling										
Pre	0 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 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
	100 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	12	12	12	12	12	12
Day 42	0 mg/kg	n	7	7	7	7	7	7	7	7	7	7	7
	100 mg/kg	n	8	8	8	8	8	8	8	8	8	8	8
	300 mg/kg	n	6	6	6	6	6	6	6	6	6	6	6
	1000 mg/kg	n	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.

Not significantly different from HBM 0 mg/kg

Table 3 - 3

Study No. : SR17144

## Detailed clinical observation (on the hand)

Sex : Female (satellite)

Species : Rat

Stage	Group	Ease of		Muscle tone	Piloerection	Fur	Mucous membranes		Skin	Pupil size	Lacration	Salivation	Secretions/ Excretions
		Removal	Handling				Eyes	1					
Pre	0 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
Day 7	0 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
Day 14	0 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
Day 21	0 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
Day 28	0 mg/kg	n	10	10	10	10	10	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	10	10	10	10	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.

Not significantly different from HBM 0 mg/kg

Table 3 - 4

Study No. : SR17144

## Detailed clinical observation (on the hand)

Sex : Male

Species : Rat

Stage	Group	Ease of		Muscle tone	Piloerection	Fur	Mucous membranes			Pupil size	Lacration	Salivation	Secretions/Excretions
		Removal	Handling				Eyes	1	0				
Recovery	0 mg/kg	n	5	5	5	5	5	5	5	5	5	5	5
Day 7	1000 mg/kg	n	5	5	5	5	5	5	5	5	5	5	5
Recovery	0 mg/kg	n	5	5	5	5	5	5	5	5	5	5	5
Day 14	1000 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 HBM 0 mg/kg

Table 3 - 5

Study No. : SR17144

Detailed clinical observation (on the hand)

Sex : Female (satellite)

Species : Rat

Stage	Group	Ease of		Muscle tone	Piloerection	Fur	Mucous membranes			Pupil size	Lacration	Salivation	Secretions/Excretions
		Removal	Handling				Eyes	1	0				
Recovery	0 mg/kg	n	5	5	5	5	5	5	5	5	5	5	5
Day 7	1000 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 HBM 0 mg/kg

Table 4 - 1

Study No. : SR17144

Detailed clinical observation (in the open-field)

Sex : Male

Species : Rat

Stage	Group	Gait	Co-ordination		Reactivity to		Urination	Defecation	Stereotype		Bizarre behavior			
			1	1	1	1			0	1	0	0	1	1
Pre	0 mg/kg	n	12	12	12	12	10	2	9	3	12	12	12	12
	100 mg/kg	n	12	12	12	12	8	4	7	5	12	12	12	12
	300 mg/kg	n	12	12	12	12	6	6	5	7	12	12	12	12
	1000 mg/kg	n	12	12	12	12	10	2	7	5	12	12	12	12
Day 7	0 mg/kg	n	12	12	12	12	10	2	12	0	12	12	12	12
	100 mg/kg	n	12	12	12	12	9	3	11	1	12	12	12	12
	300 mg/kg	n	12	12	12	12	9	3	8	4	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12
Day 14	0 mg/kg	n	12	12	12	12	11	1	12	0	12	12	12	12
	100 mg/kg	n	12	12	12	12	12	0	9	3	12	12	12	12
	300 mg/kg	n	12	12	12	12	10	2	11	1	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	11	1	12	12	12	12
Day 21	0 mg/kg	n	12	12	12	12	11	1	12	0	12	12	12	12
	100 mg/kg	n	12	12	12	12	9	3	10	2	12	12	12	12
	300 mg/kg	n	12	12	12	12	7	5	7	5	12	12	12	12
	1000 mg/kg	n	12	12	12	12	11	1	12	0	12	12	12	12
Day 28	0 mg/kg	n	12	12	12	12	9	3	12	0	12	12	12	12
	100 mg/kg	n	12	12	12	12	10	2	10	2	12	12	12	12
	300 mg/kg	n	12	12	12	12	9	3	10	2	12	12	12	12
	1000 mg/kg	n	12	12	12	12	10	2	11	1	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.

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

ST : Steel test (two-side)

Table 4 - 2

Study No. : SR17144

Detailed clinical observation (in the open-field)

Sex : Female

Species : Rat

Stage	Group	Co-ordination of movement		Reactivity to stimuli		Searching		Urination		Defecation		Stereotype		Bizarre behavior			
		Gait	1	1	1	1	0	1	0	1	0	1	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
Pre	0 mg/kg	n	12	12	12	12	10	2	11	1	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	8	4	10	2	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	9	3	11	1	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	10	2	10	2	12	12	12	12	12	12	12
Day 7	0 mg/kg	n	12	12	12	12	10	2	12	0	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	8	4	12	0	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
Day 14	0 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	10	2	11	1	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
Day 21	0 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
Day 28	0 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
Day 35	0 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	100 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
	300 mg/kg	n	12	12	12	12	11	1	12	0	12	12	12	12	12	12	12
	1000 mg/kg	n	12	12	12	12	12	0	12	0	12	12	12	12	12	12	12
Day 42	0 mg/kg	n	7	7	7	7	7	0	7	0	7	7	7	7	7	7	7
	100 mg/kg	n	8	8	8	8	7	1	8	0	8	8	8	8	8	8	8
	300 mg/kg	n	6	6	6	6	6	0	6	0	6	6	6	6	6	6	6
	1000 mg/kg	n	8	8	8	8	8	0	8	0	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.

Not significantly different from HBM 0 mg/kg

Table 4 - 3

Study No. : SR17144

Detailed clinical observation (in the open-field)

Sex : Female (satellite)

Species : Rat

Stage	Group	Co-ordination of movement		Reactivity to stimuli		Searching		Urination		Defecation		Stereotype		Bizarre behavior			
		Gait 1	Gait 1	1	1	1	1	0	1	0	1	0	0	Unusual head movement 0	Walking backward 1	Vocalization 1	Aggression 1
Pre	0 mg/kg	n	10	10	10	10	10	8	2	9	1	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	9	1	10	0	10	10	10	10	10	10
Day 7	0 mg/kg	n	10	10	10	10	10	7	3	10	0	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	8	2	9	1	10	10	10	10	10	10
Day 14	0 mg/kg	n	10	10	10	10	10	10	0	10	0	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	0	10	0	10	10	10	10	10	10
Day 21	0 mg/kg	n	10	10	10	10	10	10	0	10	0	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	9	1	9	1	10	10	10	10	10	10
Day 28	0 mg/kg	n	10	10	10	10	10	9	1	10	0	10	10	10	10	10	10
	1000 mg/kg	n	10	10	10	10	10	10	0	10	0	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.

Not significantly different from HBM 0 mg/kg

Table 4 - 4

Study No. : SR17144

Detailed clinical observation (in the open-field)

Sex : Male

Species : Rat

Stage	Group	Co-ordination of movement			Reactivity to stimuli		Urination		Defecation		Stereotype		Bizarre behavior		
		Gait 1	1	1	Searching 1	1	0	1	0	1	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocalization 1	Aggression 1
Recovery Day 7	0 mg/kg	n	5	5	5	5	5	0	4	1	5	5	5	5	5
	1000 mg/kg	n	5	5	5	5	5	0	5	0	5	5	5	5	5
Recovery Day 14	0 mg/kg	n	5	5	5	5	4	1	5	0	5	5	5	5	5
	1000 mg/kg	n	5	5	5	5	4	1	5	0	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.

Not significantly different from HBM 0 mg/kg

Table 4 - 5

Study No. : SR17144

Detailed clinical observation (in the open-field)

Sex : Female (satellite)

Species : Rat

Stage	Group	Co-ordination of movement				Reactivity to stimuli		Urination		Defecation		Stereotype		Bizarre behavior		
		Gait 1	1	1	1	1	1	0	1	0	1	Excessive grooming 0	Unusual head movement 0	Walking backward 1	Vocalization 1	Aggression 1
Recovery Day 7	0 mg/kg	n	5	5	5	5	5	4	1	5	0	5	5	5	5	5
	1000 mg/kg	n	5	5	5	5	5	3	2	5	0	5	5	5	5	5
Recovery Day 14	0 mg/kg	n	5	5	5	5	5	5	0	5	0	5	5	5	5	5
	1000 mg/kg	n	5	5	5	5	5	5	0	5	0	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.

Not significantly different from HBM 0 mg/kg

Table 5 - 1

Study No. : SR17144

Functional observations (on the desk)  
Sex : Male

Stage : Week 4

Species : Rat

Group	n	Reactivity					Righting reflex
		Visual 4	Touch 2	Auditory 1	Pain 2	Proprioceptive 1	
0 mg/kg	n	5	5	5	5	5	5
100 mg/kg	n	5	5	5	5	5	5
300 mg/kg	n	5	5	5	5	5	5
1000 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 HBM 0 mg/kg

Table 5 - 2

Functional observations (on the desk)  
Sex : Female

Stage : Lactation Day 4

Study No. : SR17144

Species : Rat

Group	n	Reactivity					Righting reflex
		Visual 4	Touch 2	Auditory 1	Pain 2	Proprioceptive 1	
0 mg/kg	n	5	5	5	5	5	5
100 mg/kg	n	5	5	5	5	5	5
300 mg/kg	n	5	5	5	5	5	5
1000 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 HBM 0 mg/kg

Table 5 - 3

Study No. : SR17144

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

Stage : Week 4

Species : Rat

Group	n	Reactivity					Righting reflex
		Visual 4	Touch 2	Auditory 1	Pain 2	Proprioceptive 1	
0 mg/kg	n	5	5	5	5	5	5
1000 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 HBM 0 mg/kg

Table 5 - 4

Study No. : SR17144

Functional observations (on the desk)  
Sex : Male

Stage : Recovery Week 2

Species : Rat

Group	n	Reactivity					Righting reflex
		Visual 4	Touch 2	Auditory 1	Pain 2	Proprioceptive 1	
0 mg/kg	n	5	5	5	5	5	5
1000 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 HBM 0 mg/kg

Table 6 - 1

Study No. : SR17144

Sex : Male	Grip strength		Stage : Week 4	Species : Rat
	Forelimb	Hindlimb		
Test article		g	g	
Dose				
HBM	n	5	5	
0 mg/kg	Mean	1317.86	501.74	
	S.D.	102.42	66.94	
HBM	n	5	5	
100 mg/kg	Mean	1260.72	542.08	
	S.D.	186.97	51.55	
HBM	n	5	5	
300 mg/kg	Mean	1515.74	555.08	
	S.D.	128.80	61.25	
HBM	n	5	5	
1000 mg/kg	Mean	1328.12	520.60	
	S.D.	284.61	76.75	

Not significantly different from HBM 0 mg/kg

Table 6 - 2

Study No. : SR17144

Sex : Female	Grip strength		Stage : Lactation Day 4	Species : Rat
	Forelimb	Hindlimb		
Test article	g	g		
Dose				
HBM	n	5	5	
0 mg/kg	Mean	1144.94	401.38	
	S.D.	115.77	18.28	
HBM	n	5	5	
100 mg/kg	Mean	1255.12	395.40	
	S.D.	116.25	14.63	
HBM	n	5	5	
300 mg/kg	Mean	1207.40	399.06	
	S.D.	121.38	35.96	
HBM	n	5	5	
1000 mg/kg	Mean	1215.92	406.18	
	S.D.	152.40	55.72	

Not significantly different from HBM 0 mg/kg

Table 6 - 3

Study No. : SR17144

Grip strength Sex : Female (satellite)		Stage : Week 4		Species : Rat
	Forelimb	Hindlimb		
Test article		g	g	
Dose				
HBM	n	5	5	
0 mg/kg	Mean	1099.68	445.16	
	S.D.	92.34	46.91	
HBM	n	5	5	
1000 mg/kg	Mean	1067.68	385.94	
	S.D.	78.87	102.82	

Not significantly different from HBM 0 mg/kg

Table 6 - 4

Study No. : SR17144

Sex : Male	Grip strength		Stage : Recovery Week 2	Species : Rat
	Forelimb	Hindlimb		
Test article		g	g	
Dose				
HBM	n	5	5	
0 mg/kg	Mean	1403.86	489.38	
	S.D.	189.90	43.69	
HBM	n	5	5	
1000 mg/kg	Mean	1629.76	496.46	
	S.D.	284.63	93.78	

Not significantly different from HBM 0 mg/kg

Table 7 - 1

Study No. : SR17144

	Motor activity measurements		Stage : Week 4						Species : Rat	
	Sex : Male	Sex : Female	0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	0' - 60'	
Test article			No.	No.	No.	No.	No.	No.	No.	
Dose										
HBM	n	5	5	5	5	5	5	5	5	
0 mg/kg	Mean	414.2	258.0	165.2	119.4	141.2	43.4	1141.4		
	S.D.	120.2	129.7	148.7	114.3	92.0	36.0	562.4		
HBM	n	5	5	5	5	5	5	5	5	
100 mg/kg	Mean	518.2	335.4	234.8	266.4	141.6	78.8	1575.2		
	S.D.	212.0	188.0	142.6	265.9	135.7	107.8	835.5		
HBM	n	5	5	5	5	5	5	5	5	
300 mg/kg	Mean	548.0	365.6	194.0	91.0	80.2	42.8	1321.6		
	S.D.	193.0	150.0	153.0	104.5	129.3	94.0	713.9		
HBM	n	5	5	5	5	5	5	5	5	
1000 mg/kg	Mean	739.2	445.6	284.8	91.8	28.8	35.6	1625.8		
	S.D.	199.1	299.8	262.4	68.5	51.4	79.6	707.7		
	DT *									

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

DT : Dunnett test (two-side)

Table 7 - 2

Study No. : SR17144

Test article Dose	Motor activity measurements Sex : Female		Stage : Lactation Day 4					Species : Rat
	0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	0' - 60'	
HBM	n	5	5	5	5	5	5	
0 mg/kg	Mean	481.2	285.6	147.4	119.6	150.4	49.6	1233.8
	S.D.	137.2	256.8	121.0	154.3	230.0	87.9	940.9
HBM	n	5	5	5	5	5	5	
100 mg/kg	Mean	648.6	202.6	164.0	190.0	81.0	110.0	1396.2
	S.D.	306.1	108.7	86.7	123.8	82.0	118.3	423.8
HBM	n	5	5	5	5	5	5	
300 mg/kg	Mean	502.4	208.6	66.2	15.6	9.8	52.6	855.2
	S.D.	168.4	165.7	77.4	14.6	21.9	59.5	343.2
HBM	n	5	5	5	5	5	5	
1000 mg/kg	Mean	634.2	249.8	53.4	91.4	50.2	51.4	1130.4
	S.D.	175.1	158.9	53.2	88.3	79.3	75.0	295.7

Not significantly different from HBM 0 mg/kg

Table 7 - 3

Study No. : SR17144

	Motor activity measurements							Species : Rat
	Stage : Week 4							
Sex : Female (satellite)	0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	0' - 60'	
Test article	No.	No.	No.	No.	No.	No.	No.	
Dose								
HBM	n	5	5	5	5	5	5	
0 mg/kg	Mean	704.0	540.0	310.8	162.0	156.8	13.4	1887.0
	S.D.	257.1	313.5	279.9	168.5	216.1	15.1	1117.5
HBM	n	5	5	5	5	5	5	
1000 mg/kg	Mean	867.2	525.6	270.2	248.0	211.8	23.8	2146.6
	S.D.	306.3	193.9	195.1	186.0	120.3	42.5	698.8

Not significantly different from HBM 0 mg/kg

Table 7 - 4

Study No. : SR17144

	Motor activity measurements		Stage : Recovery Week 2					Species : Rat	
	Sex : Male	Sex : Female	0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	
Test article			No.	No.	No.	No.	No.	No.	No.
Dose									
HBM	n	5	5	5	5	5	5	5	5
0 mg/kg	Mean	574.6	370.6	264.6	207.4	235.4	155.6	1808.2	
	S.D.	265.0	168.1	171.3	154.7	177.9	125.7	983.9	
HBM	n	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	757.6	539.6	347.4	216.2	191.2	168.6	2220.6	
	S.D.	177.0	253.6	208.3	109.6	224.1	143.6	904.9	

Not significantly different from HBM 0 mg/kg

Table 8 - 1

Study No. : SR17144

Test article	Dose	Body weight Sex : Male		Period : Administration Day 1-28					Unit : g	Species : Rat	
		/Day		1	4	7	14	21	28		
HBM	n	12	12	12	12	12	12	12	12	12	
0 mg/kg	Mean	375.3	390.1	403.7	427.3	447.0	469.6	482.3	494.3	496.0	
	S.D.	17.0	18.7	21.9	27.6	29.8	28.1	28.4	28.1	15.4	
HBM	n	12	12	12	12	12	12	12	12	12	
100 mg/kg	Mean	373.9	388.4	404.2	430.3	452.3	474.6	494.6	500.7	500.7	
	S.D.	17.7	19.7	21.0	20.8	22.4	25.8	26.1	25.8	14.1	
HBM	n	12	12	12	12	12	12	12	12	12	
300 mg/kg	Mean	374.8	388.8	403.4	429.8	455.9	479.6	499.6	504.8	504.8	
	S.D.	17.6	21.3	24.9	27.6	28.0	31.4	31.4	31.4	16.2	
HBM	n	12	12	12	12	12	12	12	12	12	
1000 mg/kg	Mean	375.1	389.1	404.8	427.0	447.6	471.6	491.6	496.5	496.5	
	S.D.	15.7	19.0	20.6	25.4	29.5	32.9	32.9	32.9	26.1	

Not significantly different from HBM 0 mg/kg

Table 8 - 2

Study No. : SR17144

Test article Dose	Sex : Female /Day	Period : F0 before mating Day 1-14					Unit : g	Species : Rat
		1	4	7	14	Body weight gain		
HBM 0 mg/kg	n	12	12	12	12	12		
	Mean	237.0	238.8	247.8	262.0	25.0		
	S.D.	13.2	14.6	15.9	16.9	7.7		
HBM 100 mg/kg	n	12	12	12	12	12		
	Mean	235.8	241.3	245.8	254.0	18.2		
	S.D.	13.8	13.1	13.3	14.9	8.4		
HBM 300 mg/kg	n	12	12	12	12	12		
	Mean	233.8	238.4	244.0	255.9	22.1		
	S.D.	18.5	17.3	16.1	22.0	9.0		
HBM 1000 mg/kg	n	12	12	12	12	12		
	Mean	234.4	241.5	250.3	259.3	24.8		
	S.D.	13.6	15.6	14.8	15.9	6.2		

Not significantly different from HBM 0 mg/kg

Table 8 - 3

Study No. : SR17144

Test article Dose	Sex : Female /Day	Period : F0 gestation Day 0-20				Unit : g	Species : Rat
		0	7	14	20	Body weight gain	
HBM 0 mg/kg	n	12	12	12	12	12	
	Mean	264.9	304.7	345.6	431.0	166.1	
	S.D.	18.2	21.6	25.9	31.4	17.4	
HBM 100 mg/kg	n	12	12	12	12	12	
	Mean	260.5	299.3	337.4	418.9	158.4	
	S.D.	13.5	13.8	17.9	27.2	20.4	
HBM 300 mg/kg	n	11	11	11	11	11	
	Mean	258.1	298.4	336.8	420.8	162.7	
	S.D.	21.3	21.4	23.5	29.1	13.7	
HBM 1000 mg/kg	n	12	12	12	12	12	
	Mean	264.6	307.6	348.8	434.2	169.6	
	S.D.	16.2	15.5	18.6	20.3	11.3	

Not significantly different from HBM 0 mg/kg

Table 8 - 4

Study No. : SR17144

Test article Dose	Sex : Female /Day	Period : F0 lactation Day 0-4			Unit : g	Species : Rat
		0	4	Body weight gain		
HBM 0 mg/kg	n	12	12	12		
	Mean	328.9	349.9	21.0		
	S.D.	26.5	26.4	10.7		
HBM 100 mg/kg	n	12	12	12		
	Mean	318.3	341.5	23.3		
	S.D.	17.7	18.6	8.2		
HBM 300 mg/kg	n	11	11	11		
	Mean	319.4	344.6	25.3		
	S.D.	22.8	22.3	9.3		
HBM 1000 mg/kg	n	12	12	12		
	Mean	331.3	348.2	16.8		
	S.D.	19.3	16.8	9.9		

Not significantly different from HBM 0 mg/kg

Table 8 - 5

Study No. : SR17144

Test article Dose	Body weight Sex : Female (satellite) /Day	Period : Administration Day 1-28						Unit : g	Species : Rat
		1	4	7	14	21	28		
HBM 0 mg/kg	n Mean S.D.	10 235.0 9.1	10 237.0 7.6	10 244.7 9.2	10 258.4 13.2	10 269.9 11.9	10 276.6 11.4	10 41.6 11.1	
HBM 1000 mg/kg	n Mean S.D.	10 233.7 7.9	10 238.0 8.7	10 242.7 11.5	10 256.9 14.3	10 268.9 13.8	10 272.9 15.9	10 39.2 10.4	

Not significantly different from HBM 0 mg/kg

Table 8 - 6

Study No. : SR17144

Test article Dose	Body weight Sex : Male /Day	Period : Recovery Day 1-14			Unit : g	Species : Rat
		1	7	14		
HBM	n	5	5	5	5	
0 mg/kg	Mean	469.0	491.6	504.6	35.6	
	S.D.	8.0	10.2	13.2	8.8	
HBM	n	5	5	5	5	
1000 mg/kg	Mean	466.6	488.2	501.6	35.0	
	S.D.	12.4	8.8	6.8	11.3	

Not significantly different from HBM 0 mg/kg

Table 8 - 7

Study No. : SR17144

Test article Dose	Body weight Sex : Female (satellite)		Period : Recovery Day 1-14			Unit : g	Species : Rat
	/Day		1	7	14	Body weight gain	
HBM 0 mg/kg	n	5	5	5	5	5	
	Mean	275.8	284.2	296.4	20.6		
	S.D.	11.9	14.5	14.9	6.4		
HBM 1000 mg/kg	n	5	5	5	5		
	Mean	275.0	289.6	309.0	34.0		
	S.D.	19.8	20.0	29.3	20.8		

Not significantly different from HBM 0 mg/kg

Table 9 - 1

Study No. : SR17144

Test article	Food consumption Sex : Male /Day	Period : Administration Day 1-28				Unit : g	Species : Rat
		4	7	14	28		
HBM	n	12	12	12	12		
0 mg/kg	Mean	27.15	26.73	27.17	27.37		
	S.D.	1.96	1.75	1.96	1.67		
HBM	n	12	12	12	12		
100 mg/kg	Mean	27.54	27.91	27.88	28.01		
	S.D.	1.91	1.83	1.27	1.78		
HBM	n	12	12	12	12		
300 mg/kg	Mean	27.36	26.99	27.82	28.23		
	S.D.	2.27	2.04	1.73	1.38		
HBM	n	12	12	12	12		
1000 mg/kg	Mean	26.83	27.38	27.79	28.28		
	S.D.	2.76	2.75	2.82	2.76		

Not significantly different from HBM 0 mg/kg

Table 9 - 2

Study No. : SR17144

Test article	Sex : Female	Food consumption /Day			Period : F0 before mating Day 1-14	Unit : g	Species : Rat
		4	7	14			
HBM	n	12	12	12			
0 mg/kg	Mean	17.95	19.58	19.68			
	S.D.	1.83	2.24	1.33			
HBM	n	12	12	12			
100 mg/kg	Mean	18.43	19.21	19.43			
	S.D.	1.63	1.50	1.13			
HBM	n	12	12	12			
300 mg/kg	Mean	18.08	19.53	20.14			
	S.D.	1.78	1.48	2.36			
HBM	n	12	12	12			
1000 mg/kg	Mean	19.12	19.43	19.74			
	S.D.	2.21	1.62	1.45			

Not significantly different from HBM 0 mg/kg

Table 9 - 3

Study No. : SR17144

Test article	Food consumption Sex : Female /Day	Period : F0 gestation Day 0-20			Unit : g	Species : Rat
		7	14	20		
HBM	n	12	12	12		
0 mg/kg	Mean	24.30	26.24	26.38		
	S.D.	1.71	2.22	1.83		
HBM	n	12	12	12		
100 mg/kg	Mean	24.22	26.45	25.22		
	S.D.	1.58	2.16	1.82		
HBM	n	11	11	11		
300 mg/kg	Mean	25.20	27.20	26.53		
	S.D.	2.49	2.74	2.02		
HBM	n	12	12	12		
1000 mg/kg	Mean	25.13	27.96	26.40		
	S.D.	1.45	1.67	1.57		

Not significantly different from HBM 0 mg/kg

Table 9 - 4

Study No. : SR17144

Test article	Food consumption		Period : F0 lactation Day 0-4	Unit : g	Species : Rat
	Sex : Female	/Day			
Dose		4			
HBM	n	12			
0 mg/kg	Mean	35.48			
	S.D.	3.32			
HBM	n	12			
100 mg/kg	Mean	34.99			
	S.D.	5.06			
HBM	n	11			
300 mg/kg	Mean	35.50			
	S.D.	3.26			
HBM	n	12			
1000 mg/kg	Mean	35.27			
	S.D.	4.46			

Not significantly different from HBM 0 mg/kg

Table 9 - 5

Study No. : SR17144

Test article	Food consumption Sex : Female (satellite)	Period : Administration Day 1-28					Unit : g	Species : Rat
		/Day	4	7	14	21		
HBM		n	10	10	10	10	10	
0 mg/kg	Mean	18.41	19.70	20.49	20.20	20.47		
	S.D.	1.37	1.49	1.30	1.25	1.63		
HBM		n	10	10	10	10	10	
1000 mg/kg	Mean	18.04	19.23	19.80	19.33	18.83		
	S.D.	1.77	1.92	1.30	1.55	1.86		

Not significantly different from HBM 0 mg/kg

Table 9 - 6

Study No. : SR17144

Test article	Food consumption		Period : Recovery Day 1-14	Unit : g	Species : Rat
	Sex : Male	/Day			
Dose			7	14	
HBM	n		5	5	
0 mg/kg	Mean	26.92	26.22		
	S.D.	2.14	1.99		
HBM	n		5	5	
1000 mg/kg	Mean	27.44	26.92		
	S.D.	1.18	1.18		

Not significantly different from HBM 0 mg/kg

Table 9 - 7

Study No. : SR17144

Test article	Food consumption Sex : Female (satellite)		Period : Recovery Day 1-14	Unit : g	Species : Rat
	/Day				
Dose			7	14	
HBM	n	5		5	
0 mg/kg	Mean	19.96		19.92	
	S.D.	1.75		1.56	
HBM	n	5		5	
1000 mg/kg	Mean	20.26		21.88	
	S.D.	1.79		4.70	

Not significantly different from HBM 0 mg/kg

Table 10 - 1

Study No. : SR17144

Urinary findings

Sex : Male

Stage : Week 4

Species : Rat

		pH								
Test article	Dose	5.0	6.0	6.5	7.0	7.5	8.0	8.5		
HBM	n	5.0	0	0	0	0	1	4		
0 mg/kg										
HBM	n	0	0	0	0	1	0	4		
100 mg/kg										
HBM	n	0	0	0	2	0	0	3		
300 mg/kg										
HBM	n	0	4	1	0	0	0	0		
1000 mg/kg										
ST \$										
Protein										
Test article	Dose	-	±	+	2+	3+	-	+	2+	3+
HBM	n	-	0	1	2	2	0	5	0	0
0 mg/kg										
HBM	n	0	0	2	3	0	5	0	0	0
100 mg/kg										
HBM	n	0	0	5	0	0	5	0	0	0
300 mg/kg										
HBM	n	0	0	4	0	1	5	0	0	0
1000 mg/kg										

Significantly different from HBM 0 mg/kg: \$ P<0.05  
 ST : Steel test (two-side)

Table 10 - 2

Study No. : SR17144

Urinary findings

Sex : Male

Stage : Week 4

Species : Rat

Test article Dose	n	Ketone body						Urobilinogen					
		-	±	+	2+	3+	0.1	1	2	0	4	8	0
HBM 0 mg/kg	n	5	0	0	0	0	0.1	5	1	0	2	0	0
HBM 100 mg/kg	n	5	0	0	0	0	0	5	0	0	0	0	0
HBM 300 mg/kg	n	5	0	0	0	0	0	5	0	0	0	0	0
HBM 1000 mg/kg	n	5	0	0	0	0	0	5	0	0	0	0	0
<hr/>													
Bilirubin													
Test article Dose	n	-					Occult blood						
		-	±	+	2+	3+	-	±	+	2+	3+	0	0
HBM 0 mg/kg	n	5	0	0	0	0	0	5	0	0	0	0	0
HBM 100 mg/kg	n	5	0	0	0	0	0	5	0	0	0	0	0
HBM 300 mg/kg	n	5	0	0	0	0	0	5	0	0	0	0	0
HBM 1000 mg/kg	n	5	0	0	0	0	4	0	0	0	0	0	1
<hr/>													
Not significantly different from HBM 0 mg/kg													

Table 10 - 3

Study No. : SR17144

Urinary findings Sex : Male		Stage : Week 4				Species : Rat
		Color				
Test article	Dose	A	B	C	D	
HBM	n	5	0	0	0	
0 mg/kg						
HBM	n	5	0	0	0	
100 mg/kg						
HBM	n	5	0	0	0	
300 mg/kg						
HBM	n	5	0	0	0	
1000 mg/kg						

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

Not significantly different from HBM 0 mg/kg

Table 10 - 4

Study No. : SR17144

Urinary findings Sex : Male		Stage : Week 4	Species : Rat
Urine volume			
Test article		mL/21hr	
Dose			
HBM	n	5	
0 mg/kg	Mean	12.20	
	S.D.	5.32	
HBM	n	5	
100 mg/kg	Mean	10.50	
	S.D.	2.32	
HBM	n	5	
300 mg/kg	Mean	13.00	
	S.D.	2.42	
HBM	n	5	
1000 mg/kg	Mean	17.70	
	S.D.	1.75	
		DT *	

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

DT : Dunnett test (two-side)

Table 10 - 5

Study No. : SR17144

Urinary findings Sex : Male		Stage : Week 4							Species : Rat	
		Specific gravity								
<b>Test article</b>										
Dose		0	1	2	3	4	5			
HBM	n	0	0	0	1	1	3			
0 mg/kg										
HBM	n	0	0	0	0	0	5			
100 mg/kg										
HBM	n	0	0	0	0	1	4			
300 mg/kg										
HBM	n	0	0	0	0	5	0			
1000 mg/kg										
RBC										
Dose		-	±	+	2+	3+		-	±	+
HBM	n	5	0	0	0	0		5	0	0
0 mg/kg										
HBM	n	5	0	0	0	0		5	0	0
100 mg/kg										
HBM	n	5	0	0	0	0		5	0	0
300 mg/kg										
HBM	n	4	0	0	0	1		5	0	0
1000 mg/kg										

Specific gravity) 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 HBM 0 mg/kg

Table 10 - 6

Study No. : SR17144

Urinary findings Sex : Male		Stage : Week 4							Species : Rat				
		Squamous							Round				
Test article	Dose	-	±	+	2+	3+	0	-	±	+	2+	3+	0
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
0 mg/kg													
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
100 mg/kg													
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
300 mg/kg													
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
1000 mg/kg													
<hr/>													
Small round													
Test article	Dose	-	±	+	2+	3+	0	-	±	+	2+	3+	0
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
0 mg/kg													
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
100 mg/kg													
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
300 mg/kg													
HBM	n	5	0	0	0	0	0	5	0	0	0	0	0
1000 mg/kg													
<hr/>													
Not significantly different from HBM 0 mg/kg													

Table 10 - 7

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Week 4								Species : Rat											
		pH																			
<b>Test article</b>																					
<b>Dose</b>																					
HBM	n	5.0	0	6.0	0	6.5	0	7.0	0	7.5	0										
0 mg/kg											8.0										
											8.5										
HBM	n	0		5		0		0		0											
1000 mg/kg											0										
<b>W2 \$\$</b>																					
<b>Protein</b>																					
<b>Glucose</b>																					
<b>Test article</b>																					
<b>Dose</b>																					
HBM	n	-	±	+	2+	3+	-	+	2+	3+											
0 mg/kg		3		1	1	0	0	5	0	0	0										
HBM	n	1		1	3	0	0	5	0	0	0										
1000 mg/kg											0										
<b>Ketone body</b>																					
<b>Urobilinogen</b>																					
<b>EU/dL</b>																					
<b>Test article</b>																					
<b>Dose</b>																					
HBM	n	-	±	+	2+	3+	0.1	1	2	4	8										
0 mg/kg		5		0	0	0	5	0	0	0	0										
HBM	n	5		0	0	0	0	5	0	0	0										
1000 mg/kg											0										

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

W2 : Wilcoxon rank sum test (two-side)

Table 10 - 8

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Week 4										Species : Rat	
Test article	Dose	Bilirubin					Occult blood						
		-	+	2+	3+	0	-	±	1	+	2+		
HBM	n	-	5	0	0	0	-	4	1	0	0	0	0
0 mg/kg													
HBM	n	5	0	0	0	0	4	1	0	0	0	0	0
1000 mg/kg													
Color													
Test article	Dose	A      B      C      D											
		A	B	C	D								
HBM	n	5	0	0	0								
0 mg/kg													
HBM	n	5	0	0	0								
1000 mg/kg													

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

Not significantly different from HBM 0 mg/kg

Table 10 - 9

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Week 4	Species : Rat
Urine volume			
Test article		mL/21hr	
Dose			
HBM	n	5	
0 mg/kg	Mean	12.80	
	S.D.	5.29	
HBM	n	5	
1000 mg/kg	Mean	11.50	
	S.D.	8.67	

Not significantly different from HBM 0 mg/kg

Table 10 - 10

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Week 4							Species : Rat			
		Specific gravity										
Test article	Dose	0	1	2	3	4	5					
HBM	n	0	0	0	2	2	4	2				
0 mg/kg												
HBM	n	0	0	0	1	1	1	3				
1000 mg/kg												
RBC												
Test article	Dose	-	±	+	2+	3+		-	±	+	2+	3+
HBM	n	-	4	1	0	0	0	-	5	0	0	0
0 mg/kg												
HBM	n	-	4	1	0	0	0	-	5	0	0	0
1000 mg/kg												
WBC												
Test article	Dose	-	±	+	2+	3+		-	±	+	2+	3+
HBM	n	-	4	1	0	0	0	-	5	0	0	0
0 mg/kg												
HBM	n	-	4	1	0	0	0	-	5	0	0	0
1000 mg/kg												
Squamous												
Test article	Dose	-	±	+	2+	3+		-	±	+	2+	3+
HBM	n	-	5	0	0	0	0	-	5	0	0	0
0 mg/kg												
HBM	n	-	5	0	0	0	0	-	5	0	0	0
1000 mg/kg												
Round												
Test article	Dose	-	±	+	2+	3+		-	±	+	2+	3+
HBM	n	-	5	0	0	0	0	-	5	0	0	0
0 mg/kg												
HBM	n	-	5	0	0	0	0	-	5	0	0	0
1000 mg/kg												

Specific gravity) 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 HBM 0 mg/kg

Table 10 - 11

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Week 4						Species : Rat					
		Small round						Cast					
Test article	Dose	-	±	+	2+	3+	-	±	+	2+	3+		
HBM	n	-	5	0	0	0	-	5	0	0	0		
0 mg/kg													
HBM	n	5	0	0	0	0	5	0	0	0	0		
1000 mg/kg													

Not significantly different from HBM 0 mg/kg

Table 10 - 12

Study No. : SR17144

Urinary findings		Stage : Recovery Week 2								Species : Rat	
Sex : Male		pH									
<b>Test article</b>											
Dose		5.0	6.0	6.5	7.0	7.5	8.0	8.5			
HBM	n	0	0	0	0	0	0	5			
0 mg/kg											
HBM	n	0	0	0	0	0	0	5			
1000 mg/kg											
Protein											
Dose		-	±	+	2+	3+	-	+	2+	3+	
HBM	n	0	1	3	1	0	5	0	0	0	
0 mg/kg											
HBM	n	0	1	3	1	0	5	0	0	0	
1000 mg/kg											
Ketone body											
Dose		-	±	+	2+	3+	0.1	1	2	4	8
HBM	n	5	0	0	0	0	5	0	0	0	0
0 mg/kg											
HBM	n	5	0	0	0	0	5	0	0	0	0
1000 mg/kg											
 <hr/>											
Not significantly different from HBM 0 mg/kg											

Table 10 - 13

Study No. : SR17144

Urinary findings Sex : Male		Stage : Recovery Week 2										Species : Rat		
		Bilirubin					Occult blood							
Test article	Dose	-	+	2+	3+	-	±	+	2+	3+	-	+	2+	3+
HBM	n	-	5	0	0	0	-	5	0	0	-	0	0	0
0 mg/kg														
HBM	n	5	0	0	0	0	5	0	0	0	0	0	0	0
1000 mg/kg														
Color														
Test article	Dose	A	B	C	D									
HBM	n	5	0	0	0									
0 mg/kg														
HBM	n	5	0	0	0	0								
1000 mg/kg														

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

Not significantly different from HBM 0 mg/kg

Table 10 - 14

Study No. : SR17144

Urinary findings Sex : Male		Stage : Recovery Week 2	Species : Rat
Urine volume			
Test article		mL/21hr	
Dose			
HBM	n	5	
0 mg/kg	Mean	11.00	
	S.D.	2.45	
HBM	n	5	
1000 mg/kg	Mean	11.10	
	S.D.	0.65	

Not significantly different from HBM 0 mg/kg

Table 10 - 15

Study No. : SR17144

Urinary findings Sex : Male		Stage : Recovery Week 2							Species : Rat		
		Specific gravity									
<b>Test article</b>											
Dose		0	1	2	3	4	5				
HBM	n	0	0	0	0	1	4				
0 mg/kg											
HBM	n	0	0	0	0	1	4				
1000 mg/kg											
RBC											
Dose		-	±	+	2+	3+		-	±	+	2+
HBM	n	5	0	0	0	0		5	0	0	0
0 mg/kg											
HBM	n	5	0	0	0	0		5	0	0	0
1000 mg/kg											
Squamous											
Dose		-	±	+	2+	3+		-	±	+	2+
HBM	n	4	1	0	0	0		5	0	0	0
0 mg/kg											
HBM	n	3	2	0	0	0		5	0	0	0
1000 mg/kg											

Specific gravity) 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 HBM 0 mg/kg

Table 10 - 16

Study No. : SR17144

Test article Dose	Sex : Male	Stage : Recovery Week 2						Species : Rat									
		Small round			Cast												
	n	-	±	0	+	2+	0	3+	0	-	±	0	+	2+	0	3+	0
HBM 0 mg/kg																	
HBM 1000 mg/kg	n	5		0		0		0		5		0		0		0	

Not significantly different from HBM 0 mg/kg

Table 10 - 17

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2								Species : Rat	
		pH									
<b>Test article</b>											
Dose		5.0	6.0	6.5	7.0	7.5	8.0	8.5			
HBM	n	0	0	0	0	0	1	4			
0 mg/kg											
HBM	n	0	0	0	0	0	0	5			
1000 mg/kg											
Protein											
Dose		-	±	+	2+	3+		-	+	2+	3+
HBM	n	0	3	2	0	0		5	0	0	0
0 mg/kg											
HBM	n	1	1	3	0	0		5	0	0	0
1000 mg/kg											
Ketone body											
Dose		-	±	+	2+	3+		0.1	1	2	4
HBM	n	5	0	0	0	0		5	0	0	0
0 mg/kg											
HBM	n	5	0	0	0	0		5	0	0	0
1000 mg/kg											
 <hr/>											
Not significantly different from HBM 0 mg/kg											

Table 10 - 18

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2										Species : Rat	
		Bilirubin					Occult blood						
Test article	Dose	-	+	2+	3+	0	-	±	0	+	2+	3+	0
HBM	n	-	5	0	0	0	-	5	0	0	0	0	0
0 mg/kg													
HBM	n	5	0	0	0	0	5	0	0	0	0	0	0
1000 mg/kg													
<hr/>													
Color													
Test article	Dose	A	B	C	D	0	0	0	0	0	0	0	0
HBM	n	5	0	0	0	0	0	0	0	0	0	0	0
0 mg/kg													
HBM	n	5	0	0	0	0	0	0	0	0	0	0	0
1000 mg/kg													

Color) A : Pale yellow or yellow, B : Orange yellow, C : Red brown, D : Creamy white  
 Not significantly different from HBM 0 mg/kg

Table 10 - 19

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2	Species : Rat
Urine volume			
Test article		mL/21hr	
Dose			
HBM	n	5	
0 mg/kg	Mean	10.10	
	S.D.	2.33	
HBM	n	5	
1000 mg/kg	Mean	16.00	
	S.D.	6.50	

Not significantly different from HBM 0 mg/kg

Table 10 - 20

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2							Species : Rat		
		Specific gravity									
Test article	Dose	0	1	2	3	4	5				
HBM	n	0	0	0	0	3	4	3	2	2	2
0 mg/kg											
HBM	n	0	0	0	2	2	2	1			
1000 mg/kg											
RBC											
Test article	Dose	-	±	+	2+	3+		-	±	+	2+
HBM	n	-	5	0	0	0	0	-	5	0	0
0 mg/kg											
HBM	n	-	5	0	0	0	0	-	5	0	0
1000 mg/kg											
WBC											
Test article	Dose	-	±	+	2+	3+		-	±	+	2+
HBM	n	-	5	0	0	0	0	-	5	0	0
0 mg/kg											
HBM	n	-	5	0	0	0	0	-	5	0	0
1000 mg/kg											
Squamous											
Test article	Dose	-	±	+	2+	3+		-	±	+	2+
HBM	n	-	3	1	1	0	0	-	5	0	0
0 mg/kg											
HBM	n	-	2	3	0	0	0	-	5	0	0
1000 mg/kg											
Round											
Test article	Dose	-	±	+	2+	3+		-	±	+	2+
HBM	n	-	5	0	0	0	0	-	5	0	0
0 mg/kg											
HBM	n	-	5	0	0	0	0	-	5	0	0
1000 mg/kg											

Specific gravity) 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 HBM 0 mg/kg

Table 10 - 21

Study No. : SR17144

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2						Species : Rat						
		Small round						Cast						
Test article	Dose	-	±	0	+	2+	3+	-	±	0	+	2+	3+	0
HBM	n			5	0	0	0			5	0	0	0	0
0 mg/kg														
HBM	n			5	0	0	0			5	0	0	0	0
1000 mg/kg														

Not significantly different from HBM 0 mg/kg

Table 11 - 1

Study No. : SR17144

	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												
HBM	n	5	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	870.0	15.90	44.12	50.70	18.26	36.04	3.082	104.52	78.48	14.04	
	S.D.	23.3	0.66	2.02	1.24	0.52	0.48	0.547	4.27	17.37	7.46	
HBM	n	5	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	867.6	15.86	44.18	50.92	18.30	35.88	3.436	110.92	89.66	17.96	
	S.D.	25.5	0.40	1.31	1.06	0.28	0.30	0.675	14.21	26.38	10.18	
HBM	n	5	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	854.8	15.24	42.34	49.56	17.84	35.98	3.988	109.38	78.18	14.80	
	S.D.	24.3	0.17	0.44	1.13	0.50	0.18	0.422	11.54	4.31	1.72	
								DT *				
HBM	n	5	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	879.8	16.04	44.54	50.68	18.26	36.02	3.262	101.62	92.60	15.18	
	S.D.	31.0	0.23	0.51	1.54	0.46	0.23	0.495	11.95	40.61	6.92	
			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												
HBM	n	5	5	5	5	5	5	5				
0 mg/kg	Mean	60.22	3.42	0.78	0.02	22.02	18.88					
	S.D.	10.13	0.83	0.22	0.04	2.33	0.85					
HBM	n	5	5	5	5	5	5	5				
100 mg/kg	Mean	66.86	3.76	1.04	0.04	21.50	18.54					
	S.D.	20.53	2.25	0.44	0.05	0.63	1.89					
HBM	n	5	5	5	5	5	5	5				
300 mg/kg	Mean	59.50	2.80	1.06	0.02	21.26	18.66					
	S.D.	4.54	0.84	0.38	0.04	3.16	0.44					
HBM	n	5	5	5	5	5	5	5				
1000 mg/kg	Mean	73.46	3.06	0.88	0.02	22.32	18.28					
	S.D.	33.53	0.44	0.19	0.04	5.73	2.21					

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

DT : Dunnett test (two-side)

Table 11 - 2

Study No. : SR17144

Sex : Female	Hematological findings							Stage : Day 5 after delivery			Species : Rat
	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	
HBM 0 mg/kg	n 5 Mean 748.6 S.D. 25.0	5 14.76 0.30	5 42.82 1.25	5 57.22 0.29	5 19.72 0.26	5 34.50 0.35	5 9.216 0.768	5 105.94 5.57	5 78.28 25.89	5 27.10 16.68	
HBM 100 mg/kg	n 5 Mean 753.4 S.D. 36.5	5 14.46 0.52	5 41.64 1.51	5 55.30 1.15	5 19.22 0.41	5 34.74 0.18	5 7.312 1.111	5 110.78 14.53	5 89.16 23.25	5 26.50 13.61	
HBM 300 mg/kg	n 5 Mean 731.2 S.D. 50.4	5 14.20 0.70	5 40.88 1.51	5 56.06 3.21	5 19.46 0.91	5 34.72 0.52	5 9.068 4.003	5 115.60 12.87	5 95.36 23.01	5 31.60 18.92	
HBM 1000 mg/kg	n 5 Mean 787.4 S.D. 17.7	5 15.06 0.78	5 42.82 2.18	5 54.40 2.31	5 19.12 0.75	5 35.16 0.48	5 8.254 1.363	5 121.98 22.78	5 75.10 15.18	5 23.44 6.45	
							ST *				
	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					
HBM 0 mg/kg	n 5 Mean 46.14 S.D. 8.36	5 4.26 2.17	5 0.72 0.26	5 0.06 0.05	5 16.38 0.69	5 13.54 1.36					
HBM 100 mg/kg	n 5 Mean 59.58 S.D. 17.59	5 2.22 1.04	5 0.82 0.41	5 0.04 0.05	5 16.34 1.00	5 13.82 1.19					
HBM 300 mg/kg	n 5 Mean 59.36 S.D. 6.75	5 3.44 1.17	5 0.94 0.33	5 0.02 0.04	5 16.46 0.77	5 13.58 1.14					
HBM 1000 mg/kg	n 5 Mean 47.08 S.D. 15.19	5 3.44 1.53	5 1.12 0.68	5 0.02 0.04	5 16.54 0.68	5 13.28 1.81					

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

ST : Steel test (two-side)

Table 11 - 3

Study No. : SR17144

Hematological findings 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	g/dL	%	fL	pg	g/dL	%	10 <sup>4</sup> /µL	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL
Dose											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	801.4	15.32	42.12	52.56	19.12	36.36	3.424	116.48	65.08	10.76
	S.D.	18.7	0.33	0.95	0.29	0.08	0.05	0.508	18.96	17.38	8.53
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	822.0	15.54	42.80	52.08	18.92	36.30	3.260	103.02	63.08	7.00
	S.D.	15.5	0.53	1.33	0.97	0.40	0.16	0.346	15.34	14.85	2.92
<hr/>											
		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											
HBM	n	5	5	5	5	5	5				
0 mg/kg	Mean	51.00	2.36	0.94	0.02	14.80	11.50				
	S.D.	15.00	0.60	0.38	0.04	0.52	1.62				
HBM	n	5	5	5	5	5	5				
1000 mg/kg	Mean	52.78	1.80	0.92	0.00	14.72	11.72				
	S.D.	15.86	0.64	0.22	0.00	0.65	1.02				

Not significantly different from HBM 0 mg/kg

Table 11 - 4

Study No. : SR17144

	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
HBM	n	5	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	863.4	15.64	44.16	51.22	18.14	35.44	3.204	102.24	78.54	13.50	
	S.D.	53.8	0.86	2.55	2.46	0.72	0.33	0.487	7.12	7.14	5.82	
HBM	n	5	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	843.6	15.14	42.50	50.42	17.94	35.62	3.024	98.12	74.58	14.06	
	S.D.	24.0	0.42	1.19	1.83	0.59	0.16	0.761	7.37	16.50	6.15	
			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				
HBM	n	5	5	5	5	5	5	5				
0 mg/kg	Mean	61.20	2.76	1.02	0.06	19.78	18.04					
	S.D.	9.87	0.54	0.36	0.05	3.40	1.78					
HBM	n	5	5	5	5	5	5	5				
1000 mg/kg	Mean	56.00	3.24	1.26	0.02	19.26	18.20					
	S.D.	9.93	1.02	0.56	0.04	2.84	1.24					

Not significantly different from HBM 0 mg/kg

Table 11 - 5

Study No. : SR17144

Hematological findings Sex : Female (satellite)		Stage : Recovery Day 15							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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	832.6	15.06	42.24	50.74	18.08	35.64	3.280	112.48	45.22	7.56
	S.D.	32.7	0.54	1.38	0.54	0.16	0.25	0.411	13.38	10.18	1.76
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	826.0	15.40	42.76	51.76	18.64	36.04	3.216	97.52	45.94	7.86
	S.D.	20.8	0.31	0.96	0.62	0.17	0.22	0.637	9.10	19.62	4.58
					T2 *	T2 **	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											
HBM	n	5	5	5	5	5	5				
0 mg/kg	Mean	35.92	1.06	0.68	0.00	15.08	12.68				
	S.D.	8.46	0.19	0.27	0.00	0.92	1.15				
HBM	n	5	5	5	5	5	5				
1000 mg/kg	Mean	35.82	1.34	0.92	0.00	14.96	11.72				
	S.D.	14.78	0.76	0.47	0.00	0.86	1.03				

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

T2 : Student t-test (two-side)

Table 12 - 1

Study No. : SR17144

Biochemical findings Sex : Male		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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	64.0	27.4	429.0	0.50	0.066	6.20	161.0	51.6	29.0	5.46
	S.D.	2.6	3.6	68.0	0.24	0.005	3.10	11.4	3.7	23.1	0.15
HBM	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	67.8	29.2	453.2	0.58	0.072	8.04	163.2	53.8	23.2	5.44
	S.D.	10.7	5.6	32.0	0.19	0.011	3.31	23.7	9.0	6.9	0.21
HBM	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	61.0	26.0	463.2	0.48	0.074	7.84	162.8	53.4	41.8	5.32
	S.D.	5.7	1.2	96.6	0.16	0.021	3.11	15.5	8.2	24.5	0.19
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	66.4	27.2	479.4	0.46	0.076	6.40	151.0	50.0	25.8	5.20
	S.D.	9.7	2.2	47.8	0.18	0.005	4.39	7.5	9.2	10.6	0.19
<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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	13.84	0.300	145.2	4.420	104.8	9.20	6.32	0.944	2.650	48.50
	S.D.	1.65	0.035	1.3	0.167	1.1	0.21	0.76	0.063	0.126	1.67
HBM	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	12.94	0.294	144.4	4.568	104.8	9.18	6.34	0.956	2.644	48.68
	S.D.	1.47	0.027	0.5	0.228	0.8	0.29	0.47	0.128	0.163	3.45
HBM	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	12.10	0.278	144.8	4.604	105.2	9.12	6.86	0.990	2.644	49.70
	S.D.	0.88	0.022	1.3	0.174	1.6	0.23	0.71	0.109	0.137	2.70
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	12.14	0.258	145.0	4.492	104.4	9.22	6.60	1.066	2.684	51.62
	S.D.	1.56	0.033	1.0	0.122	0.5	0.36	0.51	0.022	0.089	0.54

Not significantly different from HBM 0 mg/kg

Table 12 - 2

Study No. : SR17144

Sex : Male	Biochemical findings				Stage : Day 29	Species : Rat
	$\alpha$ 1-G	$\alpha$ 2-G	$\beta$ -G	$\gamma$ -G		
Test article		%	%	%	%	
Dose						
HBM	n	5	5	5	5	
0 mg/kg	Mean	23.58	9.06	15.04	3.82	
	S.D.	0.91	0.48	1.37	1.79	
HBM	n	5	5	5	5	
100 mg/kg	Mean	21.26	9.04	16.54	4.48	
	S.D.	0.68	1.32	1.87	0.71	
HBM	n	5	5	5	5	
300 mg/kg	Mean	20.88	8.86	15.78	4.78	
	S.D.	2.21	1.13	1.08	0.70	
	DT *					
HBM	n	5	5	5	5	
1000 mg/kg	Mean	20.34	8.56	15.70	3.78	
	S.D.	1.88	0.95	0.97	0.78	
	DT *					

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

DT : Dunnett test (two-side)

Table 12 - 3

Study No. : SR17144

Biochemical findings Sex : Female		Stage : Day 5 after delivery							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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	92.8	42.8	187.8	0.56	0.060	20.60	141.4	58.0	32.2	5.70
	S.D.	19.6	3.7	18.7	0.11	0.012	10.62	13.6	14.3	14.0	0.34
HBM	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	105.6	47.4	183.8	0.58	0.052	18.20	142.2	61.0	34.8	5.82
	S.D.	35.9	10.5	40.7	0.13	0.011	11.74	16.6	8.0	19.6	0.19
HBM	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	72.4	38.2	221.4	0.86	0.048	15.60	147.2	57.2	50.0	5.76
	S.D.	9.9	7.9	90.3	0.26	0.011	5.88	18.5	9.4	64.0	0.23
DT *											
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	89.8	45.8	269.6	0.74	0.060	27.74	144.4	67.2	44.4	5.66
	S.D.	28.9	10.5	130.3	0.15	0.012	21.52	18.4	21.0	17.5	0.21
UN	mg/dL	mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	g/dL	g/dL	%
Test article											
Dose											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	14.76	0.318	143.4	4.616	105.4	10.12	7.66	0.916	2.720	47.66
	S.D.	3.93	0.036	0.5	0.226	1.1	0.27	0.97	0.098	0.261	2.63
HBM	n	5	5	5	5	5	5	5	5	5	5
100 mg/kg	Mean	17.50	0.326	143.2	4.672	104.0	10.22	8.34	0.924	2.792	47.98
	S.D.	2.82	0.026	0.8	0.170	1.0	0.44	0.74	0.091	0.123	2.51
HBM	n	5	5	5	5	5	5	5	5	5	5
300 mg/kg	Mean	14.88	0.300	142.4	4.726	103.2	10.14	7.94	0.968	2.826	49.08
	S.D.	2.09	0.021	0.9	0.118	2.5	0.39	0.36	0.091	0.129	2.33
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	17.10	0.320	142.6	4.764	103.4	10.36	8.48	0.888	2.662	47.02
	S.D.	3.62	0.025	1.5	0.321	1.5	0.55	0.92	0.039	0.086	1.09

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

DT : Dunnett test (two-side)

Table 12 - 4

Study No. : SR17144

	Biochemical findings		Stage : Day 5 after delivery		Species : Rat		
	Sex : Female		α1-G	α2-G	β-G	γ-G	
Test article		%		%	%	%	
Dose							
HBM	n	5	5	5	5	5	
0 mg/kg	Mean	20.80	10.96	16.82	3.76		
	S.D.	1.97	0.50	0.44	0.72		
HBM	n	5	5	5	5	5	
100 mg/kg	Mean	20.16	11.32	16.98	3.56		
	S.D.	1.79	1.36	1.10	0.84		
HBM	n	5	5	5	5	5	
300 mg/kg	Mean	20.80	10.58	16.14	3.40		
	S.D.	1.26	0.78	1.78	0.60		
HBM	n	5	5	5	5	5	
1000 mg/kg	Mean	19.92	11.74	16.92	4.40		
	S.D.	2.36	1.98	0.95	0.80		

Not significantly different from HBM 0 mg/kg

Table 12 - 5

Study No. : SR17144

Biochemical findings 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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	60.6	24.8	214.2	0.58	0.096	23.66	147.0	64.4	12.2	5.96
	S.D.	4.0	3.3	32.9	0.19	0.018	22.43	24.5	8.6	4.0	0.23
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	66.0	25.0	194.8	0.76	0.088	10.68	146.8	67.0	12.8	6.02
	S.D.	24.3	8.2	88.8	0.34	0.022	5.04	13.7	7.7	4.3	0.47
		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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	16.42	0.336	142.8	4.306	103.2	9.74	6.44	1.180	3.226	54.14
	S.D.	2.08	0.034	1.8	0.251	1.8	0.27	0.55	0.057	0.144	1.13
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	15.30	0.340	143.6	4.372	102.8	9.84	6.36	1.212	3.294	54.70
	S.D.	1.65	0.032	0.9	0.261	1.5	0.36	0.34	0.092	0.316	1.83
		α1-G	α2-G	β-G	γ-G						
Test article		%	%	%	%						
Dose											
HBM	n	5	5	5	5						
0 mg/kg	Mean	18.26	7.84	14.26	5.50						
	S.D.	1.26	0.54	0.69	1.31						
HBM	n	5	5	5	5						
1000 mg/kg	Mean	17.02	8.38	14.42	5.48						
	S.D.	2.34	0.71	1.92	1.00						

Not significantly different from HBM 0 mg/kg

Table 12 - 6

Study No. : SR17144

Biochemical findings 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	g/dL
Dose										
HBM	n	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	62.4	27.4	365.2	0.26	0.070	9.16	159.2	46.6	23.2
	S.D.	3.8	4.4	80.3	0.21	0.012	3.19	13.4	9.0	5.38
										0.11
HBM	n	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	66.0	28.6	371.4	0.32	0.072	9.74	153.0	45.0	16.4
	S.D.	6.1	3.8	50.7	0.18	0.019	4.47	25.3	6.2	5.26
										0.22
		UN	Crea	Na	K	Cl	Ca	IP	A/G	Albumin
Test article		mg/dL	mg/dL	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL		Albumin
Dose									g/dL	%
HBM	n	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	14.26	0.312	143.8	4.636	104.8	8.76	5.50	0.962	2.638
	S.D.	1.32	0.048	0.4	0.160	1.3	0.32	0.22	0.052	49.02
										1.33
HBM	n	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	15.12	0.326	144.8	4.456	105.2	9.08	5.92	0.950	2.560
	S.D.	1.50	0.015	0.4	0.126	0.8	0.23	0.40	0.046	48.72
										1.33
		α1-G	α2-G	β-G	γ-G					
Test article		%	%	%	%					
Dose										
HBM	n	5	5	5	5					
0 mg/kg	Mean	21.86	9.04	15.30	4.78					
	S.D.	3.55	0.83	1.57	0.77					
HBM	n	5	5	5	5					
1000 mg/kg	Mean	21.48	9.12	15.40	5.28					
	S.D.	2.93	1.08	0.61	1.31					

Significantly different from HBM 0 mg/kg: \*\* P&lt;0.01

T2 : Student t-test (two-side)

Table 12 - 7

Study No. : SR17144

Biochemical findings 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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	57.4	23.6	228.4	0.46	0.072	12.78	149.8	61.8	11.6	5.92
	S.D.	7.8	3.0	40.0	0.11	0.020	5.68	14.1	3.8	4.3	0.33
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	50.8	24.2	190.8	0.78	0.072	9.76	154.6	72.6	15.2	6.06
	S.D.	5.8	6.5	33.6	0.24	0.011	3.32	19.1	18.6	5.4	0.37
		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											
HBM	n	5	5	5	5	5	5	5	5	5	5
0 mg/kg	Mean	14.36	0.326	143.8	4.398	105.6	9.46	5.24	1.170	3.192	53.92
	S.D.	1.84	0.034	0.4	0.446	1.1	0.25	0.46	0.060	0.163	1.27
HBM	n	5	5	5	5	5	5	5	5	5	5
1000 mg/kg	Mean	14.82	0.326	143.0	4.636	104.6	9.60	5.40	1.254	3.372	55.56
	S.D.	0.92	0.043	1.0	0.228	0.9	0.12	1.11	0.135	0.355	2.51
		α1-G	α2-G	β-G	γ-G						
Test article		%	%	%	%						
Dose											
HBM	n	5	5	5	5						
0 mg/kg	Mean	16.02	8.92	14.34	6.80						
	S.D.	2.71	0.82	0.54	1.46						
HBM	n	5	5	5	5						
1000 mg/kg	Mean	15.74	8.82	13.72	6.16						
	S.D.	3.24	0.88	0.88	2.16						

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

T2 : Student t-test (two-side)

Table 13 - 1

Study No. : SR17144

Necropsy findings			Species : Rat		
Sex : Male		Stage : Day 29			
	Test article	HBM	HBM	HBM	HBM
	Dose	0	100	300	1000
Organ		mg/kg	mg/kg	mg/kg	mg/kg
Findings	Number of Animals	7	12	12	7
Epididymis		<7/7>	<12/12>	<11/12>	<7/7>
Yellowish white focus, cauda, unilateral	P	0	0	1	0
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. : SR17144

Necropsy findings Sex : Female		Stage : Day 5 after delivery			Species : Rat
Organ Findings	Number of Animals	HBM Dose mg/kg	HBM mg/kg	HBM mg/kg	HBM mg/kg
Glandular stomach Black focus, mucosa	P	<12/12> 0	<12/12> 0	<10/11> 1	<10/12> 2
Other organs & tissues		<12/12>	<12/12>	<11/11>	<12/12>

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

P : Non-graded change

Table 13 - 3

Study No. : SR17144

Necropsy findings		Stage : Non-pregnancy	Species : Rat
Sex : Female			
	Test article	HBM	
	Dose	300	
Organ		mg/kg	
Findings	Number of Animals	1	
All organs & tissues		<1/1>	

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

Table 13 - 4

Study No. : SR17144

Necropsy findings				Species : Rat
Sex : Female (satellite)		Stage : Day 29		
Organ	Test article	HBM	HBM	
Findings	Dose	0	1000	
All organs & tissues	Number of Animals	mg/kg	mg/kg	
		5	5	
	<5/5>		<5/5>	

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

Table 13 - 5

Study No. : SR17144

Necropsy findings				Species : Rat
Sex : Male		Stage : Recovery Day 15		
Organ Findings	Test article	HBM	HBM	
	Dose	0	1000	
		mg/kg	mg/kg	
All organs & tissues	Number of Animals	5	5	
<5/5>		<5/5>		

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

Table 13 - 6

Study No. : SR17144

Necropsy findings				Species : Rat
Sex : Female (satellite)		Stage : Recovery Day 15		
Organ	Test article	HBM	HBM	
Findings	Dose	0	1000	
All organs & tissues	Number of Animals	mg/kg	mg/kg	
		5	5	
	<5/5>		<5/5>	

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

Table 14 - 1

Study No. : SR17144

Organ weight Sex : Male		Stage : Day 29								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		
HBM	n	7	7	7	7	7	7	7	7		
0 mg/kg	Mean	438.9	11.223	2.556	3.121	0.710	1.361	0.310	697.4	158.940	
	S.D.	32.6	1.160	0.138	0.266	0.026	0.132	0.021	85.1	15.613	
HBM	n	12	12	12	12	12	12	12	12		
100 mg/kg	Mean	445.8	11.459	2.570	3.220	0.723	1.387	0.311	774.5	173.847	
	S.D.	21.9	1.049	0.189	0.192	0.051	0.150	0.028	131.9	28.675	
HBM	n	12	12	12	12	12	12	12	12		
300 mg/kg	Mean	448.8	11.431	2.542	3.398	0.758	1.423	0.316	736.3	164.085	
	S.D.	31.4	1.179	0.117	0.395	0.067	0.140	0.014	96.4	19.052	
HBM	n	7	7	7	7	7	7	7	7		
1000 mg/kg	Mean	439.0	10.966	2.486	3.367	0.767	1.414	0.324	746.9	169.189	
	S.D.	41.8	1.820	0.188	0.289	0.036	0.108	0.024	136.3	17.773	
		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
HBM	n	7	7	7	7	7	7	7	7	7	7
0 mg/kg	Mean	308.6	71.540	66.3	15.029	12.19	2.781	20.57	4.703	3.199	0.731
	S.D.	86.6	24.609	14.3	2.564	1.29	0.252	2.58	0.605	0.211	0.046
HBM	n	12	12	12	12	12	12	12	12	12	12
100 mg/kg	Mean	363.9	81.820	67.2	15.065	11.27	2.524	19.99	4.495	3.342	0.752
	S.D.	90.6	20.830	13.0	2.732	1.15	0.184	3.76	0.880	0.292	0.090
HBM	n	12	12	12	12	12	12	12	12	12	12
300 mg/kg	Mean	355.7	78.745	60.3	13.467	11.19	2.499	21.20	4.721	3.236	0.725
	S.D.	71.8	11.690	7.5	1.640	1.39	0.309	3.61	0.732	0.239	0.075
HBM	n	7	7	7	7	7	7	7	7	7	7
1000 mg/kg	Mean	383.0	87.159	65.0	14.890	11.09	2.536	20.69	4.737	3.034	0.697
	S.D.	74.6	15.393	7.3	1.902	1.47	0.348	3.19	0.833	0.200	0.056

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

Not significantly different from HBM 0 mg/kg

Table 14 - 2

Study No. : SR17144

Test article Dose	Organ weight Sex : Male		Stage : Day 29						Species : Rat	
	Epididymis		Prostate		Seminal vesicle		Brain			
	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g		
HBM	n	7	7	7	7	7	7	7		
0 mg/kg	Mean	1.220	0.279	649.3	147.969	2.039	0.464	2.183	0.500	
	S.D.	0.099	0.019	173.8	39.101	0.322	0.075	0.129	0.029	
HBM	n	12	12	12	12	12	12	12		
100 mg/kg	Mean	1.267	0.286	708.6	158.914	2.052	0.461	2.217	0.499	
	S.D.	0.085	0.027	125.1	26.273	0.324	0.073	0.063	0.027	
HBM	n	12	12	12	12	12	12	12		
300 mg/kg	Mean	1.288	0.288	684.0	153.859	2.106	0.472	2.193	0.489	
	S.D.	0.072	0.019	150.6	38.734	0.238	0.070	0.065	0.032	
HBM	n	7	7	7	7	7	7	7		
1000 mg/kg	Mean	1.217	0.279	699.3	161.046	2.124	0.487	2.136	0.490	
	S.D.	0.048	0.027	127.5	34.523	0.194	0.048	0.068	0.054	

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

Not significantly different from HBM 0 mg/kg

Table 14 - 3

Study No. : SR17144

Organ weight Sex : Female		Stage : Day 5 after delivery								Species : Rat	
		Body weight		Liver		Kidney		Heart			
Test article	Dose	n	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
HBM		n	12	12	12	12	12	12	12	12	
0 mg/kg		Mean	315.2	10.228	3.250	2.241	0.713	1.040	0.332	725.9	230.237
		S.D.	22.6	0.754	0.188	0.178	0.056	0.093	0.029	109.2	28.545
HBM		n	12	12	12	12	12	12	12	12	
100 mg/kg		Mean	308.4	10.098	3.272	2.232	0.725	1.022	0.333	675.6	219.991
		S.D.	18.6	1.016	0.220	0.178	0.058	0.082	0.023	98.3	36.598
HBM		n	11	11	11	11	11	11	11	11	
300 mg/kg		Mean	310.6	10.106	3.257	2.318	0.745	1.013	0.327	693.8	222.550
		S.D.	21.7	0.767	0.195	0.260	0.073	0.052	0.018	129.2	31.887
HBM		n	12	12	12	12	12	12	12	12	
1000 mg/kg		Mean	314.9	10.607	3.369	2.467	0.782	1.047	0.332	758.7	241.336
		S.D.	19.4	0.858	0.205	0.281	0.078	0.093	0.034	220.8	71.458
				DT *							
Thymus											
Test article	Dose		AB mg	RE mg/100g		AB mg	RE mg/100g		AB mg	RE mg/100g	
HBM		n	12	12	12	12	12	12	12	12	
0 mg/kg		Mean	292.2	93.273	79.4	25.257	18.11	5.773	15.80	5.064	114.0
		S.D.	53.7	19.214	9.0	2.868	1.50	0.620	2.93	1.188	13.9
HBM		n	12	12	12	12	12	12	12	12	
100 mg/kg		Mean	297.7	97.023	74.0	24.074	16.63	5.408	15.94	5.170	105.9
		S.D.	68.9	24.644	9.5	3.438	2.27	0.792	3.60	1.161	13.0
HBM		n	11	11	11	11	11	11	11	11	
300 mg/kg		Mean	264.8	85.448	83.2	26.836	16.68	5.382	15.65	5.069	107.2
		S.D.	57.3	18.472	9.5	3.122	2.65	0.822	2.51	0.940	10.9
HBM		n	12	12	12	12	12	12	12	12	
1000 mg/kg		Mean	226.7	71.924	78.9	25.191	16.49	5.220	17.13	5.459	121.2
		S.D.	45.5	13.304	10.1	3.932	3.28	0.863	3.44	1.122	17.6
			DT *	DT *							

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

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

DT : Dunnett test (two-side)

Table 14 - 4

Study No. : SR17144

Organ weight Sex : Female		Stage : Day 5 after delivery				Species : Rat
Test article Dose		Uterus		Brain		
		AB mg	RE mg/100g	AB g	RE g/100g	
HBM 0 mg/kg	n	12	12	12	12	
	Mean	691.8	220.282	2.044	0.652	
	S.D.	78.3	26.194	0.064	0.034	
HBM 100 mg/kg	n	12	12	12	12	
	Mean	669.3	217.630	2.028	0.659	
	S.D.	60.6	23.267	0.064	0.035	
HBM 300 mg/kg	n	11	11	11	11	
	Mean	654.4	211.526	2.042	0.660	
	S.D.	73.8	27.537	0.051	0.039	
HBM 1000 mg/kg	n	12	12	12	12	
	Mean	737.8	234.953	2.060	0.657	
	S.D.	72.6	25.802	0.064	0.042	

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

Not significantly different from HBM 0 mg/kg

Table 14 - 5

Study No. : SR17144

Organ weight Sex : Female (satellite)				Stage : Day 29								Species : Rat	
Test article	Dose	Body weight		Liver		Kidney		Heart		Spleen			
		g	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	
HBM	n	5	5	5	5	5	5	5	5	5	5	5	
0 mg/kg	Mean	258.2	6.982	2.708	1.880	0.730	0.908	0.354	471.8	182.748			
	S.D.	14.1	0.163	0.130	0.088	0.052	0.061	0.019	52.8	17.667			
HBM	n	5	5	5	5	5	5	5	5	5	5	5	
1000 mg/kg	Mean	255.4	6.902	2.702	1.880	0.736	0.872	0.340	528.8	206.824			
	S.D.	4.7	0.447	0.158	0.134	0.044	0.080	0.028	85.3	31.048			
<hr/>													
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		
		5	5	5	5	5	5	5	5	5	5		
HBM	n	5	5	5	5	5	5	5	5	5	5	5	
0 mg/kg	Mean	330.2	127.730	73.4	28.402	14.64	5.668	13.04	5.044	100.6	39.082		
	S.D.	30.0	5.761	8.0	2.224	1.09	0.227	3.04	1.088	10.5	4.768		
HBM	n	5	5	5	5	5	5	5	5	5	5	5	
1000 mg/kg	Mean	316.2	123.602	73.6	28.836	12.36	4.842	11.22	4.382	95.4	37.318		
	S.D.	117.6	45.917	4.2	1.911	0.92	0.398	3.23	1.218	19.4	7.404		
						T2 **		T2 **					
<hr/>													
Uterus				Brain									
Test article	Dose	AB mg	RE mg/100g	AB g	RE g/100g								
		5	5	5	5								
HBM	n	5	5	5	5								
0 mg/kg	Mean	702.2	276.622	1.942	0.752								
	S.D.	246.9	111.357	0.049	0.034								
HBM	n	5	5	5	5								
1000 mg/kg	Mean	706.6	277.144	1.986	0.778								
	S.D.	301.7	120.786	0.049	0.024								

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

Significantly different from HBM 0 mg/kg: \*\* P&lt;0.01

T2 : Student t-test (two-side)

Table 14 - 6

Study No. : SR17144

Organ weight Sex : Male		Stage : Recovery Day 15										Species : Rat	
		Body weight		Liver		Kidney		Heart		Spleen			
Test article	Dose	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g				
HBM	n	5	5	5	5	5	5	5	5	5	5		
0 mg/kg	Mean	474.4	11.226	2.366	3.122	0.656	1.352	0.282	761.0	160.232			
	S.D.	14.3	0.729	0.087	0.124	0.017	0.122	0.020	98.0	17.952			
HBM	n	5	5	5	5	5	5	5	5	5	5		
1000 mg/kg	Mean	470.8	11.182	2.374	3.132	0.664	1.502	0.318	659.6	140.064			
	S.D.	9.3	0.755	0.150	0.078	0.021	0.086	0.022	40.7	7.427			T2 *
<hr/>													
		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		
HBM	n	5	5	5	5	5	5	5	5	5	5		
0 mg/kg	Mean	347.6	73.396	59.0	12.410	11.44	2.416	19.60	4.134	3.300	0.698		
	S.D.	53.7	11.905	11.9	2.305	0.85	0.227	4.32	0.908	0.272	0.065		
HBM	n	5	5	5	5	5	5	5	5	5	5		
1000 mg/kg	Mean	296.8	63.060	65.0	13.764	11.46	2.430	17.12	3.640	3.250	0.690		
	S.D.	25.4	5.532	15.5	3.059	1.66	0.327	2.69	0.607	0.136	0.038		
<hr/>													
		Epididymis		Prostate		Seminal vesicle		Brain					
Test article	Dose	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g				
HBM	n	5	5	5	5	5	5	5	5	5	5		
0 mg/kg	Mean	1.406	0.296	968.6	204.786	2.248	0.474	2.122	0.448				
	S.D.	0.094	0.015	133.7	32.589	0.075	0.024	0.033	0.020				
HBM	n	5	5	5	5	5	5	5	5	5	5		
1000 mg/kg	Mean	1.306	0.278	827.6	175.454	2.202	0.466	2.274	0.484				
	S.D.	0.087	0.013	186.0	36.878	0.302	0.059	0.042	0.015				T2 **
													T2 *

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

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

T2 : Student t-test (two-side)

Table 14 - 7

Study No. : SR17144

Organ weight Sex : Female (satellite)				Stage : Recovery Day 15								Species : Rat		
Test article Dose	n	Body weight		Liver		Kidney		Heart		Spleen				
		g	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	AB mg	RE mg/100g		
HBM	n	5	5	5	5	5	5	5	5	5	5	5		
0 mg/kg	Mean	273.4	6.854	2.512	1.988	0.726	0.866	0.316	533.8	194.896	66.3	18.345		
HBM	n	5	5	5	5	5	5	5	5	5	5	5		
1000 mg/kg	Mean	277.8	7.390	2.664	1.948	0.700	0.926	0.332	555.2	199.192	109.1	26.348		
	S.D.	13.0	0.506	0.197	0.124	0.021	0.064	0.015						
Thymus				Adrenal		Pituitary gland		Thyroid		Ovary				
Test article Dose	n	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	AB mg	RE mg/100g	
		5	5			5	5	5	5	5	5	5	5	
HBM	n	5	5	5	5	5	5	5	5	5	5	5	5	
0 mg/kg	Mean	296.8	108.462	80.6	29.558	16.02	5.860	14.76	5.366	90.8	33.356			
	S.D.	43.2	13.733	4.2	2.464	3.35	1.156	3.87	1.209	8.7	4.527			
HBM	n	5	5	5	5	5	5	5	5	5	5	5	5	
1000 mg/kg	Mean	387.0	138.478	74.2	26.764	15.52	5.614	16.54	5.984	81.8	29.076			
	S.D.	106.9	31.915	14.5	5.048	1.35	0.592	3.14	1.188	23.4	5.641			
Uterus				Brain										
Test article Dose	n	AB mg	RE mg/100g	AB g	RE g/100g									
		5	5			5	5	5	5					
HBM	n	5	5	5	5	5	5	5	5					
0 mg/kg	Mean	806.8	293.962	2.022	0.740	5	5	5	5					
	S.D.	176.8	57.348	0.038	0.026									
HBM	n	5	5	5	5	5	5	5	5					
1000 mg/kg	Mean	734.2	269.914	2.000	0.726	5	5	5	5					
	S.D.	275.6	116.258	0.049	0.074									

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

Not significantly different from HBM 0 mg/kg

Table 15 - 1

Study No. : SR17144

Sex : Male		Histopathological findings												Species : Rat		
		Test article				Stage : Day 29										
Organ Findings	Number of Animals Grade	Dose		0 mg/kg		100 mg/kg		300 mg/kg		1000 mg/kg						
		-	1+	2+	3+	4+	-	1+	2+	3+	4+	-	1+	2+	3+	4+
Lung		7	<7>				12	<0>		<0>		7	<7>			
Accumulation, macrophage, alveolar		6	1	0	0	0	0			0		5	2	0	0	0
Mineralization, artery, focal		6	1	0	0	0	0			0		7	0	0	0	0
Trachea		7	<7>				0	<0>		<0>		7	<7>			
Submandibular gland		7	<7>				0	<0>		<0>		7	<7>			
Esophagus		7	<7>				0	<0>		<0>		7	<7>			
Stomach		7	<7>				0	<0>		<0>		7	<7>			
Duodenum		7	<7>				0	<0>		<0>		7	<7>			
Jejunum		7	<7>				0	<0>		<0>		7	<7>			
Ileum		7	<7>				0	<0>		<0>		7	<7>			
Cecum		7	<7>				0	<0>		<0>		7	<7>			
Colon		7	<7>				0	<0>		<0>		7	<7>			

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 2

Study No. : SR17144

Histopathological findings										Species : Rat			
Sex : Male			Stage : Day 29										
Organ Findings	Test article	HBM				HBM				HBM			
		Dose	0 mg/kg	100 mg/kg	300 mg/kg	1000 mg/kg							
		Number of Animals	7	12	12	7	-	1+	2+	3+	4+	-	1+
Rectum		Grade	- <7>	- <0>	- <0>	- <7>		-	1+	2+	3+	4+	- <7>
			7	0	0	0		0	0	0	0	0	7
Pancreas	Atrophy, acinar cell, focal		<7>	0	<0>	<0>		0	0	0	0	0	<7>
Liver	Microgranuloma		<7>	0	<0>	<0>		0	0	0	0	0	<7>
Heart	Inflammation, focal		<7>	0	<0>	<0>		0	0	0	0	0	<7>
Kidney	Basophilic change, renal tubule		<7>	0	<0>	<0>		0	0	0	0	0	<7>
Urinary bladder	Hyperplasia, urothelium		<7>	12	<12>	<12>		12	0	0	0	0	<7>
Testis			<7>	0	<0>	<0>		0	0	0	0	0	<7>
Epididymis	Granuloma, spermatic		<7>	0	<0>	<1>		0	1	0	0	0	<7>
Prostate	Inflammation, interstitium		<7>	0	<0>	<0>		0	0	0	0	0	<7>
Seminal vesicle			<7>	0	<0>	<0>		0	0	0	0	0	<7>
Coagulating gland			<7>	0	<0>	<0>		0	0	0	0	0	<7>

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 3

Study No. : SR17144

Histopathological findings		Species : Rat														
Sex : Male		Stage : Day 29														
Organ Findings	Test article	HBM				HBM				HBM						
		Dose	0 mg/kg	100 mg/kg	300 mg/kg	1000 mg/kg										
	Number of Animals		7	12	12	7	-	1+	2+	3+	4+	-	1+	2+	3+	4+
Cerebrum	Grade		<7>	<0>	<0>	<7>										
			7	0	0	7										
Cerebellum			<7>	<0>	<0>	<7>										
Pons			<7>	<0>	<0>	<7>										
Spinal cord			<7>	<0>	<0>	<7>										
Sciatic nerve			<7>	<0>	<0>	<7>										
Spleen			<7>	<0>	<0>	<7>										
Thymus			<7>	<0>	<0>	<7>										
Bone marrow, femur			<7>	<0>	<0>	<7>										
Submandibular lymph node			<7>	<0>	<0>	<7>										
Mesenteric lymph node			<7>	<0>	<0>	<7>										

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Table 15 - 4

Study No. : SR17144

Histopathological findings		Stage : Day 29										Species : Rat					
Sex : Male		Test article		HBM		HBM		HBM		HBM							
Organ	Findings	Dose	0 mg/kg				100 mg/kg				300 mg/kg						
		Number of Animals	-	1+	2+	3+	4+	-	1+	2+	3+	4+	-	1+	2+	3+	4+
Peyer's patch			7	<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0
Pituitary gland				<7>	0	0	0	0	<0>	0	0	0	6	1	0	0	0
Craniopharyngeal duct, remnant			7	0	0	0	0	0	<0>	0	0	0	6	1	0	0	0
Cyst, pars distalis			6	1	0	0	0	0	<0>	0	0	0	7	0	0	0	0
Thyroid				<7>	0	0	0	0	<0>	0	0	0	7	0	0	0	0
Remnant, ultimobranchial body			5	2	0	0	0	0	<0>	0	0	0	7	0	0	0	0
Parathyroid				<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0
Adrenal				<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0
Eyeball				<7>	0	0	0	0	<0>	0	0	0	6	1	0	0	0
Dysplasia, retina, focal			7	0	0	0	0	0	<0>	0	0	0	6	1	0	0	0
Harderian gland				<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0
Skeletal muscle				<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0
Femur				<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0
Mammary gland				<7>	0	0	0	0	<0>	0	0	0	7	<7>	0	0	0

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 5

Study No. : SR17144

Histopathological findings Sex : Female		Stage : Day 5 after delivery												Species : Rat				
Organ Findings	Test article	HBM				HBM				HBM				HBM				
		Dose		0 mg/kg		100 mg/kg		300 mg/kg		1000 mg/kg								
		Number of Animals	Grade	-	1+	2+	3+	4+	-	1+	2+	3+	4+	-	1+	2+	3+	4+
Lung	Accumulation, macrophage, alveolar	9	3 0 0 0	0	0	<0>	0	<0>	0	10	2 0 0 0	<12>	12	12	12	12	12	12
Trachea		12	<12>		0	<0>		0	<0>	0	<12>		12					
Submandibular gland		12	<12>		0	<0>		0	<0>	0	<12>		12					
Esophagus		12	<12>		0	<0>		0	<0>	0	<12>		12					
Stomach	Erosion, glandular stomach, focal	12	<12> 0 0 0	12	0 0 0 0	<12>	0 0 0 0	10 1 0 0 0	<11>	10 2 0 0 0	<12>		12					
Duodenum		12	<12>		0	<0>		0	<0>	0	<12>		12					
Jejunum		12	<12>		0	<0>		0	<0>	0	<12>		12					
Ileum		12	<12>		0	<0>		0	<0>	0	<12>		12					
Cecum		12	<12>		0	<0>		0	<0>	0	<12>		12					
Colon		12	<12>		0	<0>		0	<0>	0	<12>		12					

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 6

Study No. : SR17144

Sex : Female		Histopathological findings												Species : Rat			
		Test article				Stage : Day 5 after delivery											
Organ	Findings	Dose	HBM				HBM				HBM						
		Number of Animals	-	1+	2+	3+	4+	-	1+	2+	3+	4+	-	1+	2+	3+	4+
Grade			0 mg/kg	12	<12>			100 mg/kg	12	<0>			300 mg/kg	11	<0>	1000 mg/kg	12
Rectum																	
Pancreas																	
Atrophy, acinar cell, focal																	
Liver																	
Heart																	
Inflammation, focal																	
Kidney																	
Basophilic change, renal tubule																	
Infiltration, inflammatory cell																	
Mineralization																	
Urinary bladder																	
Infiltration, inflammatory cell																	
Edema, lamina propria																	
Hyperplasia, urothelium																	
Ovary																	
Uterine horn																	
Uterine cervix																	

&lt;&gt; : Number of animals examined

- : Not remarkable

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

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

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

Table 15 - 7

Study No. : SR17144

Sex : Female Histopathological findings		Stage : Day 5 after delivery												Species : Rat					
		Test article		HBM				HBM				HBM							
Organ Findings	Number of Animals	Dose		0 mg/kg				100 mg/kg				300 mg/kg				1000 mg/kg			
		-	1+	2+	3+	4+	<12>	-	1+	2+	3+	4+	11	12	-	1+	2+	3+	4+
Vagina		12	0	0	0	0	<12>	0	0	0	0	0	0	0	12	<12>			
Cerebrum		12	0	0	0	0	<12>	0	<0>	0	0	0	<0>	0	11	1	0	0	0
Mineralization		12	0	0	0	0		0	<0>	0	0	0	<0>	0	12				
Cerebellum		12					<12>	0	<0>	0	0	0	<0>	0	12				
Pons		12					<12>	0	<0>	0	0	0	<0>	0	12				
Spinal cord		12					<12>	0	<0>	0	0	0	<0>	0	12				
Sciatic nerve		12					<12>	0	<0>	0	0	0	<0>	0	12				
Spleen		12					<12>	0	<0>	0	0	0	<0>	0	11	1	0	0	0
Extramedullary hematopoiesis		12	0	0	0	0		0	<0>	0	0	0	<0>	0	12	0	0	0	0
Thymus		11	1	0	0	0	<12>	0	<0>	0	0	0	<0>	0	12	0	0	0	0
Hyperplasia, epithelial cell		12						0	<0>	0	0	0	<0>	0	12				
Bone marrow, femur		12					<12>	0	<0>	0	0	0	<0>	0	12				
Submandibular lymph node		12					<12>	0	<0>	0	0	0	<0>	0	12				
Mesenteric lymph node		12					<12>	0	<0>	0	0	0	<0>	0	12				

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 8

Study No. : SR17144

Histopathological findings		Stage : Day 5 after delivery												Species : Rat				
Sex : Female		Test article		HBM				HBM				HBM						
Organ	Findings	Dose	Number of Animals	0 mg/kg				100 mg/kg				300 mg/kg						
				-	1+	2+	3+	4+	-	1+	2+	3+	4+	-	1+	2+	3+	4+
Peyer's patch				12	0	0	0	0	0	<0>	0	<0>	0	11	1	0	0	0
Mineralization																		
Pituitary gland																		
Cyst, pars distalis				12	0	0	0	0	0	<0>	0	<0>	0	11	1	0	0	0
Thyroid																		
Remnant, ultimobranchial body				10	2	0	0	0	0	<0>	0	<0>	0	9	3	0	0	0
Parathyroid																		
				12					0	<0>	0	<0>	0	12				
Adrenal																		
				12					0	<0>	0	<0>	0	12				
Eyeball																		
Dysplasia, retina, focal				12	0	0	0	0	0	<0>	0	<0>	0	11	1	0	0	0
Harderian gland																		
				12					0	<0>	0	<0>	0	12				
Skeletal muscle																		
				12					0	<0>	0	<0>	0	12				
Femur																		
				12					0	<0>	0	<0>	0	12				
Mammary gland																		
				12					0	<0>	0	<0>	0	12				

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 9

Study No. : SR17144

Histopathological findings		Stage : Non-pregnancy	Species : Rat
Sex : Female	Test article		
Organ Findings	Dose	300 mg/kg	
	Number of Animals	1	
	Grade	- 1+ 2+ 3+ 4+ <1>	
	Stomach	1	
Urinary bladder			
		<1>	
1			

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Table 15 - 10

Study No. : SR17144

Sex : Female (satellite)		Stage : Day 29										Species : Rat			
Organ Findings	Test article	HBM		HBM											
		Dose		0 mg/kg				1000 mg/kg							
		Number of Animals	Grade	-	1+	2+	3+	4+	-	1+	2+	3+	4+		
Lung	Accumulation, macrophage, alveolar	5							<5>						
										4	1	0	0	0	
Trachea		5							<5>						
										5					
Submandibular gland		5							<5>						
										5					
Esophagus		5							<5>						
										5					
Stomach		5							<5>						
										5					
Duodenum		5							<5>						
										5					
Jejunum		5							<5>						
										5					
Ileum		5							<5>						
										5					
Cecum		5							<5>						
										5					
Colon		5							<5>						
										5					

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 11

Study No. : SR17144

Histopathological findings Sex : Female (satellite)		Stage : Day 29										Species : Rat
Organ Findings	Test article	HBM					HBM					
		Dose	0 mg/kg				1000 mg/kg					
			<5>	5	5	<5>	5	5	5	5		
Rectum			5			<5>	5					
Pancreas			5	<5>			5	<5>				
Liver			5	<5>			3	2	0	0	0	
Microgranuloma												
Heart			5	<5>			5	<5>				
Kidney			5	<5>			5	<5>				
Urinary bladder			5	<5>			5	<5>				
Ovary			5	<5>			5	<5>				
Uterine horn			5	<5>			5	<5>				
Uterine cervix			5	<5>			5	<5>				
Vagina			5	<5>			5	<5>				

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 12

Study No. : SR17144

Histopathological findings Sex : Female (satellite)		Stage : Day 29								Species : Rat	
Organ Findings	Test article	HBM				HBM				Species : Rat	
		Dose		0 mg/kg	1000 mg/kg	-		1+	2+	3+	4+
		Number of Animals	Grade	- 5 <5>	- 5 <5>	-	1+	2+	3+	4+	
Cerebrum		5			5						
Cerebellum		5		<5>		5		<5>			
Pons		5		<5>		5		<5>			
Spinal cord		5		<5>		5		<5>			
Sciatic nerve		5		<5>		5		<5>			
Spleen		5		<5>		5		<5>			
Thymus		5		<5>		5		<5>			
Bone marrow, femur		5		<5>		5		<5>			
Submandibular lymph node		5		<5>		5		<5>			
Mesenteric lymph node		5		<5>		5		<5>			
Peyer's patch		5		<5>		5		<5>			

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Table 15 - 13

Study No. : SR17144

Sex : Female (satellite)		Stage : Day 29										Species : Rat	
Organ Findings	Test article	HBM					HBM						
		Dose	0 mg/kg				1000 mg/kg						
			-	1+	2+	3+	4+	-	1+	2+	3+		
Pituitary gland			5					5					
Thyroid	Remnant, ultimobranchial body		<5>	3	2	0	0	0	4	1	0	0	0
Parathyroid			<5>	5					5				
Adrenal			<5>	5					5				
Eyeball			<5>	5					5				
Harderian gland			<5>	5					5				
Skeletal muscle			<5>	5					5				
Femur			<5>	5					5				
Mammary gland			<5>	5					5				

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Not significantly different from HBM 0 mg/kg

Table 15 - 14

Study No. : SR17144

Sex : Male		Stage : Recovery Day 15								Species : Rat			
Organ Findings	Test article	HBM				HBM							
	Dose	0 mg/kg				1000 mg/kg							
	Number of Animals	5				5							
Grade		-	1+	2+	3+	4+	-	1+	2+	3+	4+		
Urinary bladder			<5>					<5>					
		5					5						

&lt;&gt; : Number of animals examined

- : Not remarkable

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

Table 16

Study No. : SR17144

Estrous cycles Generation : F0				Species : Rat
Test article Dose	/Before mating			
	n	Mean length of estrous cycle (Days)	Number of estrus	Number of animals with acyclic or irregular cycle
HBM 0 mg/kg	Mean	4.00	3.0	12 (0)
	S.D.	0.00	0.4	
HBM 100 mg/kg	Mean	4.00	3.3	12 (0)
	S.D.	0.00	0.5	
HBM 300 mg/kg	Mean	4.04	3.2	12 (0)
	S.D.	0.14	0.4	
HBM 1000 mg/kg	Mean	4.21	3.3	12 (0)
	S.D.	0.40	0.6	

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

Not significantly different from HBM 0 mg/kg

Table 17 - 1

Study No. : SR17144

Test article 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 (%)		
HBM 0 mg/kg	n Mean S.D.	12 1.7 0.7	12 (12/12) 100.0	12 (12/12) 100.0			(12/12) 100.0	(12/12) 100.0		
HBM 100 mg/kg	n Mean S.D.	12 2.0 1.2	12 (12/12) 100.0	12 (12/12) 100.0			(12/12) 100.0	(12/12) 100.0		
HBM 300 mg/kg	n Mean S.D.	12 1.6 0.8	12 (12/12) 100.0	12 (11/12) 91.7			(12/12) 100.0	(11/12) 91.7		
HBM 1000 mg/kg	n Mean S.D.	12 2.3 1.2	12 (12/12) 100.0	12 (12/12) 100.0			(12/12) 100.0	(12/12) 100.0		

Not significantly different from HBM 0 mg/kg

Table 17 - 2

Study No. : SR17144

Test article 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 (%)		
HBM 0 mg/kg	n Mean S.D.	12 1.7 0.7	12 (12/12) 100.0	12 (12/12) 100.0			(12/12) 100.0	(12/12) 100.0		
HBM 100 mg/kg	n Mean S.D.	12 2.0 1.2	12 (12/12) 100.0	12 (12/12) 100.0			(12/12) 100.0	(12/12) 100.0		
HBM 300 mg/kg	n Mean S.D.	12 1.6 0.8	12 (12/12) 100.0	12 (11/12) 91.7			(12/12) 100.0	(11/12) 91.7		
HBM 1000 mg/kg	n Mean S.D.	12 2.3 1.2	12 (12/12) 100.0	12 (12/12) 100.0			(12/12) 100.0	(12/12) 100.0		

Not significantly different from HBM 0 mg/kg

Table 18 - 1

Study No. : SR17144

Test article Dose	Delivery data Generation : F0					Species : Rat					
	Gestation period (day)	Number of implantation	Birth index (%)	Number of offspring	Number of live newborns			Sex ratio (offspring) (%)	Number of dead newborns		Gestation index (%)
					M	F	Total		Dead	Cannibalism	
HBM 0 mg/kg	n Mean S.D.	12 22.00 0.00	12 15.4	12 93.06 14.3	12 8.5 3.4	12 5.8 2.9	12 14.3 1.9	102/172 59.3	12 0.0 0.0	12 0.0 0.0	12/12 100.0 0.00
HBM 100 mg/kg	n Mean S.D.	12 22.25 0.45	12 14.8	12 95.55 14.1	12 7.2 3.1	12 6.8 1.9	12 14.0 2.7	86/168 51.2	12 0.0 0.0	12 0.1 0.3	12/12 100.0 0.00
HBM 300 mg/kg	n Mean S.D.	11 22.18 0.40	11 15.0	11 86.95 13.1	11 6.3 2.1	11 6.8 1.8	11 13.1 2.2	69/144 47.9	11 0.0 0.0	11 0.0 0.0	11/11 100.0 0.00
HBM 1000 mg/kg	n Mean S.D.	12 22.17 0.39	12 16.3	12 90.93 14.9	12 7.8 1.9	12 7.0 1.7	12 14.8 1.7	94/178 52.8	12 0.1 0.3	12 0.1 0.3	12/12 100.0 0.00

M : Male, F : Female

Not significantly different from HBM 0 mg/kg

Table 18 - 2

Study No. : SR17144

Delivery data Generation : F0				Species : Rat
Test article		Number of corpora lutea	Implantation index (%)	Nursing index (%)
HBM	n	12	12	12/12
0 mg/kg	Mean	15.9	96.73	100.0
	S.D.	1.4	4.45	
HBM	n	12	12	12/12
100 mg/kg	Mean	15.6	94.48	100.0
	S.D.	3.2	5.87	
HBM	n	11	11	11/11
300 mg/kg	Mean	15.3	98.29	100.0
	S.D.	1.2	2.93	
HBM	n	12	12	12/12
1000 mg/kg	Mean	16.4	99.51	100.0
	S.D.	1.6	1.70	

Not significantly different from HBM 0 mg/kg

Table 18 - 3

Study No. : SR17144

Delivery data (External examination of offspring)				Day after birth : 0
Generation : F0	HBM	HBM	HBM	Species : Rat
Test article				
Dose	0	100	300	1000
Dose unit	mg/kg	mg/kg	mg/kg	mg/kg
Number of dams	12	12	11	12
Number of offspring	172	168	144	178
Number of dams with anomalous offspring (incidence %)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Number of offspring with any anomaly (incidence %)	0(0.00)	0(0.00)	0(0.00)	0(0.00)

Not significantly different from HBM 0 mg/kg

Table 19

Study No. : SR17144

Clinical sign of offspring Generation : F0		Species : Rat						
Test article	Dose	Day after birth	0	1	2	3	4	
	Clinical signs	Time	1	1	1	1	1	
HBM	Number of dams examined		12	12	12	12	12	
0 mg/kg	Number of offspring		172	172	172	172	171	
	Number of dams with anomalous offspring		0	0	0	0	0	
HBM	Number of dams examined		12	12	12	12	12	
100 mg/kg	Number of offspring		167	167	167	166	164	
	Number of dams with anomalous offspring		0	0	0	0	0	
HBM	Number of dams examined		11	11	11	11	11	
300 mg/kg	Number of offspring		144	144	144	144	144	
	Number of dams with anomalous offspring		0	0	0	0	0	
HBM	Number of dams examined		12	12	12	12	12	
1000 mg/kg	Number of offspring		178	178	178	178	178	
	Number of dams with anomalous offspring		0	0	0	0	0	

F0 lactation)1 : Daily examination

Table 20

Study No. : SR17144

## Litter size and viability index of offspring

Generation : F0

Species : Rat

Test article Dose		/Day after birth					Species : Rat
		0 All pups	0 Live pups	0 Viability index (%)	4 Live pups	4 Viability index (%)	
HBM	Total	172	172		171		
0 mg/kg	n	12	12	12	12	12	
	Mean			100.00		99.24	
	S.D.			0.00		2.63	
HBM	Total	169	168		164		
100 mg/kg	n	12	12	12	12	12	
	Mean			99.53		98.28	
	S.D.			1.62		3.16	
HBM	Total	144	144		144		
300 mg/kg	n	11	11	11	11	11	
	Mean			100.00		100.00	
	S.D.			0.00		0.00	
HBM	Total	179	178		178		
1000 mg/kg	n	12	12	12	12	12	
	Mean			99.44		100.00	
	S.D.			1.93		0.00	

Not significantly different from HBM 0 mg/kg

Table 21

Study No. : SR17144

		Body weight of offspring		Unit : g	Species : Rat		
		Generation : F0					
Test article	Dose	/Day after birth					
		0	4				
HBM 0 mg/kg	Male	n	12	12			
		Mean	6.584	10.803			
		S.D.	0.340	0.650			
	Female	n	12	12			
		Mean	6.090	10.098			
		S.D.	0.318	0.621			
HBM 100 mg/kg	Male	n	11	11			
		Mean	6.690	11.036			
		S.D.	0.621	0.819			
	Female	n	12	12			
		Mean	6.553	10.869			
		S.D.	0.853	1.691			
HBM 300 mg/kg	Male	n	11	11			
		Mean	7.145	11.727			
		S.D.	0.706	1.120			
	Female	n	11	11			
		Mean	6.656	10.936			
		S.D.	0.581	1.172			
HBM 1000 mg/kg	Male	n	12	12			
		Mean	6.654	10.528			
		S.D.	0.586	1.090			
	Female	n	12	12			
		Mean	6.319	10.062			
		S.D.	0.527	0.972			

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

ST : Steel test (two-side)

Table 22

Study No. : SR17144

Necropsy findings of offspring Generation : F0				Species : Rat
	HBM 0 mg/kg	HBM 100 mg/kg	HBM 300 mg/kg	HBM 1000 mg/kg
Test article				
Dose	0	100	300	1000
Dose unit	mg/kg	mg/kg	mg/kg	mg/kg
Number of dams	12	12	11	12
Number of live offspring examined on Day 4 of birth	171	164	144	178
Finding absent	170	164	144	178
Multifocal yellowish white focuses of liver	1	0	0	0
Number of dead offspring examined on Day 0-4 of birth	0	3 <sup>a</sup>	0	1
Finding absent	0	2	0	1
Trauma on dorsal skin <sup>b</sup>	0	1	0	0

a: One of 3 died of an accident on Day 0.

b: The finding is because of an accident.

Clinical sign Sex : Male		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			
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		
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 : Before administration, 2 : After administration

Clinical sign Sex : Male		Period : Administration Day 1-29 Dose : HBM 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 : Before administration, 2 : After administration, 3 : Necropsy day

Animal No.	Clinical signs	Period : Administration Day 1-29												Species : Rat								
		Day		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	2		
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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Animal No.	Clinical signs	Day 10-18												Species : Rat								
		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	1	2	1	2	1	2
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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Animal No.	Clinical signs	Day 19-27												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	2	1	2
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 : Before administration, 2 : After administration

Clinical sign Sex : Male		Period : Administration Day 1-29 Dose : HBM 100 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 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Male		Period : Administration Day 1-29 Dose : HBM 300 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		
		Time		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	
Animal No.	Clinical signs	Time		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
Animal No.	Clinical signs	Time		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 : Before administration, 2 : After administration

Clinical sign Sex : Male		Period : Administration Day 1-29 Dose : HBM 300 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 : Before administration, 2 : After administration, 3 : Necropsy day

Animal No.	Clinical signs	Period : Administration Day 1-29												Species : Rat					
		Day		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	
10401	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10402	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10403	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10404	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10405	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10406	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10407	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10408	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10409	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10410	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10411	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10412	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Animal No.		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	1	2	
10401	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10402	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10403	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10404	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10405	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10406	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10407	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10408	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10409	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10410	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10411	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10412	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Animal No.		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	
10401	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10402	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10403	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10404	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10405	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10406	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10407	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10408	Reddish urine	-	-	-	-	-	-	-	-	+	-	-	+	-	+	-	-	-	
10409	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10410	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10411	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10412	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Administration)1 : Before administration, 2 : After administration

Clinical sign Sex : Male		Period : Administration Day 1-29 Dose : HBM 1000 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	Reddish urine	-	-	-	
10409	No abnormality	-	-	-	
10410	No abnormality	-	-	-	
10411	No abnormality	-	-	-	
10412	No abnormality	-	-	-	

Administration)1 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Female		Period : F0 before mating Day 1-14, F0 mating Day 15-18												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	
		Time		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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Animal No.		Day		10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Animal No.	Clinical signs	Time		1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1
				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; F0 mating)1 : Before administration, 2 : After administration

Clinical sign Sex : Female		Period : F0 gestation Day 0-26												Species : Rat					
Animal No.	Clinical signs	Day 0		1		2		3		4		5		6		7			
		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 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	
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	
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 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Female		Period : F0 lactation Day 0-5 Dose : HBM 0 mg/kg										Species : Rat		
Animal No.	Clinical signs	Day	0	1	2	3	4	5	Time	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		-	-	-	-	-	-	-	-	-	-	-	-

F0 lactation)1 : Before administration, 2 : After administration, 3 : Necropsy day

Animal No.	Clinical signs	Period : F0 before mating Day 1-14, F0 mating Day 15-18												Species : Rat						
		Day		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	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 10-18												Species : Rat						
		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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50256	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50257	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50258	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50259	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50260	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50261	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50262	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

F0 before mating; F0 mating)1 : Before administration, 2 : After administration

Clinical sign Sex : Female		Period : F0 gestation Day 0-26												Species : Rat					
Animal No.	Clinical signs	Day 0		1		2		3		4		5		6		7			
		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		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	
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		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	
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 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Female		Period : F0 lactation Day 0-5 Dose : HBM 100 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 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Female		Period : F0 before mating Day 1-14, F0 mating Day 15-18 Dose : HBM 300 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
		Time	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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		Day	10	11	12	13	14	15	16	17	18	Time	1	2	1	2	1	2	1	2
Animal No.	Clinical signs	Time	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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

F0 before mating; F0 mating)1 : Before administration, 2 : After administration

Clinical sign 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
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 : Before administration, 2 : After administration, 3 : Necropsy day

Animal No. 50358 : Non-pregnancy

\$ : Excluded data from calculation

Clinical sign Sex : Female		Period : F0 lactation Day 0-5 Dose : HBM 300 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		-	-	-	-	-	-	-	-	-	-	-	
50359	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50360	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50361	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50362	No abnormality		-	-	-	-	-	-	-	-	-	-	-	

F0 lactation)1 : Before administration, 2 : After administration, 3 : Necropsy day

Animal No.	Clinical signs	Period : F0 before mating Day 1-14, F0 mating Day 15-18												Species : Rat						
		Day		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	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 10-18												Species : Rat						
		Time	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
		Day	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
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; F0 mating)1 : Before administration, 2 : After administration

Clinical sign Sex : Female		Period : F0 gestation Day 0-26												Species : Rat					
Animal No.	Clinical signs	Day 0		1		2		3		4		5		6		7			
		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	Reddish urine	-	-	-	-	+	+	+	-	+	-	-	-	-	-	-	-	-	
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	
50451	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50452	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50453	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50454	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50455	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
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	
50451	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50452	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50453	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50454	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50455	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50456	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50457	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50458	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50459	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50460	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50461	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50462	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

F0 gestation)1 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Female		Period : F0 lactation Day 0-5 Dose : HBM 1000 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		-	-	-	-	-	-	-	-	-	-	-	
50456	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50457	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50458	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50459	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50460	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50461	No abnormality		-	-	-	-	-	-	-	-	-	-	-	
50462	No abnormality		-	-	-	-	-	-	-	-	-	-	-	

F0 lactation)1 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign 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	
		Time		1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	
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
		Time		1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	
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	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	
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 : Before administration, 2 : After administration

Clinical sign Sex : Female (satellite)		Period : Administration Day 1-29 Dose : HBM 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 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign 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		
50651	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50652	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50653	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50654	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50655	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50656	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50657	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50658	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50659	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
50660	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
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	
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
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50651	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50652	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50653	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50654	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50655	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50656	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50657	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50658	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50659	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50660	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
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
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
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50651	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50652	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50653	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50654	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50655	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50656	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50657	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50658	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50659	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50660	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Administration)1 : Before administration, 2 : After administration

Clinical sign Sex : Female (satellite)		Period : Administration Day 1-29 Dose : HBM 1000 mg/kg			Species : Rat
Animal No.	Clinical signs	Day	28	29	
		Time	1	2	3
50651	No abnormality		-	-	-
50652	No abnormality		-	-	-
50653	No abnormality		-	-	-
50654	No abnormality		-	-	-
50655	No abnormality		-	-	-
50656	No abnormality		-	-	-
50657	No abnormality		-	-	-
50658	No abnormality		-	-	-
50659	No abnormality		-	-	-
50660	Reddish urine		+	+	

Administration)1 : Before administration, 2 : After administration, 3 : Necropsy day

Clinical sign Sex : Male		Period : Recovery Day 1-15 Dose : HBM 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	1	2	
10103	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10104	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10105	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10109	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10111	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Animal No.		Day 10		11		12		13		14		15									
Animal No.	Clinical signs	Time	1	2	1	2	1	2	1	2	1	2	1	2	3						
		-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10103	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10104	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10105	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10109	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10111	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						

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

Clinical sign Sex : Male		Period : Recovery Day 1-15 Dose : HBM 1000 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	1	2	
10403	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10407	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10408	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10411	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10412	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						
10403	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10407	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10408	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10411	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
10412	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-						

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

Clinical sign Sex : Female (satellite)		Period : Recovery Day 1-15															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
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	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 Sex : Female (satellite)		Period : Recovery Day 1-15 Dose : HBM 1000 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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50660	Reddish urine	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Animal No.		Day		10	11	12	13	14	15									
Animal No.	Clinical signs	Time		1	2	1	2	1	2	1	2	1	2	1	2	1	2	3
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
50656	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50657	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50658	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50659	No abnormality	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50660	Reddish urine	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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			Dose : HBM 100 mg/kg				
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting		
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			Dose : HBM 300 mg/kg				
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting		
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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 7			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Detailed clinical observation (in the cage)			Stage : Day 7 Dose : HBM 100 mg/kg			Species : Rat
Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 7 Dose : HBM 300 mg/kg			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting	
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 : Day 7 Dose : HBM 1000 mg/kg			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting	
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			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 14			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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 14			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 : Day 14			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 21			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 : Day 21			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 28			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 28			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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 28			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 : Day 28			Species : Rat
	Sex : Male	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Pre administration			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
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 : Pre administration			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Pre administration			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 7 Dose : HBM 0 mg/kg			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 7 Dose : HBM 100 mg/kg			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 7 Dose : HBM 300 mg/kg			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 7 Dose : HBM 1000 mg/kg			Species : Rat
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 Dose : HBM 0 mg/kg			Species : Rat
Sex : Female						
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 14			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
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 14			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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			Species : Rat
Sex : Female			Dose : HBM 1000 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 21			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
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 21			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 21			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 21		Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	
50451		1	1	1	0	0
50452		1	1	1	0	0
50453		1	1	1	0	0
50454		1	1	1	0	0
50455		1	1	1	0	0
50456		1	1	1	0	0
50457		1	1	1	0	0
50458		1	1	1	0	0
50459		1	1	1	0	0
50460		1	1	1	0	0
50461		1	1	1	0	0
50462		1	1	1	0	0
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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 28			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 28			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 28			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Day 35			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
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 35			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 35			Species : Rat
	Sex : Female	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Detailed clinical observation (in the cage)			Stage : Day 42			Species : Rat
Sex : Female			Dose : HBM 0 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
50151	1	1	1	0	0	1
50153	1	1	1	0	0	1
50154	1	1	1	0	0	1
50156	1	1	1	0	0	1
50158	1	1	1	0	0	1
50159	1	1	1	0	0	1
50161	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.

Detailed clinical observation (in the cage)			Stage : Day 42			Species : Rat
Sex : Female			Dose : HBM 100 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
50251	1	1	1	0	0	1
50252	1	1	1	0	0	1
50254	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
50260	1	1	1	0	0	1
50261	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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
Animal No.						
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
50359	1	1	1	0	0	1
50360	1	1	1	0	0	1
n	6	6	6	6	6	6

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			Dose : HBM 1000 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
50451	1	1	1	0	0	1
50452	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
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.

Animal No.	Detailed clinical observation (in the cage)			Stage : Pre administration			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 14			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 21			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	
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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 28			Species : Rat
	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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.

Detailed clinical observation (in the cage)			Stage : Recovery Day 7			Species : Rat
Sex : Male			Dose : HBM 0 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
10103	1	1	1	0	0	1
10104	1	1	1	0	0	1
10105	1	1	1	0	0	1
10109	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 Dose : HBM 1000 mg/kg			Species : Rat
Sex : Male						
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
10403	1	1	1	0	0	1
10407	1	1	1	0	0	1
10408	1	1	1	0	0	1
10411	1	1	1	0	0	1
10412	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 : Male			Dose : HBM 0 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
10103	1	1	1	0	0	1
10104	1	1	1	0	0	1
10105	1	1	1	0	0	1
10109	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 Dose : HBM 1000 mg/kg			Species : Rat
Sex : Male						
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive circling	Self biting
10403	1	1	1	0	0	1
10407	1	1	1	0	0	1
10408	1	1	1	0	0	1
10411	1	1	1	0	0	1
10412	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 : HBM 0 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 : HBM 1000 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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
50660	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 : HBM 0 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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 : HBM 1000 mg/kg			
Animal No.	Body position/ Posture	Respiratory pattern	Tremor/ Convulsion	Rolling	Repetitive 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
50660	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.

Sex : Male	Detailed clinical observation (on the hand)											Species : Rat
	Stage : Pre administration Dose : HBM 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/ 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 : Pre administration		Dose : HBM 100 mg/kg						Lacration	Salivation	
Animal No.	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size		
10201	1	1	2	1	1	1	0	1	1	1	1
10202	1	1	2	1	1	1	0	1	1	1	1
10203	1	1	2	1	1	1	0	1	1	1	1
10204	1	1	2	1	1	1	0	1	1	1	1
10205	1	1	2	1	1	1	0	1	1	1	1
10206	1	1	2	1	1	1	0	1	1	1	1
10207	1	1	2	1	1	1	0	1	1	1	1
10208	1	1	2	1	1	1	0	1	1	1	1
10209	1	1	2	1	1	1	0	1	1	1	1
10210	1	1	2	1	1	1	0	1	1	1	1
10211	1	1	2	1	1	1	0	1	1	1	1
10212	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/ 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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Pre administration			Species : Rat					
	Sex : Male	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
10302		1	1	2	1	1	1	0	1	1	1	1
10303		1	1	2	1	1	1	0	1	1	1	1
10304		1	1	2	1	1	1	0	1	1	1	1
10305		1	1	2	1	1	1	0	1	1	1	1
10306		1	1	2	1	1	1	0	1	1	1	1
10307		1	1	2	1	1	1	0	1	1	1	1
10308		1	1	2	1	1	1	0	1	1	1	1
10309		1	1	2	1	1	1	0	1	1	1	1
10310		1	1	2	1	1	1	0	1	1	1	1
10311		1	1	2	1	1	1	0	1	1	1	1
10312		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/ 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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Pre administration			Species : Rat					
	Sex : Male	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
10402		1	1	2	1	1	1	0	1	1	1	1
10403		1	1	2	1	1	1	0	1	1	1	1
10404		1	1	2	1	1	1	0	1	1	1	1
10405		1	1	2	1	1	1	0	1	1	1	1
10406		1	1	2	1	1	1	0	1	1	1	1
10407		1	1	2	1	1	1	0	1	1	1	1
10408		1	1	2	1	1	1	0	1	1	1	1
10409		1	1	2	1	1	1	0	1	1	1	1
10410		1	1	2	1	1	1	0	1	1	1	1
10411		1	1	2	1	1	1	0	1	1	1	1
10412		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/ 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 Dose : HBM 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/ 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 7 Dose : HBM 100 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/ 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 Dose : HBM 300 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

Animal No.	Secretions/ 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 7 Dose : HBM 1000 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/ 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 Dose : HBM 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/ 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 14 Dose : HBM 100 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/ 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 14 Dose : HBM 300 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

Animal No.	Secretions/ 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 Dose : HBM 1000 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/ 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.

Sex : Male	Detailed clinical observation (on the hand)											Species : Rat
	Stage : Day 21 Dose : HBM 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/ 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 : Day 21 Dose : HBM 100 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
10202	1	1	2	1	1	1	0	1	1	1	1
10203	1	1	2	1	1	1	0	1	1	1	1
10204	1	1	2	1	1	1	0	1	1	1	1
10205	1	1	2	1	1	1	0	1	1	1	1
10206	1	1	2	1	1	1	0	1	1	1	1
10207	1	1	2	1	1	1	0	1	1	1	1
10208	1	1	2	1	1	1	0	1	1	1	1
10209	1	1	2	1	1	1	0	1	1	1	1
10210	1	1	2	1	1	1	0	1	1	1	1
10211	1	1	2	1	1	1	0	1	1	1	1
10212	1	1	2	1	1	1	0	1	1	1	1
n	12	12	12	12	12	12	12	12	12	12	12


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Animal No.	Secretions/ 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 Dose : HBM 300 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

Animal No.	Secretions/ 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 Dose : HBM 1000 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/ 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 Dose : HBM 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/ 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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Day 28			Species : Rat					
	Sex : Male	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
10202		1	1	2	1	1	1	0	1	1	1	1
10203		1	1	2	1	1	1	0	1	1	1	1
10204		1	1	2	1	1	1	0	1	1	1	1
10205		1	1	2	1	1	1	0	1	1	1	1
10206		1	1	2	1	1	1	0	1	1	1	1
10207		1	1	2	1	1	1	0	1	1	1	1
10208		1	1	2	1	1	1	0	1	1	1	1
10209		1	1	2	1	1	1	0	1	1	1	1
10210		1	1	2	1	1	1	0	1	1	1	1
10211		1	1	2	1	1	1	0	1	1	1	1
10212		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/ 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.

Animal No.	Sex : Male		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
10301	1	1	2	1	1	1	0	1	1	1	1
10302	1	1	2	1	1	1	0	1	1	1	1
10303	1	1	2	1	1	1	0	1	1	1	1
10304	1	1	2	1	1	1	0	1	1	1	1
10305	1	1	2	1	1	1	0	1	1	1	1
10306	1	1	2	1	1	1	0	1	1	1	1
10307	1	1	2	1	1	1	0	1	1	1	1
10308	1	1	2	1	1	1	0	1	1	1	1
10309	1	1	2	1	1	1	0	1	1	1	1
10310	1	1	2	1	1	1	0	1	1	1	1
10311	1	1	2	1	1	1	0	1	1	1	1
10312	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/ 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 28 Dose : HBM 1000 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/ 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.

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		
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	12	

Animal No.	Secretions/ Excretions	
	0	1
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.

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
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
50256		1	1	2	1	1	1	0	1	1	1	1
50257		1	1	2	1	1	1	0	1	1	1	1
50258		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		12	12	12	12	12	12	12	12	12	12	12

Animal No.	Secretions/ 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/ 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/ 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		
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	12	

Animal No.	Secretions/ Excretions											
	0	0	0	0	0	0	0	0	0	0	0	0
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.

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
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
50256	1	1	2	1	1	1	0	1	1	1	1
50257	1	1	2	1	1	1	0	1	1	1	1
50258	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	12	12	12	12	12	12	12	12	12	12	12

Animal No.	Secretions/ 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.	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
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/ 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.	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
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/ 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		
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	12	

Animal No.	Secretions/ Excretions											
	0	0	0	0	0	0	0	0	0	0	0	0
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.

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
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
50256	1	1	2	1	1	1	0	1	1	1	1
50257	1	1	2	1	1	1	0	1	1	1	1
50258	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	12	12	12	12	12	12	12	12	12	12	12

Animal No.	Secretions/ 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.	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	
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/ Excretions	
	0	
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.	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	
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/ Excretions	
	0	
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
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/ Excretions	
	0	
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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Day 21			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
50256		1	1	2	1	1	1	0	1	1	1	1
50257		1	1	2	1	1	1	0	1	1	1	1
50258		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		12	12	12	12	12	12	12	12	12	12	12

Animal No.	Secretions/ 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.	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
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/ 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.	Sex : Female		Detailed clinical observation (on the hand)		Stage : Day 21		Mucous membranes	Skin	Pupil size	Species : Rat	
	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes				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/ Excretions	
	0	
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 28 Dose : HBM 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	
<hr/>												
<hr/>												
Secretions/ Excretions												
Animal No.												
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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Day 28			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
50256		1	1	2	1	1	1	0	1	1	1	1
50257		1	1	2	1	1	1	0	1	1	1	1
50258		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		12	12	12	12	12	12	12	12	12	12	12

Animal No.	Secretions/ 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.	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
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/ 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 28			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/ 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		
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	12	

Animal No.	Secretions/ Excretions											
	0	0	0	0	0	0	0	0	0	0	0	0
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.

Animal No.	Sex : Female		Detailed clinical observation (on the hand)		Stage : Day 35		Species : Rat				
	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
50256	1	1	2	1	1	1	0	1	1	1	1
50257	1	1	2	1	1	1	0	1	1	1	1
50258	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	12	12	12	12	12	12	12	12	12	12	12

Animal No.	Secretions/ 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.	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		
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/ Excretions	
	0	1
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.	Sex : Female		Detailed clinical observation (on the hand)		Stage : Day 35		Mucous membranes	Skin	Pupil size	Species : Rat	
	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes				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/ 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 42			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
50153		1	1	2	1	1	1	0	1	1	1	1
50154		1	1	2	1	1	1	0	1	1	1	1
50156		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
50161		1	1	2	1	1	1	0	1	1	1	1
n		7	7	7	7	7	7	7	7	7	7	7

Animal No.	Secretions/ Excretions
50151	0
50153	0
50154	0
50156	0
50158	0
50159	0
50161	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 : 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
50254		1	1	2	1	1	1	0	1	1	1	1
50256		1	1	2	1	1	1	0	1	1	1	1
50257		1	1	2	1	1	1	0	1	1	1	1
50258		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
n		8	8	8	8	8	8	8	8	8	8	8

Animal No.	Secretions/ Excretions	
50251	0	
50252	0	
50254	0	
50256	0	
50257	0	
50258	0	
50260	0	
50261	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.

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
50352	1	1	2	1	1	1	1	0	1	1	1	1
50353	1	1	2	1	1	1	1	0	1	1	1	1
50356	1	1	2	1	1	1	1	0	1	1	1	1
50357	1	1	2	1	1	1	1	0	1	1	1	1
50359	1	1	2	1	1	1	1	0	1	1	1	1
50360	1	1	2	1	1	1	1	0	1	1	1	1
n	6	6	6	6	6	6	6	6	6	6	6	6

Animal No.	Secretions/ Excretions
50352	0
50353	0
50356	0
50357	0
50359	0
50360	0
n	6

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
50451		1	1	2	1	1	1	0	1	1	1	1
50452		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
n		8	8	8	8	8	8	8	8	8	8	8

Animal No.	Secretions/ Excretions	
50451	0	
50452	0	
50454	0	
50455	0	
50456	0	
50457	0	
50458	0	
50459	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.

Animal No.	Detailed clinical observation (on the hand)		Stage : Pre administration		Species : Rat				
	Sex : Female (satellite)		Dose : HBM 0 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes				
50551	1	1	2	1	1	0	1	1	1
50552	1	1	2	1	1	0	1	1	1
50553	1	1	2	1	1	0	1	1	1
50554	1	1	2	1	1	0	1	1	1
50555	1	1	2	1	1	0	1	1	1
50556	1	1	2	1	1	0	1	1	1
50557	1	1	2	1	1	0	1	1	1
50558	1	1	2	1	1	0	1	1	1
50559	1	1	2	1	1	0	1	1	1
50560	1	1	2	1	1	0	1	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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)		Dose : HBM 1000 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes			
50651	1	1	2	1	1	1	0	1	1
50652	1	1	2	1	1	1	0	1	1
50653	1	1	2	1	1	1	0	1	1
50654	1	1	2	1	1	1	0	1	1
50655	1	1	2	1	1	1	0	1	1
50656	1	1	2	1	1	1	0	1	1
50657	1	1	2	1	1	1	0	1	1
50658	1	1	2	1	1	1	0	1	1
50659	1	1	2	1	1	1	0	1	1
50660	1	1	2	1	1	1	0	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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)	Sex : Female (satellite)	Dose : HBM 0 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
50551	1	1	2	1	1	0	1	1	1
50552	1	1	2	1	1	0	1	1	1
50553	1	1	2	1	1	0	1	1	1
50554	1	1	2	1	1	0	1	1	1
50555	1	1	2	1	1	0	1	1	1
50556	1	1	2	1	1	0	1	1	1
50557	1	1	2	1	1	0	1	1	1
50558	1	1	2	1	1	0	1	1	1
50559	1	1	2	1	1	0	1	1	1
50560	1	1	2	1	1	0	1	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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)		Dose : HBM 1000 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes			
50651	1	1	2	1	1	1	0	1	1
50652	1	1	2	1	1	1	0	1	1
50653	1	1	2	1	1	1	0	1	1
50654	1	1	2	1	1	1	0	1	1
50655	1	1	2	1	1	1	0	1	1
50656	1	1	2	1	1	1	0	1	1
50657	1	1	2	1	1	1	0	1	1
50658	1	1	2	1	1	1	0	1	1
50659	1	1	2	1	1	1	0	1	1
50660	1	1	2	1	1	1	0	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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 14		Species : Rat				
	Sex : Female (satellite)	Sex : Female (satellite)	Dose : HBM 0 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
50551	1	1	2	1	1	0	1	1	1
50552	1	1	2	1	1	0	1	1	1
50553	1	1	2	1	1	0	1	1	1
50554	1	1	2	1	1	0	1	1	1
50555	1	1	2	1	1	0	1	1	1
50556	1	1	2	1	1	0	1	1	1
50557	1	1	2	1	1	0	1	1	1
50558	1	1	2	1	1	0	1	1	1
50559	1	1	2	1	1	0	1	1	1
50560	1	1	2	1	1	0	1	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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)	Sex : Female (satellite)	Dose : HBM 1000 mg/kg	Eyes	Mucous membranes	Skin	Pupil size	Lacration	Salivation
50651	1	1	2	1	1	0	1	1	1
50652	1	1	2	1	1	0	1	1	1
50653	1	1	2	1	1	0	1	1	1
50654	1	1	2	1	1	0	1	1	1
50655	1	1	2	1	1	0	1	1	1
50656	1	1	2	1	1	0	1	1	1
50657	1	1	2	1	1	0	1	1	1
50658	1	1	2	1	1	0	1	1	1
50659	1	1	2	1	1	0	1	1	1
50660	1	1	2	1	1	0	1	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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 21		Species : Rat				
	Sex : Female (satellite)	Sex : Female (satellite)	Dose : HBM 0 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes			
50551	1	1	2	1	1	1	0	1	1
50552	1	1	2	1	1	1	0	1	1
50553	1	1	2	1	1	1	0	1	1
50554	1	1	2	1	1	1	0	1	1
50555	1	1	2	1	1	1	0	1	1
50556	1	1	2	1	1	1	0	1	1
50557	1	1	2	1	1	1	0	1	1
50558	1	1	2	1	1	1	0	1	1
50559	1	1	2	1	1	1	0	1	1
50560	1	1	2	1	1	1	0	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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 21		Dose : HBM 1000 mg/kg		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/ 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 28		Species : Rat				
	Sex : Female (satellite)		Dose : HBM 0 mg/kg		Mucous membranes	Skin	Pupil size	Lacration	Salivation
Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes				
50551	1	1	2	1	1	0	1	1	1
50552	1	1	2	1	1	0	1	1	1
50553	1	1	2	1	1	0	1	1	1
50554	1	1	2	1	1	0	1	1	1
50555	1	1	2	1	1	0	1	1	1
50556	1	1	2	1	1	0	1	1	1
50557	1	1	2	1	1	0	1	1	1
50558	1	1	2	1	1	0	1	1	1
50559	1	1	2	1	1	0	1	1	1
50560	1	1	2	1	1	0	1	1	1
n	10	10	10	10	10	10	10	10	10

Animal No.	Secretions/ 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		Dose : HBM 1000 mg/kg		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/ 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 : Recovery Day 7			Species : Rat					
	Sex : Male	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
10109		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

Animal No.	Secretions/ Excretions
10103	0
10104	0
10105	0
10109	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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Recovery Day 7			Species : Rat					
	Sex : Male	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacration	Salivation
10403		1	1	2	1	1	1	0	1	1	1	1
10407		1	1	2	1	1	1	0	1	1	1	1
10408		1	1	2	1	1	1	0	1	1	1	1
10411		1	1	2	1	1	1	0	1	1	1	1
10412		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/ Excretions
10403	0
10407	0
10408	0
10411	0
10412	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 : Male	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
10109		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

Animal No.	Secretions/ Excretions
10103	0
10104	0
10105	0
10109	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.

Animal No.	Detailed clinical observation (on the hand)			Stage : Recovery Day 14				Species : Rat				
	Sex : Male	Ease of Removal	Ease of Handling	Muscle tone	Piloerection	Fur	Eyes	Mucous membranes	Skin	Pupil size	Lacration	Salivation
10403		1	1	2	1	1	1	0	1	1	1	1
10407		1	1	2	1	1	1	0	1	1	1	1
10408		1	1	2	1	1	1	0	1	1	1	1
10411		1	1	2	1	1	1	0	1	1	1	1
10412		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/ Excretions
10403	0
10407	0
10408	0
10411	0
10412	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
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/ 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.

Detailed clinical observation (on the hand)				Stage : Recovery Day 7				Species : Rat			
Sex : Female (satellite)		Dose : HBM 1000 mg/kg									
Animal No.	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
50660	1	1	2	1	1	1	0	1	1	1	1
n	5	5	5	5	5	5	5	5	5	5	5

Secretions/ Excretions	
Animal No.	
50656	0
50657	0
50658	0
50659	0
50660	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
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/ 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
50660		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/ Excretions
50656	0
50657	0
50658	0
50659	0
50660	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 (in the open-field)										Species : Rat
	Stage : Pre administration Dose : HBM 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	1	0	0	0	1	1	1
10103	1	1	1	1	0	1	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 : Pre administration				Dose : HBM 100 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	1	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	1	1	0	0	1	1	1
10206	1	1	1	1	1	1	0	0	1	1	1
10207	1	1	1	1	0	1	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	1	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 : Pre administration Dose : HBM 300 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	1	1	0	0	1	1	1
10302	1	1	1	1	1	1	0	0	1	1	1
10303	1	1	1	1	1	1	0	0	1	1	1
10304	1	1	1	1	1	0	0	0	1	1	1
10305	1	1	1	1	1	1	0	0	1	1	1
10306	1	1	1	1	1	1	0	0	1	1	1
10307	1	1	1	1	0	1	0	0	1	1	1
10308	1	1	1	1	0	0	0	0	1	1	1
10309	1	1	1	1	0	1	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 : Pre administration Dose : HBM 1000 mg/kg								Vocalization	Aggression	
Animal No.	Gait	Co-ordination of movement	Reactivity to stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward		
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	0	1	0	0	1	1	1
10405	1	1	1	1	1	1	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	1	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	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 : Day 7 Dose : HBM 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	1	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 Dose : HBM 100 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	1	0	0	0	1	1	1
10205	1	1	1	1	0	0	0	0	1	1	1
10206	1	1	1	1	1	1	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 7 Dose : HBM 300 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	1	1	0	0	1	1	1
10306	1	1	1	1	1	1	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	1	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 : Day 7 Dose : HBM 1000 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 Dose : HBM 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	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 Dose : HBM 100 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	1	0	0	1	1	1
10206	1	1	1	1	0	1	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 Dose : HBM 300 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	1	1	0	0	1	1	1
10306	1	1	1	1	0	0	0	0	1	1	1
10307	1	1	1	1	1	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 Dose : HBM 1000 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	1	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 Dose : HBM 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	1	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 Dose : HBM 100 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	1	1	0	0	1	1	1
10206	1	1	1	1	1	1	0	0	1	1	1
10207	1	1	1	1	0	0	0	0	1	1	1
10208	1	1	1	1	1	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 Dose : HBM 300 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	1	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	1	1	0	0	1	1	1
10306	1	1	1	1	1	0	0	0	1	1	1
10307	1	1	1	1	1	0	0	0	1	1	1
10308	1	1	1	1	0	0	0	0	1	1	1
10309	1	1	1	1	1	1	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	1	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 : Day 21 Dose : HBM 1000 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	1	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 Dose : HBM 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	0	0	0	1	1	1
10102	1	1	1	1	0	0	0	0	1	1	1
10103	1	1	1	1	1	0	0	0	1	1	1
10104	1	1	1	1	0	0	0	0	1	1	1
10105	1	1	1	1	1	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 Dose : HBM 100 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	1	0	0	0	1	1	1
10204	1	1	1	1	0	0	0	0	1	1	1
10205	1	1	1	1	0	1	0	0	1	1	1
10206	1	1	1	1	0	1	0	0	1	1	1
10207	1	1	1	1	0	0	0	0	1	1	1
10208	1	1	1	1	1	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 Dose : HBM 300 mg/kg								Vocalization	Aggression
Animal No.	Gait	Co-ordination of movement	Reactivity to stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	
10301	1	1	1	1	0	0	0	0	1	1
10302	1	1	1	1	0	0	0	0	1	1
10303	1	1	1	1	0	0	0	0	1	1
10304	1	1	1	1	0	0	0	0	1	1
10305	1	1	1	1	1	1	0	0	1	1
10306	1	1	1	1	1	1	0	0	1	1
10307	1	1	1	1	0	0	0	0	1	1
10308	1	1	1	1	0	0	0	0	1	1
10309	1	1	1	1	0	0	0	0	1	1
10310	1	1	1	1	0	0	0	0	1	1
10311	1	1	1	1	0	0	0	0	1	1
10312	1	1	1	1	1	0	0	0	1	1
n	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 Dose : HBM 1000 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	1	0	0	1	1	1
10407	1	1	1	1	1	0	0	0	1	1	1
10408	1	1	1	1	0	0	0	0	1	1	1
10409	1	1	1	1	1	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.

Animal No.	Detailed clinical observation (in the open-field)			Stage : Pre administration				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	1	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	1	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 Dose : HBM 100 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	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	1	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	1	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)			Stage : Pre administration				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	1	1	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	1	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	1	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 Dose : HBM 1000 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	1	0	0	1	1	1
50454	1	1	1	1	1	0	0	0	1	1	1
50455	1	1	1	1	0	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.

Animal No.	Detailed clinical observation (in the open-field)			Stage : Day 7 Dose : HBM 0 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
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	0	0	0	0	1	1	1
50157		1	1	1	1	0	0	0	0	1	1	1
50158		1	1	1	1	1	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 Dose : HBM 100 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	1	0	0	0	1	1	1
50253	1	1	1	1	0	0	0	0	1	1	1
50254	1	1	1	1	1	0	0	0	1	1	1
50255	1	1	1	1	1	0	0	0	1	1	1
50256	1	1	1	1	1	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.

Sex : Female	Detailed clinical observation (in the open-field)										Species : Rat
	Stage : Day 7 Dose : HBM 300 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)			Stage : Day 7 Dose : HBM 1000 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	0	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)			Stage : Day 14				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 14 Dose : HBM 100 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.

Sex : Female	Detailed clinical observation (in the open-field)										Species : Rat
	Stage : Day 14 Dose : HBM 300 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	1	0	0	0	1	1	1
50353	1	1	1	1	0	0	0	0	1	1	1
50354	1	1	1	1	1	1	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.

Sex : Female	Detailed clinical observation (in the open-field)										Species : Rat
	Stage : Day 14 Dose : HBM 1000 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	0	0	0	0	1	1	1
50455	1	1	1	1	0	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)			Stage : Day 21				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 Dose : HBM 100 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)			Stage : Day 21				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)			Stage : Day 21			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	0	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)			Stage : Day 28				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)			Stage : Day 28			Species : Rat				
	Gait	Co-ordination of movement	Reactivity to stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
Animal No.											
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.

Sex : Female	Detailed clinical observation (in the open-field)										Species : Rat
	Stage : Day 28 Dose : HBM 300 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.

Animal No.	Detailed clinical observation (in the open-field)			Stage : Day 28			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	0	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)			Stage : Day 35				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 35 Dose : HBM 100 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)			Stage : Day 35				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	1	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)				Stage : Day 35				Species : Rat			
Sex : Female				Dose : HBM 1000 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	0	0	0	0	1	1	1
50455	1	1	1	1	0	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.

Detailed clinical observation (in the open-field)			Stage : Day 42			Species : Rat					
Sex : Female			Dose : HBM 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
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
50158	1	1	1	1	0	0	0	0	1	1	1
50159	1	1	1	1	0	0	0	0	1	1	1
50161	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.

Detailed clinical observation (in the open-field) Sex : Female				Stage : Day 42 Dose : HBM 100 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
50251	1	1	1	1	0	0	0	0	1	1	1
50252	1	1	1	1	0	0	0	0	1	1	1
50254	1	1	1	1	0	0	0	0	1	1	1
50256	1	1	1	1	1	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
50260	1	1	1	1	0	0	0	0	1	1	1
50261	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)			Stage : Day 42			Species : Rat					
Sex : Female			Dose : HBM 300 mg/kg								
Animal No.	Gait	Co-ordination of movement	Reactivity to stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
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
50359	1	1	1	1	0	0	0	0	1	1	1
50360	1	1	1	1	0	0	0	0	1	1	1
n	6	6	6	6	6	6	6	6	6	6	6

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) Sex : Female			Stage : Day 42 Dose : HBM 1000 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
50454	1	1	1	1	0	0	0	0	1	1	1
50455	1	1	1	1	0	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
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.

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	1	0	0	1	1	1
50558		1	1	1	1	1	0	0	0	1	1	1
50559		1	1	1	1	1	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	1	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
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	1	0	0	0	1	1	1
50553		1	1	1	1	0	0	0	0	1	1	1
50554		1	1	1	1	1	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	1	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.

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
50651		1	1	1	1	1	1	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	1	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 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.

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
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
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 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.

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
50651		1	1	1	1	1	1	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
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 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	1	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.

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
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
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.

Detailed clinical observation (in the open-field)			Stage : Recovery Day 7						Species : Rat		
Sex : Male			Dose : HBM 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
10103	1	1	1	1	0	1	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
10109	1	1	1	1	0	0	0	0	1	1	1
10111	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)			Stage : Recovery Day 7						Species : Rat		
Sex : Male			Dose : HBM 1000 mg/kg								
Animal No.	Gait	Co-ordination of movement	Reactivity to stimuli	Searching	Urination	Defecation	Excessive grooming	Unusual head movement	Walking backward	Vocalization	Aggression
10403	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
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	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						Species : Rat		
Sex : Male			Dose : HBM 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
10103	1	1	1	1	1	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
10109	1	1	1	1	0	0	0	0	1	1	1
10111	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)			Stage : Recovery Day 14 Dose : HBM 1000 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.											
10403	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	1	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	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 7			Species : Rat				
	Sex : Female (satellite)			Dose : HBM 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
50556	1	1	1	1	0	0	0	0	1	1	1
50557	1	1	1	1	1	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) Sex : Female (satellite)			Stage : Recovery Day 7 Dose : HBM 1000 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	1	0	0	0	1	1	1
50659	1	1	1	1	0	0	0	0	1	1	1
50660	1	1	1	1	1	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)			Stage : Recovery Day 14			Species : Rat				
	Sex : Female (satellite)			Dose : HBM 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
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) Sex : Female (satellite)			Stage : Recovery Day 14 Dose : HBM 1000 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
50660	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.

Functional observations (on the desk)		Stage : Week 4 Dose : HBM 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
10109		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 Dose : HBM 100 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
10208		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 Dose : HBM 300 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
10306		4	2	1	2	1	1
10309		4	2	1	2	1	1
10312		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 Dose : HBM 1000 mg/kg				Species : Rat	
Sex : Male		Visual reactivity	Touch reactivity	Auditory reactivity	Pain reactivity	Proprioceptive reactivity	Righting reflex
Animal No.							
10403		4	2	1	2	1	1
10407		4	2	1	2	1	1
10408		4	2	1	2	1	1
10411		4	2	1	2	1	1
10412		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 Dose : HBM 0 mg/kg					Species : Rat
Sex : Female		Visual reactivity	Touch reactivity	Auditory reactivity	Pain reactivity	Proprioceptive reactivity	Righting reflex
Animal No.							
50152		4	2	1	2	1	1
50155		4	2	1	2	1	1
50157		4	2	1	2	1	1
50160		4	2	1	2	1	1
50162		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 Dose : HBM 100 mg/kg				Species : Rat	
Sex : Female		Visual reactivity	Touch reactivity	Auditory reactivity	Pain reactivity	Proprioceptive reactivity	Righting reflex
Animal No.							
50253		4	2	1	2	1	1
50254		4	2	1	2	1	1
50255		4	2	1	2	1	1
50259		4	2	1	2	1	1
50262		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 Dose : HBM 300 mg/kg				Species : Rat	
Sex : Female		Visual reactivity	Touch reactivity	Auditory reactivity	Pain reactivity	Proprioceptive reactivity	Righting reflex
Animal No.							
50351		4	2	1	2	1	1
50354		4	2	1	2	1	1
50355		4	2	1	2	1	1
50361		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 Dose : HBM 1000 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
50453		4	2	1	2	1	1
50460		4	2	1	2	1	1
50461		4	2	1	2	1	1
50462		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 : HBM 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 : HBM 1000 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
50660	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 : HBM 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
10109		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.

Animal No.	Functional observations (on the desk)			Stage : Recovery Week 2		Species : Rat
	Sex : Male	Visual reactivity	Touch reactivity	Auditory reactivity	Pain reactivity	
10403		4	2	1	2	1
10407		4	2	1	2	1
10408		4	2	1	2	1
10411		4	2	1	2	1
10412		4	2	1	2	1
n		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.

Animal No.	Grip strength		Stage : Week 4				Species : Rat	
	Sex : Male		Dose : HBM 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	1083	1091	1271	1148.3	500	438	512	483.3
10104	1210	1507	1417	1378.0	433	518	584	511.7
10105	1324	1256	1474	1351.3	441	488	476	468.3
10109	1619	1314	1293	1408.7	422	486	396	434.7
10111	1140	1110	1659	1303.0	660	569	603	610.7
n	5	5	5	5	5	5	5	5
Mean	1275.2	1255.6	1422.8	1317.86	491.2	499.8	514.2	501.74
S.D.	212.2	169.5	156.8	102.42	99.1	48.1	84.0	66.94

Animal No.	Grip strength		Stage : Week 4				Species : Rat	
	Sex : Male		Dose : HBM 100 mg/kg					
	Forelimb, 1st	Forelimb, 2nd	Forelimb, 3rd	Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	Hindlimb
10202	g	g	g	g	g	g	g	g
10202	1112	1026	992	1043.3	529	603	589	573.7
10204	1298	1258	1414	1323.3	407	552	396	451.7
10208	1072	1145	1026	1081.0	575	569	521	555.0
10209	1354	1545	1426	1441.7	577	540	611	576.0
10210	1482	1275	1486	1414.3	580	559	523	554.0
n	5	5	5	5	5	5	5	5
Mean	1263.6	1249.8	1268.8	1260.72	533.6	564.6	528.0	542.08
S.D.	170.8	192.9	239.0	186.97	73.8	23.9	83.8	51.55

Animal No.	Grip strength		Stage : Week 4				Species : Rat	
	Sex : Male		Dose : HBM 300 mg/kg	Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	
	Forelimb, 1st	Forelimb, 2nd	Forelimb, 3rd	Forelimb				
10302	1215	1488	1477	1393.3	505	459	420	461.3
10303	1531	1526	1685	1580.7	591	584	472	549.0
10306	1644	1626	1677	1649.0	503	549	615	555.7
10309	1249	1458	1381	1362.7	652	538	699	629.7
10312	1642	1515	1622	1593.0	606	525	608	579.7
n	5	5	5	5	5	5	5	5
Mean	1456.2	1522.6	1568.4	1515.74	571.4	531.0	562.8	555.08
S.D.	210.1	63.5	133.9	128.80	65.5	45.8	114.0	61.25

Animal No.	Grip strength		Stage : Week 4				Species : Rat	
	Sex : Male		Dose : HBM 1000 mg/kg					
	Forelimb, 1st	Forelimb, 2nd	Forelimb, 3rd	Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	Hindlimb
10403	g	g	g	g	g	g	g	g
10403	1144	1055	1236	1145.0	452	412	444	436.0
10407	1371	1632	1479	1494.0	440	506	446	464.0
10408	1612	1504	1670	1595.3	569	455	640	554.7
10411	1089	836	835	920.0	477	490	587	518.0
10412	1460	1412	1587	1486.3	612	624	655	630.3
n	5	5	5	5	5	5	5	5
Mean	1335.2	1287.8	1361.4	1328.12	510.0	497.4	554.4	520.60
S.D.	218.3	331.3	336.4	284.61	76.2	79.4	103.0	76.75

Animal No.	Grip strength		Stage : Lactation Day 4				Species : Rat	
	Sex : Female		Dose : HBM 0 mg/kg	Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	
	g	g	g	g	g	g	g	g
50152	1165	1313	1325	1267.7	392	424	352	389.3
50155	1000	1240	1357	1199.0	424	400	343	389.0
50157	1223	1184	1116	1174.3	401	472	397	423.3
50160	1158	1179	1035	1124.0	447	374	437	419.3
50162	971	919	989	959.7	327	471	360	386.0
n	5	5	5	5	5	5	5	5
Mean	1103.4	1167.0	1164.4	1144.94	398.2	428.2	377.8	401.38
S.D.	111.0	148.8	167.9	115.77	45.2	43.3	38.9	18.28

Animal No.	Grip strength		Stage : Lactation Day 4				Species : Rat
	Sex : Female		Forelimb	Hindlimb	Hindlimb	Hindlimb	
	g	g	g	g	g	g	g
50253	1070	1101	1076	1082.3	370	414	348
50254	1209	1170	1375	1251.3	367	438	439
50255	1454	1355	1417	1408.7	404	345	416
50259	1292	1278	1268	1279.3	394	403	418
50262	1261	1028	1473	1254.0	316	377	482
n	5	5	5	5	5	5	5
Mean	1257.2	1186.4	1321.8	1255.12	370.2	395.4	420.6
S.D.	139.0	131.8	156.6	116.25	34.1	35.7	48.5
							395.40
							14.63

Animal No.	Grip strength		Stage : Lactation Day 4				Species : Rat
	Sex : Female		Forelimb	Hindlimb	Hindlimb	Hindlimb	
	g	g	g	g	g	g	g
50351	1047	1324	1323	1231.3	495	461	404
50354	1163	1466	1367	1332.0	400	381	343
50355	1045	1126	1068	1079.7	376	370	356
50361	1356	1327	1252	1311.7	455	408	390
50362	1162	1031	1054	1082.3	375	386	382.3
n	5	5	5	5	5	5	5
Mean	1154.6	1254.8	1212.8	1207.40	420.2	401.2	375.8
S.D.	126.8	174.1	144.6	121.38	52.9	36.2	25.3
							35.96

Animal No.	Grip strength		Stage : Lactation Day 4				Species : Rat	
	Sex : Female		Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd		
	g	g	g	g	g	g	g	
50451	1375	1158	1397	1310.0	528	395	497	473.3
50453	1220	1293	1320	1277.7	341	309	305	318.3
50460	1241	1017	1046	1101.3	445	409	402	418.7
50461	1265	1452	1415	1377.3	357	401	476	411.3
50462	998	1056	986	1013.3	367	470	391	409.3
n	5	5	5	5	5	5	5	5
Mean	1219.8	1195.2	1232.8	1215.92	407.6	396.8	414.2	406.18
S.D.	137.6	178.9	202.2	152.40	78.3	57.5	76.3	55.72

Animal No.	Grip strength		Stage : Week 4				Species : Rat
	Sex : Female (satellite)		Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	
	g	g	g	g	g	g	g
50556	994	1035	1186	1071.7	552	489	459
50557	974	936	949	953.0	368	470	532
50558	1184	1192	1196	1190.7	519	380	429
50559	1049	1299	1065	1137.7	409	357	346
50560	1289	1046	1101	1145.3	413	522	432
n	5	5	5	5	5	5	5
Mean	1098.0	1101.6	1099.4	1099.68	452.2	443.6	439.6
S.D.	134.6	143.3	100.8	92.34	78.9	71.5	66.8
							445.16
							46.91

Animal No.	Grip strength		Stage : Week 4				Species : Rat
	Sex : Female (satellite)		Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	
	g	g	g	g	g	g	g
50656	1018	1080	970	1022.7	385	413	380
50657	1030	1170	1044	1081.3	323	326	351
50658	1095	1051	1198	1114.7	572	639	475
50659	1313	980	1189	1160.7	280	253	430
50660	1023	1001	853	959.0	320	314	328
n	5	5	5	5	5	5	5
Mean	1095.8	1056.4	1050.8	1067.68	376.0	389.0	392.8
S.D.	125.4	74.8	147.0	78.87	115.8	151.0	59.7
							102.82

Animal No.	Grip strength		Stage : Recovery Week 2				Species : Rat	
	Sex : Male		Dose : HBM 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	1404	1247	1012	1221.0	414	601	524	513.0
10104	1459	1246	1409	1371.3	552	596	400	516.0
10105	1848	1651	1622	1707.0	462	590	548	533.3
10109	1491	1230	1108	1276.3	433	439	449	440.3
10111	1489	1587	1255	1443.7	365	523	445	444.3
n	5	5	5	5	5	5	5	5
Mean	1538.2	1392.2	1281.2	1403.86	445.2	549.8	473.2	489.38
S.D.	176.7	208.4	242.7	189.90	69.4	69.6	61.1	43.69

Animal No.	Grip strength		Stage : Recovery Week 2				Species : Rat	
	Sex : Male		Dose : HBM 1000 mg/kg					
	Forelimb, 1st	Forelimb, 2nd	Forelimb, 3rd	Forelimb	Hindlimb, 1st	Hindlimb, 2nd	Hindlimb, 3rd	Hindlimb
10403	g	g	g	g	g	g	g	g
10403	1507	1393	1275	1391.7	465	406	453	441.3
10407	1654	1314	1366	1444.7	564	572	569	568.3
10408	2016	1912	1754	1894.0	649	504	721	624.7
10411	1311	1512	1481	1434.7	418	432	410	420.0
10412	1892	2178	1881	1983.7	409	423	452	428.0
n	5	5	5	5	5	5	5	5
Mean	1676.0	1661.8	1551.4	1629.76	501.0	467.4	521.0	496.46
S.D.	284.8	369.0	257.6	284.63	103.1	69.4	126.5	93.78

Motor activity measurements		Stage : Week 4						Species : Rat	
Sex : Male		Dose : HBM 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	308	89	0	0	0	0	0	397	
10104	490	389	267	261	204	84	1695		
10105	527	370	366	165	198	75	1701		
10109	262	165	119	168	95	40	849		
10111	484	277	74	3	209	18	1065		
n	5	5	5	5	5	5	5		
Mean	414.2	258.0	165.2	119.4	141.2	43.4	1141.4		
S.D.	120.2	129.7	148.7	114.3	92.0	36.0	562.4		

Motor activity measurements		Stage : Week 4						Species : Rat	
Sex : Male		Dose : HBM 100 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.	
10202	601	356	365	686	236	168	2412		
10204	752	468	216	247	61	4	1748		
10208	184	18	2	8	0	0	212		
10209	584	485	260	74	83	0	1486		
10210	470	350	331	317	328	222	2018		
n	5	5	5	5	5	5	5		
Mean	518.2	335.4	234.8	266.4	141.6	78.8	1575.2		
S.D.	212.0	188.0	142.6	265.9	135.7	107.8	835.5		

Motor activity measurements		Stage : Week 4						Species : Rat	
Sex : Male		Dose : HBM 300 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	588	403	220	127	104	3	1445		
10303	767	489	296	50	0	0	0	1602	
10306	475	257	3	0	0	0	0	735	
10309	651	513	374	257	297	211	2303		
10312	259	166	77	21	0	0	0	523	
n	5	5	5	5	5	5	5		
Mean	548.0	365.6	194.0	91.0	80.2	42.8	1321.6		
S.D.	193.0	150.0	153.0	104.5	129.3	94.0	713.9		

Motor activity measurements		Stage : Week 4						Species : Rat	
Sex : Male		Dose : HBM 1000 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.	
10403	998	854	696	162	9	0	2719		
10407	792	634	341	144	15	0	1926		
10408	636	405	139	43	0	0	1223		
10411	467	189	247	110	120	178	1311		
10412	803	146	1	0	0	0	950		
n	5	5	5	5	5	5	5		
Mean	739.2	445.6	284.8	91.8	28.8	35.6	1625.8		
S.D.	199.1	299.8	262.4	68.5	51.4	79.6	707.7		

Motor activity measurements		Stage : Lactation Day 4						Species : Rat
Sex : Female		0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	
Animal No.	No.	No.	No.	No.	No.	No.	No.	No.
50152	351	113	126	73	0	0	663	
50155	407	0	43	0	0	0	450	
50157	706	645	344	389	550	203	2837	
50160	439	239	167	89	131	45	1110	
50162	503	431	57	47	71	0	1109	
n	5	5	5	5	5	5	5	
Mean	481.2	285.6	147.4	119.6	150.4	49.6	1233.8	
S.D.	137.2	256.8	121.0	154.3	230.0	87.9	940.9	

Motor activity measurements		Stage : Lactation Day 4						Species : Rat	
Sex : Female		Dose : HBM 100 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.	
50253	657	71	61	308	136	0	1233		
50254	724	204	254	153	187	244	1766		
50255	1106	240	114	322	3	0	1785		
50259	296	139	137	29	79	82	762		
50262	460	359	254	138	0	224	1435		
n	5	5	5	5	5	5	5		
Mean	648.6	202.6	164.0	190.0	81.0	110.0	1396.2		
S.D.	306.1	108.7	86.7	123.8	82.0	118.3	423.8		

Motor activity measurements		Stage : Lactation Day 4						Species : Rat
Sex : Female		Dose : HBM 300 mg/kg		0' - 60'				
		0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	
Animal No.	No.	No.	No.	No.	No.	No.	No.	
50351	224	92	46	0	0	130	492	
50354	661	498	182	31	0	30	1402	
50355	550	112	0	22	0	0	684	
50361	484	161	103	25	49	101	923	
50362	593	180	0	0	0	2	775	
n	5	5	5	5	5	5	5	
Mean	502.4	208.6	66.2	15.6	9.8	52.6	855.2	
S.D.	168.4	165.7	77.4	14.6	21.9	59.5	343.2	

Motor activity measurements		Stage : Lactation Day 4						Species : Rat
Sex : Female		0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'	
Animal No.	No.	No.	No.	No.	No.	No.	No.	No.
50451	559	235	134	0	17	165	1110	
50453	777	441	4	175	0	0	1397	
50460	845	311	24	183	0	0	1363	
50461	577	4	25	5	46	0	657	
50462	413	258	80	94	188	92	1125	
n	5	5	5	5	5	5	5	
Mean	634.2	249.8	53.4	91.4	50.2	51.4	1130.4	
S.D.	175.1	158.9	53.2	88.3	79.3	75.0	295.7	

Motor activity measurements								Species : Rat
Sex : Female (satellite)								
0' - 10'		10' - 20'		20' - 30'		30' - 40'		Stage : Week 4
Dose : HBM 0 mg/kg		40' - 50'		50' - 60'		0' - 60'		
Animal No.	No.	No.	No.	No.	No.	No.	No.	
50556	1058	1030	785	337	518	8	3736	
50557	578	313	128	335	188	29	1571	
50558	792	588	346	138	0	0	1864	
50559	365	225	132	0	0	0	722	
50560	727	544	163	0	78	30	1542	
n	5	5	5	5	5	5	5	
Mean	704.0	540.0	310.8	162.0	156.8	13.4	1887.0	
S.D.	257.1	313.5	279.9	168.5	216.1	15.1	1117.5	

Motor activity measurements								Species : Rat	
Sex : Female (satellite)		Stage : Week 4							
		0' - 10'	10' - 20'	20' - 30'	30' - 40'	40' - 50'	50' - 60'		
Animal No.	No.	No.	No.	No.	No.	No.	No.		
50656	432	198	195	28	86	0	939		
50657	1150	625	187	68	157	0	2187		
50658	673	543	546	421	234	21	2438		
50659	1104	704	380	331	177	0	2696		
50660	977	558	43	392	405	98	2473		
n	5	5	5	5	5	5	5		
Mean	867.2	525.6	270.2	248.0	211.8	23.8	2146.6		
S.D.	306.3	193.9	195.1	186.0	120.3	42.5	698.8		

Motor activity measurements		Stage : Recovery Week 2						Species : Rat	
Sex : Male		Dose : HBM 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	214	139	54	69	86	38	600		
10104	897	541	314	289	221	240	2502		
10105	639	444	361	392	316	192	2344		
10109	707	476	469	261	494	297	2704		
10111	416	253	125	26	60	11	891		
n	5	5	5	5	5	5	5		
Mean	574.6	370.6	264.6	207.4	235.4	155.6	1808.2		
S.D.	265.0	168.1	171.3	154.7	177.9	125.7	983.9		

Motor activity measurements		Stage : Recovery Week 2						Species : Rat	
Sex : Male		Dose : HBM 1000 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.	
10403	569	508	254	217	144	176	1868		
10407	876	624	262	165	90	373	2390		
10408	883	227	344	173	0	0	1627		
10411	901	912	704	403	578	222	3720		
10412	559	427	173	123	144	72	1498		
n	5	5	5	5	5	5	5		
Mean	757.6	539.6	347.4	216.2	191.2	168.6	2220.6		
S.D.	177.0	253.6	208.3	109.6	224.1	143.6	904.9		

Animal No.	Body weight Sex : Male /Day		Period : Administration Day 1-28 Dose : HBM 0 mg/kg					Unit : g	Species : Rat
	1	4	7	14	21	28	Body weight gain		
10101	356	371	381	405	427	449	93		
10102	355	374	389	409	428	452	97		
10103	372	386	399	425	439	462	90		
10104	370	383	389	408	437	464	94		
10105	382	392	401	415	439	469	87		
10106	390	406	426	466	487	505	115		
10107	406	421	436	462	482	503	97		
10108	372	375	385	404	415	449	77		
10109	378	396	416	443	463	478	100		
10110	347	360	371	386	397	415	68		
10111	388	401	415	436	458	475	87		
10112	388	416	436	469	492	514	126		
n	12	12	12	12	12	12	12		
Mean	375.3	390.1	403.7	427.3	447.0	469.6	94.3		
S.D.	17.0	18.7	21.9	27.6	29.8	28.1	15.4		

Animal No.	Body weight Sex : Male		Period : Administration Day 1-28 Dose : HBM 100 mg/kg					Unit : g	Species : Rat	
	/Day		1	4	7	14	21	28	Body weight gain	
10201		382	401	419	447	476	498	516		
10202		382	398	416	432	457	466	484	84	
10203		402	414	419	434	459	484	502	82	
10204		379	391	412	434	453	481	502	102	
10205		384	397	413	444	469	495	511		
10206		401	419	437	471	492	526	550	125	
10207		365	382	395	426	438	455	473	90	
10208		362	376	392	422	444	465	483	103	
10209		364	380	401	426	454	473	491	109	
10210		368	387	408	432	451	477	495	109	
10211		354	369	382	412	430	449	467	95	
10212		344	347	356	384	405	426	444	82	
n		12	12	12	12	12	12	12		
Mean		373.9	388.4	404.2	430.3	452.3	474.6	500.7		
S.D.		17.7	19.7	21.0	20.8	22.4	25.8	24.1		

Animal No.	Body weight Sex : Male		Period : Administration Day 1-28 Dose : HBM 300 mg/kg					Unit : g	Species : Rat	
	/Day		1	4	7	14	21	28	Body weight gain	
10301		352	360	370	399	428	448	468	96	
10302		380	391	401	426	442	466	477	86	
10303		368	385	400	434	456	477	490	109	
10304		384	400	414	440	468	490	523	106	
10305		403	420	435	461	496	523	553	120	
10306		380	396	413	437	464	481	509	101	
10307		339	349	354	365	400	419	448	80	
10308		367	376	394	420	440	461	481	94	
10309		365	375	391	421	443	463	483	98	
10310		382	404	421	452	477	509	539	127	
10311		394	417	442	467	499	529	559	135	
10312		383	392	406	436	458	489	519	106	
n		12	12	12	12	12	12	12	12	
Mean		374.8	388.8	403.4	429.8	455.9	479.6	509.6	104.8	
S.D.		17.6	21.3	24.9	27.6	28.0	31.4	34.2	16.2	

Animal No.	Body weight Sex : Male		Period : Administration Day 1-28 Dose : HBM 1000 mg/kg					Unit : g	Species : Rat	
	/Day		1	4	7	14	21	28	Body weight gain	
10401		339	345	363	391	410	439	497	100	
10402		393	407	427	451	468	497	507	104	
10403		374	389	403	429	451	477	507	103	
10404		368	378	385	390	404	423	451	55	
10405		361	371	383	409	430	451	477	90	
10406		376	398	418	452	478	507	536	131	
10407		369	386	399	413	436	458	486	89	
10408		387	392	412	418	436	453	481	66	
10409		367	381	395	418	429	452	480	85	
10410		389	415	431	474	508	542	570	153	
10411		388	404	421	440	457	473	499	85	
10412		390	403	420	439	464	487	514	97	
n		12	12	12	12	12	12	12	12	
Mean		375.1	389.1	404.8	427.0	447.6	471.6	496.5		
S.D.		15.7	19.0	20.6	25.4	29.5	32.9	36.1		

Animal No.	Body weight Sex : Female		Period : F0 before mating Day 1-14 Dose : HBM 0 mg/kg			Unit : g	Species : Rat	
	/Day		1	4	7	14	Body weight gain	
50151		244	249	263	272	28		
50152		229	238	254	267	38		
50153		229	229	244	255	26		
50154		249	244	256	270	21		
50155		230	227	223	237	7		
50156		249	252	268	278	29		
50157		257	261	264	290	33		
50158		242	250	261	265	23		
50159		225	220	236	251	26		
50160		251	252	249	276	25		
50161		217	216	227	235	18		
50162		222	227	228	248	26		
n		12	12	12	12	12		
Mean		237.0	238.8	247.8	262.0	25.0		
S.D.		13.2	14.6	15.9	16.9	7.7		

Animal No.	Body weight Sex : Female		Period : F0 gestation Day 0-20 Dose : HBM 0 mg/kg			Unit : g	Species : Rat	
	/Day		0	7	14	20	Body weight gain	
50151		274	305	338	429	155		
50152		271	314	351	431	160		
50153		253	286	319	395	142		
50154		275	315	348	436	161		
50155		237	278	323	408	171		
50156		273	320	370	469	196		
50157		297	344	388	484	187		
50158		277	311	354	443	166		
50159		255	302	336	411	156		
50160		279	326	381	469	190		
50161		238	270	298	381	143		
50162		250	285	341	416	166		
n		12	12	12	12	12		
Mean		264.9	304.7	345.6	431.0	166.1		
S.D.		18.2	21.6	25.9	31.4	17.4		

Animal No.	Body weight Sex : Female		Period : F0 lactation Day 0-4 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	/Day	0			
		4	Body weight gain		
50151		320	349	29	
50152		364	379	15	
50153		315	341	26	
50154		342	361	19	
50155		313	331	18	
50156		333	370	37	
50157		360	394	34	
50158		333	343	10	
50159		320	344	24	
50160		368	367	-1	
50161		283	297	14	
50162		296	323	27	
n		12	12	12	
Mean		328.9	349.9	21.0	
S.D.		26.5	26.4	10.7	

Animal No.	Body weight Sex : Female		Period : F0 before mating Day 1-14 Dose : HBM 100 mg/kg			Unit : g	Species : Rat	
	/Day		1	4	7	14	Body weight gain	
50251		223	238	251	262	39		
50252		231	238	242	238	7		
50253		228	235	245	247	19		
50254		241	244	253	259	18		
50255		245	249	246	267	22		
50256		224	224	225	238	14		
50257		247	259	261	259	12		
50258		252	254	252	268	16		
50259		253	255	253	263	10		
50260		251	253	266	278	27		
50261		216	223	230	234	18		
50262		219	223	225	235	16		
n		12	12	12	12	12		
Mean		235.8	241.3	245.8	254.0	18.2		
S.D.		13.8	13.1	13.3	14.9	8.4		

Animal No.	Body weight Sex : Female		Period : F0 gestation Day 0-20 Dose : HBM 100 mg/kg			Unit : g	Species : Rat	
	/Day		0	7	14	20	Body weight gain	
50251		271	305	347	446	175		
50252		253	298	336	418	165		
50253		251	279	310	387	136		
50254		266	290	322	396	130		
50255		268	310	359	448	180		
50256		234	283	311	363	129		
50257		265	308	340	423	158		
50258		264	305	344	431	167		
50259		270	310	357	456	186		
50260		282	319	350	418	136		
50261		261	308	355	434	173		
50262		241	277	318	407	166		
n		12	12	12	12	12		
Mean		260.5	299.3	337.4	418.9	158.4		
S.D.		13.5	13.8	17.9	27.2	20.4		

Animal No.	Body weight Sex : Female		Period : F0 lactation Day 0-4 Dose : HBM 100 mg/kg	Unit : g	Species : Rat
	/Day	0	4	Body weight gain	
50251		320	350	30	
50252		317	345	28	
50253		294	319	25	
50254		308	332	24	
50255		349	367	18	
50256		296	318	22	
50257		317	318	1	
50258		316	351	35	
50259		334	358	24	
50260		333	357	24	
50261		338	361	23	
50262		297	322	25	
n		12	12	12	
Mean		318.3	341.5	23.3	
S.D.		17.7	18.6	8.2	

Animal No.	Body weight Sex : Female		Period : F0 before mating Day 1-14 Dose : HBM 300 mg/kg			Unit : g	Species : Rat	
	/Day		1	4	7	14	Body weight gain	
50351		236	243	246	260	24		
50352		219	230	240	250	31		
50353		226	229	228	245	19		
50354		236	239	239	247	11		
50355		239	239	242	246	7		
50356		217	219	234	237	20		
50357		254	255	269	273	19		
50358		250	253	255	280	30		
50359		212	225	234	245	33		
50360		266	270	271	302	36		
50361		246	251	254	267	21		
50362		205	208	216	219	14		
n		12	12	12	12	12		
Mean		233.8	238.4	244.0	255.9	22.1		
S.D.		18.5	17.3	16.1	22.0	9.0		

Animal No.	Body weight Sex : Female		Period : F0 gestation Day 0-20 Dose : HBM 300 mg/kg			Unit : g	Species : Rat
	/Day	0	7	14	20	Body weight gain	
50351		269	313	348	423	154	
50352		257	300	336	424	167	
50353		248	293	336	415	167	
50354		253	298	343	442	189	
50355		253	303	338	416	163	
50356		238	272	306	385	147	
50357		276	313	353	435	159	
50358	\$	281 \$	321 \$	337 \$	357 \$	76 \$	
50359		249	282	317	391	142	
50360		308	344	390	481	173	
50361		261	298	331	437	176	
50362		227	266	307	380	153	
n		11	11	11	11	11	
Mean		258.1	298.4	336.8	420.8	162.7	
S.D.		21.3	21.4	23.5	29.1	13.7	

Animal No. 50358 : Non-pregnancy

\$ : Excepted data from calculation

Animal No.	Body weight Sex : Female		Period : F0 lactation Day 0-4 Dose : HBM 300 mg/kg	Unit : g	Species : Rat
	/Day	0	4	Body weight gain	
50351		349	365	16	
50352		321	352	31	
50353		336	370	34	
50354		309	350	41	
50355		314	336	22	
50356		285	306	21	
50357		336	353	17	
50359		293	316	23	
50360		357	374	17	
50361		308	347	39	
50362		305	322	17	
n		11	11	11	
Mean		319.4	344.6	25.3	
S.D.		22.8	22.3	9.3	

Animal No.	Body weight Sex : Female		Period : F0 before mating Day 1-14 Dose : HBM 1000 mg/kg			Unit : g	Species : Rat	
	/Day		1	4	7	14	Body weight gain	
50451		226	227	240	250	24		
50452		235	246	257	262	27		
50453		228	234	236	248	20		
50454		234	239	255	267	33		
50455		238	235	256	259	21		
50456		250	260	265	270	20		
50457		204	214	222	227	23		
50458		221	223	235	240	19		
50459		244	261	270	284	40		
50460		234	249	249	260	26		
50461		247	248	250	268	21		
50462		252	262	269	276	24		
n		12	12	12	12	12		
Mean		234.4	241.5	250.3	259.3	24.8		
S.D.		13.6	15.6	14.8	15.9	6.2		

Animal No.	Body weight Sex : Female		Period : F0 gestation Day 0-20 Dose : HBM 1000 mg/kg			Unit : g	Species : Rat	
	/Day		0	7	14	20	Body weight gain	
50451		251	298	335	403	152		
50452		274	306	343	425	151		
50453		251	293	335	432	181		
50454		272	314	357	440	168		
50455		279	322	375	464	185		
50456		277	321	366	439	162		
50457		238	284	333	420	182		
50458		243	288	320	404	161		
50459		290	335	380	465	175		
50460		256	299	337	424	168		
50461		269	312	344	444	175		
50462		275	319	360	450	175		
n		12	12	12	12	12		
Mean		264.6	307.6	348.8	434.2	169.6		
S.D.		16.2	15.5	18.6	20.3	11.3		

Animal No.	Body weight Sex : Female		Period : F0 lactation Day 0-4 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
	/Day	0	4	Body weight gain	
50451		324	336	12	
50452		322	350	28	
50453		311	334	23	
50454		345	349	4	
50455		344	372	28	
50456		359	363	4	
50457		323	347	24	
50458		295	316	21	
50459		340	361	21	
50460		336	336	0	
50461		318	342	24	
50462		359	372	13	
n		12	12	12	
Mean		331.3	348.2	16.8	
S.D.		19.3	16.8	9.9	

Animal No.	Body weight Sex : Female (satellite)		Period : Administration Day 1-28 Dose : HBM 0 mg/kg				Unit : g	Species : Rat
	/Day	1	4	7	14	21	28	
50551		243	244	256	270	281	286	43
50552		228	236	238	239	253	267	39
50553		215	223	227	236	253	266	51
50554		245	249	253	277	288	296	51
50555		232	232	236	257	268	276	44
50556		242	240	252	265	272	271	29
50557		243	241	246	256	265	263	20
50558		236	240	241	257	272	284	48
50559		233	229	246	256	264	268	35
50560		233	236	252	271	283	289	56
n		10	10	10	10	10	10	
Mean		235.0	237.0	244.7	258.4	269.9	276.6	41.6
S.D.		9.1	7.6	9.2	13.2	11.9	11.4	11.1

Animal No.	Body weight Sex : Female (satellite)		Period : Administration Day 1-28 Dose : HBM 1000 mg/kg					Unit : g	Species : Rat	
	/Day		1	4	7	14	21	28	Body weight gain	
50651		228	233	249	266	273	279	51		
50652		233	238	237	254	264	274	41		
50653		229	236	239	246	254	264	35		
50654		245	250	255	256	272	281	36		
50655		233	238	235	256	264	271	38		
50656		231	234	237	254	264	266	35		
50657		244	249	265	284	296	294	50		
50658		243	245	245	269	284	288	45		
50659		230	237	241	254	270	276	46		
50660		221	220	224	230	248	236	15		
n		10	10	10	10	10	10	10		
Mean		233.7	238.0	242.7	256.9	268.9	272.9	39.2		
S.D.		7.9	8.7	11.5	14.3	13.8	15.9	10.4		

Animal No.	Body weight /Day			Period : Recovery Day 1-14 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	1	7	14			
10103	459	477	483	24		
10104	464	489	512	48		
10105	468	490	501	33		
10109	478	504	512	34		
10111	476	498	515	39		
n	5	5	5	5		
Mean	469.0	491.6	504.6	35.6		
S.D.	8.0	10.2	13.2	8.8		

Animal No.	Body weight /Day			Period : Recovery Day 1-14 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
	1	7	14			
10403	474	494	509	35		
10407	453	476	493	40		
10408	455	483	506	51		
10411	469	490	496	27		
10412	482	498	504	22		
n	5	5	5	5		
Mean	466.6	488.2	501.6	35.0		
S.D.	12.4	8.8	6.8	11.3		

Animal No.	Body weight Sex : Female (satellite)			Period : Recovery Day 1-14 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	/Day	1	7			
50556		279	293	308	29	
50557		259	264	275	16	
50558		277	289	303	26	
50559		272	275	287	15	
50560		292	300	309	17	
n		5	5	5	5	
Mean		275.8	284.2	296.4	20.6	
S.D.		11.9	14.5	14.9	6.4	

Animal No.	Body weight Sex : Female (satellite)			Period : Recovery Day 1-14 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
	/Day	1	7			
50656		265	274	288	23	
50657		297	317	330	33	
50658		289	305	350	61	
50659		277	275	284	7	
50660		247	277	293	46	
n		5	5	5	5	
Mean		275.0	289.6	309.0	34.0	
S.D.		19.8	20.0	29.3	20.8	

Animal No.	Food consumption Sex : Male /Day				Period : Administration Day 1-28 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	4	7	14	28			
10101	28.1	26.9	28.2	28.9			
10102	25.1	26.3	26.2	27.4			
10103	25.0	24.7	25.0	24.6			
10104	26.4	25.5	26.6	27.8			
10105	28.2	27.0	26.5	28.2			
10106	27.8	28.0	30.2	28.4			
10107	30.5	29.5	29.9	29.4			
10108	26.4	25.7	26.4	29.2			
10109	27.5	28.2	28.2	26.2			
10110	24.7	24.3	24.3	24.8			
10111	25.7	25.2	25.2	25.6			
10112	30.4	29.4	29.3	27.9			
n	12	12	12	12			
Mean	27.15	26.73	27.17	27.37			
S.D.	1.96	1.75	1.96	1.67			

Animal No.	Food consumption Sex : Male /Day				Period : Administration Day 1-28 Dose : HBM 100 mg/kg	Unit : g	Species : Rat
	4	7	14	28			
10201	27.0	27.7	27.8	27.3			
10202	28.5	28.0	27.0	24.7			
10203	28.3	31.2	27.3	29.2			
10204	26.3	26.5	26.6	27.3			
10205	27.3	27.8	27.9	30.1			
10206	31.3	31.0	31.1	31.1			
10207	26.6	26.5	26.9	26.1			
10208	27.0	27.7	27.8	26.7			
10209	27.7	27.6	28.3	28.8			
10210	28.7	29.1	28.8	27.4			
10211	28.6	27.1	28.6	29.1			
10212	23.2	24.7	26.4	28.3			
n	12	12	12	12			
Mean	27.54	27.91	27.88	28.01			
S.D.	1.91	1.83	1.27	1.78			

Animal No.	Food consumption Sex : Male /Day				Period : Administration Day 1-28 Dose : HBM 300 mg/kg	Unit : g	Species : Rat
	4	7	14	28			
10301	24.1	24.3	26.3	26.8			
10302	28.9	26.7	27.4	27.8			
10303	27.9	27.2	28.5	28.3			
10304	29.0	28.0	29.4	29.2			
10305	29.3	26.7	28.4	29.1			
10306	27.3	28.4	28.7	26.8			
10307	23.7	23.3	23.2	25.7			
10308	28.0	27.7	28.3	29.1			
10309	25.0	25.6	27.1	28.1			
10310	29.5	29.3	29.6	30.8			
10311	30.3	30.6	28.9	29.2			
10312	25.3	26.1	28.0	27.8			
n	12	12	12	12			
Mean	27.36	26.99	27.82	28.23			
S.D.	2.27	2.04	1.73	1.38			

Animal No.	Food consumption Sex : Male /Day				Period : Administration Day 1-28 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
	4	7	14	28			
10401	20.4	23.1	24.5	28.1			
10402	28.7	30.1	30.4	30.9			
10403	26.5	26.3	27.1	26.5			
10404	25.0	24.9	24.2	26.2			
10405	24.6	24.3	26.4	26.7			
10406	28.0	29.0	29.7	28.6			
10407	26.3	25.7	26.0	26.3			
10408	26.6	26.9	26.0	25.6			
10409	27.5	28.1	28.7	28.8			
10410	31.7	33.0	34.4	35.7			
10411	28.8	28.4	28.1	27.5			
10412	27.8	28.8	28.0	28.4			
n	12	12	12	12			
Mean	26.83	27.38	27.79	28.28			
S.D.	2.76	2.75	2.82	2.76			

Animal No.	Food consumption Sex : Female /Day			Period : F0 before mating Day 1-14 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	4	7	14			
50151	19.7	21.7	19.8			
50152	19.2	21.0	20.2			
50153	17.8	20.2	19.0			
50154	19.2	22.5	21.7			
50155	14.8	14.9	17.5			
50156	19.5	21.6	19.8			
50157	19.6	20.4	22.1			
50158	20.0	19.6	19.8			
50159	17.0	19.8	19.3			
50160	16.8	17.8	20.2			
50161	16.5	19.0	18.4			
50162	15.3	16.5	18.3			
n	12	12	12			
Mean	17.95	19.58	19.68			
S.D.	1.83	2.24	1.33			

Animal No.	Food consumption Sex : Female /Day			Period : F0 gestation Day 0-20 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	7	14	20			
50151	23.3	23.7	25.3			
50152	24.4	27.5	28.0			
50153	24.0	25.1	25.5			
50154	25.7	25.7	27.8			
50155	22.6	26.3	24.1			
50156	24.7	28.0	27.6			
50157	27.2	27.3	28.0			
50158	24.8	26.7	25.7			
50159	24.6	26.8	24.6			
50160	26.4	30.3	30.0			
50161	21.0	21.4	24.5			
50162	22.9	26.1	25.5			
n	12	12	12			
Mean	24.30	26.24	26.38			
S.D.	1.71	2.22	1.83			

Food consumption Sex : Female /Day		Period : F0 lactation Day 0-4 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
Animal No.	4			
50151	38.5			
50152	36.2			
50153	32.3			
50154	39.9			
50155	32.7			
50156	38.8			
50157	38.3			
50158	36.2			
50159	35.2			
50160	28.2			
50161	34.9			
50162	34.5			
n	12			
Mean	35.48			
S.D.	3.32			

Animal No.	Food consumption Sex : Female /Day			Period : F0 before mating Day 1-14 Dose : HBM 100 mg/kg	Unit : g	Species : Rat
	4	7	14			
50251	20.7	20.6	20.1			
50252	16.3	17.8	18.2			
50253	18.6	21.1	18.6			
50254	19.0	20.6	20.1			
50255	17.4	18.2	20.4			
50256	17.3	18.6	19.1			
50257	20.6	17.7	18.3			
50258	16.4	17.7	19.1			
50259	19.7	20.2	20.3			
50260	20.4	21.7	21.9			
50261	17.7	18.1	18.4			
50262	17.0	18.2	18.7			
n	12	12	12			
Mean	18.43	19.21	19.43			
S.D.	1.63	1.50	1.13			

Animal No.	Food consumption Sex : Female /Day			Period : F0 gestation Day 0-20 Dose : HBM 100 mg/kg	Unit : g	Species : Rat
	7	14	20			
50251	24.4	26.4	26.7			
50252	24.9	27.6	26.8			
50253	21.7	22.9	23.7			
50254	22.0	24.4	22.1			
50255	23.4	27.8	28.1			
50256	23.8	23.2	23.0			
50257	24.2	25.8	25.5			
50258	23.2	26.2	24.0			
50259	25.0	27.1	27.1			
50260	26.1	28.1	25.8			
50261	27.3	30.5	25.5			
50262	24.6	27.4	24.3			
n	12	12	12			
Mean	24.22	26.45	25.22			
S.D.	1.58	2.16	1.82			

Food consumption Sex : Female <u>/Day</u>		Period : F0 lactation Day 0-4 Dose : HBM 100 mg/kg	Unit : g	Species : Rat
Animal No.	4			
50251	38.2			
50252	35.3			
50253	32.5			
50254	37.1			
50255	34.5			
50256	29.0			
50257	25.1			
50258	43.2			
50259	39.4			
50260	31.3			
50261	40.1			
50262	34.2			
n	12			
Mean	34.99			
S.D.	5.06			

Animal No.	Food consumption Sex : Female /Day			Period : F0 before mating Day 1-14 Dose : HBM 300 mg/kg	Unit : g	Species : Rat
	4	7	14			
50351	18.2	20.2	21.8			
50352	20.4	19.3	20.3			
50353	15.9	17.2	19.4			
50354	19.7	21.9	22.9			
50355	16.2	18.6	17.7			
50356	17.1	19.9	17.9			
50357	19.7	21.4	19.8			
50358	19.1	19.7	22.7			
50359	18.1	17.9	18.7			
50360	18.8	20.8	23.6			
50361	19.2	19.8	21.0			
50362	14.6	17.6	15.9			
n	12	12	12			
Mean	18.08	19.53	20.14			
S.D.	1.78	1.48	2.36			

Animal No.	Food consumption Sex : Female /Day			Period : F0 gestation Day 0-20 Dose : HBM 300 mg/kg	Unit : g	Species : Rat
	7	14	20			
50351	28.4	29.7	28.7			
50352	26.6	29.1	27.8			
50353	24.9	28.0	27.2			
50354	28.1	31.1	29.3			
50355	24.1	27.1	24.5			
50356	22.4	24.0	23.2			
50357	24.8	25.8	27.0			
50358	26.0 \$	29.9 \$	27.1 \$			
50359	22.9	24.0	24.8			
50360	29.2	31.0	28.7			
50361	22.9	24.4	25.6			
50362	22.9	25.0	25.0			
n	11	11	11			
Mean	25.20	27.20	26.53			
S.D.	2.49	2.74	2.02			

Animal No. 50358 : Non-pregnancy

\$ : Excepted data from calculation

Food consumption Sex : Female /Day		Period : F0 lactation Day 0-4 Dose : HBM 300 mg/kg	Unit : g	Species : Rat
Animal No.	4			
50351	32.6			
50352	36.1			
50353	42.0			
50354	36.7			
50355	33.6			
50356	34.3			
50357	36.4			
50359	35.1			
50360	37.1			
50361	37.5			
50362	29.1			
n	11			
Mean	35.50			
S.D.	3.26			

Animal No.	Food consumption Sex : Female /Day			Period : F0 before mating Day 1-14 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
	4	7	14			
50451	18.2	19.6	18.6			
50452	20.8	20.6	20.0			
50453	16.4	17.9	19.1			
50454	19.6	21.4	20.6			
50455	19.1	21.6	20.3			
50456	20.6	18.2	20.1			
50457	17.1	17.3	16.7			
50458	15.7	18.7	17.7			
50459	21.9	20.6	21.7			
50460	19.7	16.8	20.4			
50461	17.5	19.7	20.8			
50462	22.8	20.7	20.9			
n	12	12	12			
Mean	19.12	19.43	19.74			
S.D.	2.21	1.62	1.45			

Animal No.	Food consumption Sex : Female /Day			Period : F0 gestation Day 0-20 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
	7	14	20			
50451	23.1	26.7	23.7			
50452	25.7	27.8	26.8			
50453	24.2	27.8	26.2			
50454	25.8	27.8	26.9			
50455	27.1	30.8	27.8			
50456	24.1	28.3	28.1			
50457	24.5	27.6	26.6			
50458	24.5	24.9	23.3			
50459	27.0	31.1	27.8			
50460	22.9	27.2	27.4			
50461	26.5	27.1	25.2			
50462	26.2	28.4	27.0			
n	12	12	12			
Mean	25.13	27.96	26.40			
S.D.	1.45	1.67	1.57			

Food consumption Sex : Female /Day		Period : F0 lactation Day 0-4 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
Animal No.	4			
50451	30.7			
50452	40.2			
50453	33.3			
50454	30.0			
50455	41.5			
50456	36.8			
50457	37.3			
50458	31.9			
50459	40.0			
50460	27.7			
50461	36.3			
50462	37.5			
n	12			
Mean	35.27			
S.D.	4.46			

Animal No.	Food consumption Sex : Female (satellite)		Period : Administration Day 1-28 Dose : HBM 0 mg/kg			Unit : g	Species : Rat
	/Day		4	7	14	21	28
50551		20.6	21.6	21.0	19.9	21.5	
50552		17.7	18.4	19.0	19.2	19.6	
50553		17.6	17.3	19.7	21.1	21.7	
50554		19.4	20.1	22.2	21.5	20.9	
50555		17.2	19.2	22.2	21.0	22.3	
50556		18.8	21.1	20.5	20.0	20.2	
50557		15.8	18.2	18.8	18.2	16.8	
50558		19.1	19.1	20.3	19.6	19.9	
50559		18.5	20.5	19.3	19.2	19.7	
50560		19.4	21.5	21.9	22.3	22.1	
n		10	10	10	10	10	
Mean		18.41	19.70	20.49	20.20	20.47	
S.D.		1.37	1.49	1.30	1.25	1.63	

Animal No.	Food consumption Sex : Female (satellite)		Period : Administration Day 1-28 Dose : HBM 1000 mg/kg			Unit : g	Species : Rat
	/Day		4	7	14	21	28
50651		19.1	21.0	20.2	19.8	19.6	
50652		17.4	18.0	20.4	18.3	19.1	
50653		18.2	18.2	18.9	18.4	18.7	
50654		19.9	20.1	20.3	20.3	20.0	
50655		18.2	18.3	18.9	17.6	17.8	
50656		16.4	18.9	20.1	19.7	18.2	
50657		21.3	23.3	21.5	21.8	21.1	
50658		17.6	18.6	21.2	21.0	20.5	
50659		17.3	19.6	19.5	19.6	18.9	
50660		15.0	16.3	17.0	16.8	14.4	
n		10	10	10	10	10	
Mean		18.04	19.23	19.80	19.33	18.83	
S.D.		1.77	1.92	1.30	1.55	1.86	

Animal No.	Food consumption Sex : Male /Day		Period : Recovery Day 1-14 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
	7	14			
10103	24.0	23.3			
10104	28.7	28.1			
10105	29.1	28.0			
10109	27.2	25.4			
10111	25.6	26.3			
n	5	5			
Mean	26.92	26.22			
S.D.	2.14	1.99			

Food consumption Sex : Male <u>/Day</u>		Period : Recovery Day 1-14 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
Animal No.		7	14	
10403		26.3	26.5	
10407		26.2	25.2	
10408		28.8	28.2	
10411		27.5	27.8	
10412		28.4	26.9	
n		5	5	
Mean		27.44	26.92	
S.D.		1.18	1.18	

Food consumption Sex : Female (satellite)		Period : Recovery Day 1-14 Dose : HBM 0 mg/kg	Unit : g	Species : Rat
Animal No.	/Day	7	14	
50556		21.1	20.6	
50557		17.6	18.1	
50558		20.6	21.0	
50559		18.7	18.4	
50560		21.8	21.5	
n		5	5	
Mean		19.96	19.92	
S.D.		1.75	1.56	

Food consumption Sex : Female (satellite)		Period : Recovery Day 1-14 Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
Animal No.	/Day	7	14	
50656		19.9	19.7	
50657		22.2	20.9	
50658		21.6	30.0	
50659		17.6	17.9	
50660		20.0	20.9	
n		5	5	
Mean		20.26	21.88	
S.D.		1.79	4.70	

Sex : Male	Urinary findings							Species : Rat
	pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	
Animal No.							EU/dL	
10103	8.5	2+	-	-	0.1	-	-	A
10104	8.5	+	-	-	0.1	-	-	A
10105	8.0	±	-	-	0.1	-	-	A
10109	8.5	+	-	-	0.1	-	-	A
10111	8.5	2+	-	-	0.1	-	-	A
n	5	5	5	5	5	5	5	5

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

Urinary findings		Stage : Week 4	Species : Rat
Sex : Male		Dose : HBM 0 mg/kg	
Urine volume			
Animal No.		mL/24hr	
10103		8.0	
10104		9.0	
10105		20.0	
10109		15.5	
10111		8.5	
n		5	
Mean		12.20	
S.D.		5.32	

Animal No.	Specific gravity	Urinary findings		Stage : Week 4			Species : Rat
		Sex : Male		Dose : HBM 0 mg/kg	Round	Small round	
10103	5	-	-	-	-	-	-
10104	5	-	-	-	-	-	-
10105	3	-	-	-	-	-	-
10109	4	-	-	-	-	-	-
10111	5	-	-	-	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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
	pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	
Animal No.							EU/dL	
10202	8.5	+	-	-	0.1	-	-	A
10204	8.5	2+	-	-	0.1	-	-	A
10208	7.5	+	-	-	0.1	-	-	A
10209	8.5	2+	-	-	0.1	-	-	A
10210	8.5	2+	-	-	0.1	-	-	A
n	5	5	5	5	5	5	5	5

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

Urinary findings		Stage : Week 4	Species : Rat
Sex : Male		Dose : HBM 100 mg/kg	
Urine volume			
Animal No.		mL/24hr	
10202		10.0	
10204		9.5	
10208		8.5	
10209		10.0	
10210		14.5	
n		5	
Mean		10.50	
S.D.		2.32	

Urinary findings		Stage : Week 4					Species : Rat
Sex : Male	Specific gravity	RBC	WBC	Squamous	Round	Small round	
<b>Animal No.</b>							
10202	5	-	-	-	-	-	-
10204	5	-	-	-	-	-	-
10208	5	-	-	-	-	-	-
10209	5	-	-	-	-	-	-
10210	5	-	-	-	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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
	pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	
Animal No.							EU/dL	
10302	8.5	+	-	-	0.1	-	-	A
10303	8.5	+	-	-	0.1	-	-	A
10306	7.0	+	-	-	0.1	-	-	A
10309	8.5	+	-	-	0.1	-	-	A
10312	7.0	+	-	-	0.1	-	-	A
n	5	5	5	5	5	5	5	5

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

Urinary findings		Stage : Week 4	Species : Rat
Sex : Male		Dose : HBM 300 mg/kg	
Urine volume			
Animal No.		mL/24hr	
10302		17.0	
10303		12.5	
10306		13.0	
10309		12.0	
10312		10.5	
n		5	
Mean		13.00	
S.D.		2.42	

Urinary findings		Stage : Week 4					Species : Rat
Sex : Male	Specific gravity	RBC	WBC	Squamous	Round	Small round	
<b>Animal No.</b>							
10302	4	-	-	-	-	-	-
10303	5	-	-	-	-	-	-
10306	5	-	-	-	-	-	-
10309	5	-	-	-	-	-	-
10312	5	-	-	-	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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
	pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	
Animal No.							EU/dL	
10403	6.0	+	-	-	0.1	-	-	A
10407	6.0	+	-	-	0.1	-	-	A
10408	6.5	3+	-	-	0.1	-	3+	A
10411	6.0	+	-	-	0.1	-	-	A
10412	6.0	+	-	-	0.1	-	-	A
n	5	5	5	5	5	5	5	5

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

Urinary findings		Stage : Week 4	Species : Rat
Sex : Male		Dose : HBM 1000 mg/kg	
Urine volume			
Animal No.		mL/24hr	
10403		19.5	
10407		17.5	
10408		17.5	
10411		19.0	
10412		15.0	
n		5	
Mean		17.70	
S.D.		1.75	

Animal No.	Specific gravity	Urinary findings		Stage : Week 4		Species : Rat	
		Sex : Male		Dose : HBM 1000 mg/kg	Round	Small round	Cast
10403	4	-	-	-	-	-	-
10407	4	-	-	-	-	-	-
10408	4	3+	-	-	-	-	-
10411	4	-	-	-	-	-	-
10412	4	-	-	-	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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<

Urinary findings Sex : Female (satellite)		Stage : Week 4 Dose : HBM 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		8.5	+	-	-	0.1	-	-	A
50559		8.5	-	-	-	0.1	-	-	A
50560		8.5	±	-	-	0.1	-	±	A
n		5	5	5	5	5	5	5	5

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

Urinary findings Sex : Female (satellite)		Stage : Week 4 Dose : HBM 0 mg/kg	Species : Rat
Urine volume			
Animal No.	mL/24hr		
50556	18.5		
50557	9.5		
50558	5.5		
50559	14.0		
50560	16.5		
n	5		
Mean	12.80		
S.D.	5.29		

Urinary findings Sex : Female (satellite)		Stage : Week 4 Dose : HBM 0 mg/kg					Species : Rat
Specific gravity	RBC	WBC	Squamous	Round	Small round	Cast	
<b>Animal No.</b>							
50556	3	-	-	-	-	-	-
50557	4	-	-	-	-	-	-
50558	5	-	-	-	-	-	-
50559	4	-	-	-	-	-	-
50560	3	±	-	-	-	-	-
n	5	5	5	5	5	5	

Specific gravity) 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<

Urinary findings Sex : Female (satellite)		Stage : Week 4 Dose : HBM 1000 mg/kg						Species : Rat	
Animal No.		pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	Color
50656		6.0	+	-	-	0.1	-	-	A
50657		6.0	±	-	-	0.1	-	-	A
50658		6.0	+	-	-	0.1	-	±	A
50659		6.0	-	-	-	0.1	-	-	A
50660		6.0	+	-	-	0.1	-	-	A
n		5	5	5	5	5	5	5	5

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

Urinary findings Sex : Female (satellite)		Stage : Week 4 Dose : HBM 1000 mg/kg	Species : Rat
Urine volume			
Animal No.	mL/24hr		
50656	6.5		
50657	26.5		
50658	6.0		
50659	11.5		
50660	7.0		
n	5		
Mean	11.50		
S.D.	8.67		

Urinary findings Sex : Female (satellite)		Stage : Week 4 Dose : HBM 1000 mg/kg					Species : Rat
	Specific gravity	RBC	WBC	Squamous	Round	Small round	Cast
<b>Animal No.</b>							
50656	5	-	-	-	-	-	-
50657	3	-	-	-	-	-	-
50658	5	±	-	-	-	-	-
50659	4	-	-	-	-	-	-
50660	5	-	-	-	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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
	pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	
Stage : Recovery Week 2 Dose : HBM 0 mg/kg								
Animal No.					EU/dL			
10103	8.5	2+	-	-	0.1	-	-	A
10104	8.5	+	-	-	0.1	-	-	A
10105	8.5	±	-	-	0.1	-	-	A
10109	8.5	+	-	-	0.1	-	-	A
10111	8.5	+	-	-	0.1	-	-	A
n	5	5	5	5	5	5	5	5

Color) 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 : HBM 0 mg/kg	
Urine volume			
Animal No.		mL/24hr	
10103		9.5	
10104		10.0	
10105		12.5	
10109		14.5	
10111		8.5	
n		5	
Mean		11.00	
S.D.		2.45	

Animal No.	Urinary findings		Stage : Recovery Week 2			Species : Rat	
	Specific gravity	RBC	WBC	Squamous	Round	Small round	
10103	5	-	-	-	-	-	-
10104	5	-	-	-	-	-	-
10105	5	-	-	-	-	-	-
10109	4	-	-	-	-	-	-
10111	5	-	-	±	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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
	pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	
Stage : Recovery Week 2 Dose : HBM 1000 mg/kg								
Animal No.					EU/dL			
10403	8.5	±	-	-	0.1	-	-	A
10407	8.5	+	-	-	0.1	-	-	A
10408	8.5	+	-	-	0.1	-	-	A
10411	8.5	2+	-	-	0.1	-	-	A
10412	8.5	+	-	-	0.1	-	-	A
n	5	5	5	5	5	5	5	5

Color) 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 : HBM 1000 mg/kg	
Urine volume			
Animal No.		mL/24hr	
10403		11.5	
10407		11.5	
10408		11.5	
10411		10.0	
10412		11.0	
n		5	
Mean		11.10	
S.D.		0.65	

Urinary findings		Stage : Recovery Week 2					Species : Rat
Sex : Male	Specific gravity	RBC	WBC	Squamous	Round	Small round	
<b>Animal No.</b>							
10403	4	-	-	-	-	-	-
10407	5	-	-	±	-	-	-
10408	5	-	-	±	-	-	-
10411	5	-	-	-	-	-	-
10412	5	-	-	-	-	-	-
n	5	5	5	5	5	5	5

Specific gravity) 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<

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2 Dose : HBM 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		8.5	+	-	-	0.1	-	-	A
50559		8.0	+	-	-	0.1	-	-	A
50560		8.5	±	-	-	0.1	-	-	A
n		5	5	5	5	5	5	5	5

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

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2 Dose : HBM 0 mg/kg	Species : Rat
Urine volume			
Animal No.	mL/24hr		
50556	7.0		
50557	10.5		
50558	10.0		
50559	9.5		
50560	13.5		
n	5		
Mean	10.10		
S.D.	2.33		

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2 Dose : HBM 0 mg/kg					Species : Rat
Specific gravity	RBC	WBC	Squamous	Round	Small round	Cast	
<b>Animal No.</b>							
50556	5	-	-	+	-	-	-
50557	4	-	-	-	-	-	-
50558	5	-	-	±	-	-	-
50559	4	-	-	-	-	-	-
50560	4	-	-	-	-	-	-
n	5	5	5	5	5	5	

Specific gravity) 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<

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2 Dose : HBM 1000 mg/kg						Species : Rat	
Animal No.		pH	Protein	Glucose	Ketone body	Urobilinogen	Bilirubin	Occult blood	Color
50656		8.5	+	-	-	0.1	-	-	A
50657		8.5	±	-	-	0.1	-	-	A
50658		8.5	+	-	-	0.1	-	-	A
50659		8.5	+	-	-	0.1	-	-	A
50660		8.5	-	-	-	0.1	-	-	A
n		5	5	5	5	5	5	5	5

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

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2 Dose : HBM 1000 mg/kg	Species : Rat
Urine volume			
Animal No.	mL/24hr		
50656	10.5		
50657	21.5		
50658	9.5		
50659	14.5		
50660	24.0		
n	5		
Mean	16.00		
S.D.	6.50		

Urinary findings Sex : Female (satellite)		Stage : Recovery Week 2 Dose : HBM 1000 mg/kg					Species : Rat
Specific gravity	RBC	WBC	Squamous	Round	Small round	Cast	
<b>Animal No.</b>							
50656	4	-	-	-	-	-	-
50657	3	-	-	-	-	-	-
50658	5	-	-	±	-	-	-
50659	4	-	-	±	-	-	-
50660	3	-	-	±	-	-	-
n	5	5	5	5	5	5	

Specific gravity) 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<

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		853	16.2	44.0	51.6	19.0	36.8	2.87	103.5	87.2	18.7	64.2
10102		880	16.2	45.3	51.5	18.4	35.8	2.51	108.0	69.4	7.2	58.2
10106		905	16.6	46.7	51.6	18.3	35.5	2.70	109.7	72.6	8.9	59.4
10107		865	15.6	43.2	49.9	18.0	36.1	3.67	99.3	59.3	10.6	45.7
10108		847	14.9	41.4	48.9	17.6	36.0	3.66	102.1	103.9	24.8	73.6
n		5	5	5	5	5	5	5	5	5	5	5
Mean		870.0	15.90	44.12	50.70	18.26	36.04	3.082	104.52	78.48	14.04	60.22
S.D.		23.3	0.66	2.02	1.24	0.52	0.48	0.547	4.27	17.37	7.46	10.13
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	
10101		3.5	0.7	0.1	18.6	17.6						
10102		3.4	0.6	0.0	21.2	19.7						
10106		3.7	0.6	0.0	24.9	19.6						
10107		2.1	0.9	0.0	22.9	18.8						
10108		4.4	1.1	0.0	22.5	18.7						
n		5	5	5	5	5						
Mean		3.42	0.78	0.02	22.02	18.88						
S.D.		0.83	0.22	0.04	2.33	0.85						

Hematological findings Sex : Male				Stage : Day 29 Dose : HBM 100 mg/kg				Species : Rat			
Animal No.	RBC $10^4/\mu\text{L}$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet $10^4/\mu\text{L}$	WBC $10^2/\mu\text{L}$	Neutrophil $10^2/\mu\text{L}$	Lymphocyte $10^2/\mu\text{L}$
10201	861	15.8	44.2	51.3	18.4	35.7	3.84	102.4	51.4	9.9	39.7
10203	877	16.2	44.9	51.2	18.5	36.1	3.66	134.8	89.4	16.3	67.4
10205	907	16.3	45.6	50.3	18.0	35.7	3.96	110.6	112.7	35.7	68.7
10206	843	15.7	44.1	52.3	18.6	35.6	3.44	108.5	79.1	14.3	61.4
10207	850	15.3	42.1	49.5	18.0	36.3	2.28	98.3	115.7	13.6	97.1
n	5	5	5	5	5	5	5	5	5	5	5
Mean	867.6	15.86	44.18	50.92	18.30	35.88	3.436	110.92	89.66	17.96	66.86
S.D.	25.5	0.40	1.31	1.06	0.28	0.30	0.675	14.21	26.38	10.18	20.53
Monocyte $10^2/\mu\text{L}$		Eosinophil $10^2/\mu\text{L}$	Basophil $10^2/\mu\text{L}$	PT sec	APTT sec						
Animal No.	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	sec	sec						
10201	1.3	0.5	0.0	20.7	17.9						
10203	4.0	1.7	0.0	21.9	20.3						
10205	7.3	0.9	0.1	21.5	16.8						
10206	2.5	0.9	0.0	21.1	16.9						
10207	3.7	1.2	0.1	22.3	20.8						
n	5	5	5	5	5						
Mean	3.76	1.04	0.04	21.50	18.54						
S.D.	2.25	0.44	0.05	0.63	1.89						

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		
10301		842	15.1	41.9	49.8	17.9	36.0	3.75	103.2	79.2	15.5	58.3		
10304		818	15.2	42.0	51.3	18.6	36.2	3.73	111.2	75.3	12.6	59.5		
10305		873	15.3	42.7	48.9	17.5	35.8	3.80	128.7	73.1	15.8	52.7		
10307		867	15.5	42.9	49.5	17.9	36.1	4.73	103.7	78.9	13.4	62.3		
10308		874	15.1	42.2	48.3	17.3	35.8	3.93	100.1	84.4	16.7	64.7		
n		5	5	5	5	5	5	5	5	5	5	5		
Mean		854.8	15.24	42.34	49.56	17.84	35.98	3.988	109.38	78.18	14.80	59.50		
S.D.		24.3	0.17	0.44	1.13	0.50	0.18	0.422	11.54	4.31	1.72	4.54		
Monocyte		Eosinophil	Basophil	PT	APTT									
Animal No.		10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	sec	sec								
10301		4.2	1.1	0.1	20.8	19.1								
10304		2.3	0.9	0.0	21.0	19.0								
10305		2.9	1.7	0.0	26.5	18.8								
10307		2.5	0.7	0.0	18.0	18.3								
10308		2.1	0.9	0.0	20.0	18.1								
n		5	5	5	5	5								
Mean		2.80	1.06	0.02	21.26	18.66								
S.D.		0.84	0.38	0.04	3.16	0.44								

Hematological findings Sex : Male				Stage : Day 29 Dose : HBM 1000 mg/kg				Species : Rat			
	RBC 10 <sup>4</sup> /µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet 10 <sup>4</sup> /µL	WBC 10 <sup>2</sup> /µL	Neutrophil 10 <sup>2</sup> /µL	Lymphocyte 10 <sup>2</sup> /µL
Animal No.											
10401	838	15.8	44.3	52.9	18.9	35.7	3.62	93.7	68.0	13.9	50.2
10402	859	15.9	44.3	51.6	18.5	35.9	3.38	88.7	88.4	11.5	72.7
10404	909	16.1	44.6	49.1	17.7	36.1	2.44	106.4	59.7	9.8	46.8
10405	885	16.0	44.1	49.8	18.1	36.3	3.21	99.9	162.1	27.2	130.1
10406	908	16.4	45.4	50.0	18.1	36.1	3.66	119.4	84.8	13.5	67.5
n	5	5	5	5	5	5	5	5	5	5	5
Mean	879.8	16.04	44.54	50.68	18.26	36.02	3.262	101.62	92.60	15.18	73.46
S.D.	31.0	0.23	0.51	1.54	0.46	0.23	0.495	11.95	40.61	6.92	33.53
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	Monocyte 10 <sup>2</sup> /µL	Eosinophil 10 <sup>2</sup> /µL	Basophil 10 <sup>2</sup> /µL	PT sec	APTT						
Animal No.											
10401	2.9	1.0	0.0	22.7	APTT						
10402	3.4	0.8	0.0	20.0	APTT						
10404	2.5	0.6	0.0	32.0	APTT						
10405	3.6	1.1	0.1	19.5	APTT						
10406	2.9	0.9	0.0	17.4	APTT						
n	5	5	5	5	APTT						
Mean	3.06	0.88	0.02	22.32	APTT						
S.D.	0.44	0.19	0.04	5.73	APTT						

Hematological findings Sex : Female		Stage : Day 5 after delivery Dose : HBM 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		
50152		748	14.8	42.9	57.4	19.8	34.5	9.73	106.4	63.7	16.5	43.4		
50155		780	15.1	44.2	56.7	19.4	34.2	10.24	103.6	80.6	31.0	43.0		
50157		738	14.7	42.3	57.3	19.9	34.8	9.03	100.3	56.7	9.8	44.7		
50160		714	14.3	41.0	57.4	20.0	34.9	8.32	104.3	121.9	53.2	60.6		
50162		763	14.9	43.7	57.3	19.5	34.1	8.76	115.1	68.5	25.0	39.0		
n		5	5	5	5	5	5	5	5	5	5	5		
Mean		748.6	14.76	42.82	57.22	19.72	34.50	9.216	105.94	78.28	27.10	46.14		
S.D.		25.0	0.30	1.25	0.29	0.26	0.35	0.768	5.57	25.89	16.68	8.36		
Monocyte		Eosinophil	Basophil	PT	APTT									
Animal No.		10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	sec	sec								
50152		3.1	0.6	0.1	16.8	13.5								
50155		5.8	0.7	0.1	15.2	12.4								
50157		1.4	0.8	0.0	16.9	14.3								
50160		6.9	1.1	0.1	16.6	15.4								
50162		4.1	0.4	0.0	16.4	12.1								
n		5	5	5	5	5								
Mean		4.26	0.72	0.06	16.38	13.54								
S.D.		2.17	0.26	0.05	0.69	1.36								

Hematological findings Sex : Female				Stage : Day 5 after delivery Dose : HBM 100 mg/kg					Species : Rat		
Animal No.	RBC $10^4/\mu\text{L}$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet $10^4/\mu\text{L}$	WBC $10^2/\mu\text{L}$	Neutrophil $10^2/\mu\text{L}$	Lymphocyte $10^2/\mu\text{L}$
50253	716	14.1	40.3	56.3	19.7	35.0	7.38	95.7	81.8	30.7	49.5
50254	765	14.6	42.1	55.0	19.1	34.7	7.68	124.0	95.4	15.6	75.4
50255	810	15.3	44.0	54.3	18.9	34.8	5.43	109.0	122.0	35.6	81.8
50259	746	14.0	40.4	54.2	18.8	34.7	7.71	127.3	88.9	41.4	44.9
50262	730	14.3	41.4	56.7	19.6	34.5	8.36	97.9	57.7	9.2	46.3
n	5	5	5	5	5	5	5	5	5	5	5
Mean	753.4	14.46	41.64	55.30	19.22	34.74	7.312	110.78	89.16	26.50	59.58
S.D.	36.5	0.52	1.51	1.15	0.41	0.18	1.111	14.53	23.25	13.61	17.59
Monocyte $10^2/\mu\text{L}$		Eosinophil $10^2/\mu\text{L}$	Basophil $10^2/\mu\text{L}$	PT sec	APTT sec						
Animal No.	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	sec	APTT sec						
50253	1.3	0.3	0.0	17.5	14.0						
50254	3.4	0.9	0.1	16.0	12.4						
50255	3.3	1.2	0.1	16.3	15.0						
50259	1.4	1.2	0.0	17.0	14.9						
50262	1.7	0.5	0.0	14.9	12.8						
n	5	5	5	5	5						
Mean	2.22	0.82	0.04	16.34	13.82						
S.D.	1.04	0.41	0.05	1.00	1.19						

Hematological findings Sex : Female			Stage : Day 5 after delivery Dose : HBM 300 mg/kg						Species : Rat		
Animal No.	RBC $10^4/\mu\text{L}$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet $10^4/\mu\text{L}$	WBC $10^2/\mu\text{L}$	Neutrophil $10^2/\mu\text{L}$	Lymphocyte $10^2/\mu\text{L}$
50351	666	13.6	39.8	59.8	20.4	34.2	15.17	129.8	130.8	63.4	61.0
50354	699	13.9	40.5	57.9	19.9	34.3	9.59	128.0	92.6	27.4	62.7
50355	779	14.0	39.9	51.2	18.0	35.1	6.54	104.4	71.7	19.9	48.1
50361	730	14.1	40.7	55.8	19.3	34.6	9.45	102.3	102.1	32.0	65.8
50362	782	15.4	43.5	55.6	19.7	35.4	4.59	113.5	79.6	15.3	59.2
n	5	5	5	5	5	5	5	5	5	5	5
Mean	731.2	14.20	40.88	56.06	19.46	34.72	9.068	115.60	95.36	31.60	59.36
S.D.	50.4	0.70	1.51	3.21	0.91	0.52	4.003	12.87	23.01	18.92	6.75
Monocyte $10^2/\mu\text{L}$		Eosinophil $10^2/\mu\text{L}$	Basophil $10^2/\mu\text{L}$	PT sec	APTT						
Animal No.	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	sec							
50351	5.0	1.3	0.1	16.2							
50354	1.8	0.7	0.0	16.4							
50355	3.0	0.7	0.0	16.8							
50361	3.6	0.7	0.0	15.4							
50362	3.8	1.3	0.0	17.5							
n	5	5	5	5							
Mean	3.44	0.94	0.02	16.46							
S.D.	1.17	0.33	0.04	0.77							

Hematological findings Sex : Female				Stage : Day 5 after delivery Dose : HBM 1000 mg/kg					Species : Rat		
	RBC 10 <sup>4</sup> /µL	HGB g/dL	HCT %	MCV	MCH	MCHC g/dL	Reticulocyte %	Platelet 10 <sup>4</sup> /µL	WBC 10 <sup>2</sup> /µL	Neutrophil 10 <sup>2</sup> /µL	Lymphocyte 10 <sup>2</sup> /µL
Animal No.				fL	pg						
50451	766	14.7	41.5	54.2	19.2	35.4	8.71	134.6	94.2	32.2	56.2
50453	781	15.3	44.5	57.0	19.6	34.4	9.23	110.9	84.1	14.7	64.8
50460	793	15.5	43.5	54.9	19.5	35.6	9.49	152.3	69.4	22.1	42.6
50461	783	13.9	39.7	50.7	17.8	35.0	7.69	119.6	54.1	26.4	24.6
50462	814	15.9	44.9	55.2	19.5	35.4	6.15	92.5	73.7	21.8	47.2
n	5	5	5	5	5	5	5	5	5	5	5
Mean	787.4	15.06	42.82	54.40	19.12	35.16	8.254	121.98	75.10	23.44	47.08
S.D.	17.7	0.78	2.18	2.31	0.75	0.48	1.363	22.78	15.18	6.45	15.19
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	Monocyte 10 <sup>2</sup> /µL	Eosinophil 10 <sup>2</sup> /µL	Basophil 10 <sup>2</sup> /µL	PT sec	APTT						
Animal No.											
50451	4.8	1.0	0.0	17.2							
50453	3.9	0.6	0.1	16.6							
50460	4.0	0.7	0.0	16.8							
50461	0.8	2.3	0.0	15.4							
50462	3.7	1.0	0.0	16.7							
n	5	5	5	5							
Mean	3.44	1.12	0.02	16.54							
S.D.	1.53	0.68	0.04	0.68							

Hematological findings Sex : Female (satellite)			Stage : Day 29 Dose : HBM 0 mg/kg						Species : Rat		
Animal No.	RBC $10^4/\mu\text{L}$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet $10^4/\mu\text{L}$	WBC $10^2/\mu\text{L}$	Neutrophil $10^2/\mu\text{L}$	Lymphocyte $10^2/\mu\text{L}$
50551	796	15.3	42.0	52.8	19.2	36.4	3.59	115.2	59.8	5.4	51.3
50552	828	15.8	43.5	52.5	19.1	36.3	3.82	139.1	71.8	25.2	42.9
50553	781	14.9	40.9	52.4	19.1	36.4	3.94	130.3	91.8	11.9	76.6
50554	812	15.4	42.4	52.2	19.0	36.3	2.89	106.5	54.5	5.8	45.3
50555	790	15.2	41.8	52.9	19.2	36.4	2.88	91.3	47.5	5.5	38.9
n	5	5	5	5	5	5	5	5	5	5	5
Mean	801.4	15.32	42.12	52.56	19.12	36.36	3.424	116.48	65.08	10.76	51.00
S.D.	18.7	0.33	0.95	0.29	0.08	0.05	0.508	18.96	17.38	8.53	15.00
Monocyte $10^2/\mu\text{L}$		Eosinophil $10^2/\mu\text{L}$	Basophil $10^2/\mu\text{L}$	PT sec	APTT sec						
Animal No.	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	sec	APTT sec						
50551	1.5	1.5	0.1	14.9	10.0						
50552	3.1	0.6	0.0	14.2	10.3						
50553	2.7	0.6	0.0	15.6	14.1						
50554	2.3	1.1	0.0	14.5	11.4						
50555	2.2	0.9	0.0	14.8	11.7						
n	5	5	5	5	5						
Mean	2.36	0.94	0.02	14.80	11.50						
S.D.	0.60	0.38	0.04	0.52	1.62						

Hematological findings Sex : Female (satellite)				Stage : Day 29 Dose : HBM 1000 mg/kg				Species : Rat			
Animal No.	RBC $10^4/\mu\text{L}$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet $10^4/\mu\text{L}$	WBC $10^2/\mu\text{L}$	Neutrophil $10^2/\mu\text{L}$	Lymphocyte $10^2/\mu\text{L}$
50651	845	16.1	44.1	52.2	19.1	36.5	3.07	120.8	73.8	10.7	59.4
50652	814	15.6	42.9	52.7	19.2	36.4	3.23	91.1	58.1	8.9	43.9
50653	805	15.0	41.5	51.6	18.6	36.1	3.61	96.8	41.5	5.9	32.7
50654	817	15.0	41.4	50.7	18.4	36.2	3.59	118.1	62.3	6.4	53.2
50655	829	16.0	44.1	53.2	19.3	36.3	2.80	88.3	79.7	3.1	74.7
n	5	5	5	5	5	5	5	5	5	5	5
Mean	822.0	15.54	42.80	52.08	18.92	36.30	3.260	103.02	63.08	7.00	52.78
S.D.	15.5	0.53	1.33	0.97	0.40	0.16	0.346	15.34	14.85	2.92	15.86
Monocyte $10^2/\mu\text{L}$		Eosinophil $10^2/\mu\text{L}$	Basophil $10^2/\mu\text{L}$	PT sec	APTT sec						
Animal No.	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	10 <sup>2</sup> /μL	sec	sec						
50651	2.6	1.1	0.0	14.6	11.4						
50652	1.2	1.2	0.0	14.9	12.3						
50653	2.1	0.8	0.0	13.8	13.1						
50654	2.0	0.7	0.0	14.7	11.4						
50655	1.1	0.8	0.0	15.6	10.4						
n	5	5	5	5	5						
Mean	1.80	0.92	0.00	14.72	11.72						
S.D.	0.64	0.22	0.00	0.65	1.02						

Hematological findings Sex : Male				Stage : Recovery Day 15 Dose : HBM 0 mg/kg					Species : Rat		
Animal No.	RBC $10^4/\mu\text{L}$	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet $10^4/\mu\text{L}$	WBC $10^2/\mu\text{L}$	Neutrophil $10^2/\mu\text{L}$	Lymphocyte $10^2/\mu\text{L}$
10103	946	16.8	47.1	49.8	17.8	35.7	2.55	111.0	87.1	14.6	69.0
10104	879	16.2	46.2	52.6	18.4	35.1	2.85	93.3	72.2	10.3	57.0
10105	815	15.0	42.2	51.8	18.4	35.5	3.67	103.2	75.5	7.1	64.5
10109	817	15.5	44.2	54.1	19.0	35.1	3.35	97.1	85.3	12.9	69.5
10111	860	14.7	41.1	47.8	17.1	35.8	3.60	106.6	72.6	22.6	46.0
n	5	5	5	5	5	5	5	5	5	5	5
Mean	863.4	15.64	44.16	51.22	18.14	35.44	3.204	102.24	78.54	13.50	61.20
S.D.	53.8	0.86	2.55	2.46	0.72	0.33	0.487	7.12	7.14	5.82	9.87
Monocyte $10^2/\mu\text{L}$		Eosinophil $10^2/\mu\text{L}$	Basophil $10^2/\mu\text{L}$	PT sec	APTT sec						
Animal No.	10^2/ $\mu\text{L}$	10^2/ $\mu\text{L}$	10^2/ $\mu\text{L}$	sec	sec						
10103	2.8	0.6	0.1	16.5	16.6						
10104	3.4	1.4	0.1	16.2	16.2						
10105	2.5	1.4	0.0	24.1	18.4						
10109	2.0	0.8	0.1	20.4	18.3						
10111	3.1	0.9	0.0	21.7	20.7						
n	5	5	5	5	5						
Mean	2.76	1.02	0.06	19.78	18.04						
S.D.	0.54	0.36	0.05	3.40	1.78						

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
10403		841	15.4	43.1	51.2	18.3	35.7	3.48	102.0	95.8	19.4	69.7
10407		845	15.3	42.8	50.7	18.1	35.7	2.65	91.3	71.8	14.4	53.3
10408		806	14.7	41.5	51.5	18.2	35.4	4.11	108.3	62.2	7.6	51.6
10411		871	14.7	41.1	47.2	16.9	35.8	2.21	90.9	56.4	8.1	43.8
10412		855	15.6	44.0	51.5	18.2	35.5	2.67	98.1	86.7	20.8	61.6
n		5	5	5	5	5	5	5	5	5	5	5
Mean		843.6	15.14	42.50	50.42	17.94	35.62	3.024	98.12	74.58	14.06	56.00
S.D.		24.0	0.42	1.19	1.83	0.59	0.16	0.761	7.37	16.50	6.15	9.93
Monocyte		Eosinophil	Basophil	PT	APTT							
Animal No.		10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	sec	sec						
10403		4.7	1.9	0.1	19.8	18.3						
10407		3.0	1.1	0.0	23.8	19.5						
10408		2.2	0.8	0.0	18.9	19.3						
10411		3.8	0.7	0.0	17.2	17.2						
10412		2.5	1.8	0.0	16.6	16.7						
n		5	5	5	5	5						
Mean		3.24	1.26	0.02	19.26	18.20						
S.D.		1.02	0.56	0.04	2.84	1.24						

Hematological findings Sex : Female (satellite)		Stage : Recovery Day 15 Dose : HBM 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		807	14.7	41.6	51.5	18.2	35.3	3.39	110.9	46.0	9.1	35.0	
50557		863	15.5	43.5	50.4	18.0	35.6	3.81	131.3	34.1	5.8	27.0	
50558		793	14.3	40.2	50.7	18.0	35.6	3.40	115.7	57.3	9.5	46.1	
50559		866	15.5	43.4	50.1	17.9	35.7	2.70	93.9	35.9	5.8	28.6	
50560		834	15.3	42.5	51.0	18.3	36.0	3.10	110.6	52.8	7.6	42.9	
n		5	5	5	5	5	5	5	5	5	5	5	
Mean		832.6	15.06	42.24	50.74	18.08	35.64	3.280	112.48	45.22	7.56	35.92	
S.D.		32.7	0.54	1.38	0.54	0.16	0.25	0.411	13.38	10.18	1.76	8.46	
Monocyte		Eosinophil	Basophil	PT	APTT								
Animal No.		10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	sec	sec							
50556		1.0	0.9	0.0	16.1	12.5							
50557		1.0	0.3	0.0	14.6	12.5							
50558		0.9	0.8	0.0	13.9	12.3							
50559		1.0	0.5	0.0	15.9	11.5							
50560		1.4	0.9	0.0	14.9	14.6							
n		5	5	5	5	5							
Mean		1.06	0.68	0.00	15.08	12.68							
S.D.		0.19	0.27	0.00	0.92	1.15							

Hematological findings Sex : Female (satellite)				Stage : Recovery Day 15 Dose : HBM 1000 mg/kg					Species : Rat		
Animal No.	RBC 10 <sup>4</sup> /µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Reticulocyte %	Platelet 10 <sup>4</sup> /µL	WBC 10 <sup>2</sup> /µL	Neutrophil 10 <sup>2</sup> /µL	Lymphocyte 10 <sup>2</sup> /µL
50656	852	15.7	43.4	50.9	18.4	36.2	2.58	81.8	31.9	4.7	26.1
50657	806	15.0	41.4	51.4	18.6	36.2	3.14	99.0	41.1	7.9	31.0
50658	809	15.2	42.5	52.5	18.8	35.8	4.21	102.7	74.0	15.7	54.4
50659	819	15.4	42.6	52.0	18.8	36.2	2.77	99.4	25.7	4.7	19.6
50660	844	15.7	43.9	52.0	18.6	35.8	3.38	104.7	57.0	6.3	48.0
n	5	5	5	5	5	5	5	5	5	5	5
Mean	826.0	15.40	42.76	51.76	18.64	36.04	3.216	97.52	45.94	7.86	35.82
S.D.	20.8	0.31	0.96	0.62	0.17	0.22	0.637	9.10	19.62	4.58	14.78
Monocyte 10 <sup>2</sup> /µL		Eosinophil 10 <sup>2</sup> /µL	Basophil 10 <sup>2</sup> /µL	PT sec	APTT sec						
Animal No.	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	10 <sup>2</sup> /µL	sec	sec						
50656	0.7	0.4	0.0	14.2	12.2						
50657	1.4	0.8	0.0	15.8	11.7						
50658	2.6	1.3	0.0	15.9	10.0						
50659	0.8	0.6	0.0	14.1	12.0						
50660	1.2	1.5	0.0	14.8	12.7						
n	5	5	5	5	5						
Mean	1.34	0.92	0.00	14.96	11.72						
S.D.	0.76	0.47	0.00	0.86	1.03						

Biochemical findings										Species : Rat							
Sex : Male		Stage : Day 29															
		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	μmol/L	mg/dL	mg/dL	g/dL	mg/dL		
10101		63	31	404	0.3	0.07	3.1	149	49	16	5.5	12.9					
10102		63	25	411	0.5	0.07	10.2	168	57	22	5.3	12.6					
10106		65	23	381	0.5	0.06	4.3	153	49	16	5.4	16.4					
10107		61	27	400	0.3	0.07	4.6	177	54	70	5.7	12.7					
10108		68	31	549	0.9	0.06	8.8	158	49	21	5.4	14.6					
n		5	5	5	5	5	5	5	5	5	5	5					
Mean		64.0	27.4	429.0	0.50	0.066	6.20	161.0	51.6	29.0	5.46	13.84					
S.D.		2.6	3.6	68.0	0.24	0.005	3.10	11.4	3.7	23.1	0.15	1.65					
		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		0.28	144	4.43	105	9.0	5.6	0.88	2.58	46.9	23.7	8.4					
10102		0.34	145	4.64	105	9.0	5.7	1.02	2.67	50.4	23.9	9.3					
10106		0.31	146	4.51	106	9.5	6.5	0.93	2.60	48.1	24.0	8.7					
10107		0.25	147	4.30	105	9.3	6.3	1.00	2.86	50.1	24.3	9.5					
10108		0.32	144	4.22	103	9.2	7.5	0.89	2.54	47.0	22.0	9.4					
n		5	5	5	5	5	5	5	5	5	5	5					
Mean		0.300	145.2	4.420	104.8	9.20	6.32	0.944	2.650	48.50	23.58	9.06					
S.D.		0.035	1.3	0.167	1.1	0.21	0.76	0.063	0.126	1.67	0.91	0.48					
		β-G	γ-G														
Animal No.		%	%														
10101		14.9	6.1														
10102		13.9	2.5														
10106		14.5	4.7														
10107		14.5	1.6														
10108		17.4	4.2														
n		5	5														
Mean		15.04	3.82														
S.D.		1.37	1.79														

Biochemical findings										Species : Rat		
Sex : Male		Stage : Day 29 Dose : HBM 100 mg/kg										
Animal No.	AST	ALT	ALP	γ-GTP	T-Bil	TBA	Glucose	T-Cho	TG	TP	UN	
	IU/L	IU/L	IU/L	IU/L	mg/dL	μmol/L	mg/dL	mg/dL	mg/dL	g/dL	mg/dL	
10201	61	25	483	0.5	0.07	6.6	172	50	17	5.2	13.8	
10203	79	35	461	0.8	0.06	7.1	152	63	20	5.7	14.3	
10205	80	35	455	0.6	0.09	13.9	164	58	34	5.6	12.8	
10206	60	28	399	0.3	0.07	6.8	196	58	26	5.4	10.5	
10207	59	23	468	0.7	0.07	5.8	132	40	19	5.3	13.3	
n	5	5	5	5	5	5	5	5	5	5	5	
Mean	67.8	29.2	453.2	0.58	0.072	8.04	163.2	53.8	23.2	5.44	12.94	
S.D.	10.7	5.6	32.0	0.19	0.011	3.31	23.7	9.0	6.9	0.21	1.47	
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	%	%	%	%	
	0.31	145	4.39	105	8.8	6.2	0.95	2.53	48.7	21.1	9.9	
10201	0.32	144	4.66	104	9.4	6.6	0.93	2.75	48.3	21.2	8.9	
10203	0.31	144	4.37	105	9.5	5.6	0.76	2.42	43.2	22.3	10.8	
10205	0.26	144	4.92	104	9.0	6.5	1.09	2.81	52.1	20.4	7.7	
10206	0.27	145	4.50	106	9.2	6.8	1.05	2.71	51.1	21.3	7.9	
n	5	5	5	5	5	5	5	5	5	5	5	
Mean	0.294	144.4	4.568	104.8	9.18	6.34	0.956	2.644	48.68	21.26	9.04	
S.D.	0.027	0.5	0.228	0.8	0.29	0.47	0.128	0.163	3.45	0.68	1.32	
β-G      γ-G												
Animal No.	%	%										
	10201	16.0	4.3									
10203	16.0	5.6										
10205	19.8	3.9										
10206	15.9	3.9										
10207	15.0	4.7										
n	5	5										
Mean	16.54	4.48										
S.D.	1.87	0.71										

Biochemical findings										Species : Rat	
Sex : Male		Stage : Day 29 Dose : HBM 300 mg/kg									
Animal No.	AST	ALT	ALP	γ-GTP	T-Bil	TBA	Glucose	T-Cho	TG	TP	UN
	IU/L	IU/L	IU/L	IU/L	mg/dL	μmol/L	mg/dL	mg/dL	mg/dL	g/dL	mg/dL
10301	56	27	430	0.4	0.08	5.9	167	48	49	5.3	10.7
10304	57	27	325	0.7	0.04	9.9	178	46	48	5.5	11.9
10305	69	26	590	0.3	0.07	5.9	176	66	76	5.4	12.6
10307	58	26	480	0.4	0.09	12.3	145	50	15	5.4	12.3
10308	65	24	491	0.6	0.09	5.2	148	57	21	5.0	13.0
n	5	5	5	5	5	5	5	5	5	5	5
Mean	61.0	26.0	463.2	0.48	0.074	7.84	162.8	53.4	41.8	5.32	12.10
S.D.	5.7	1.2	96.6	0.16	0.021	3.11	15.5	8.2	24.5	0.19	0.88
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	%	%	%
	0.28	144	4.66	105	9.1	5.9	0.89	2.50	47.2	21.6	8.8
10301	0.25	144	4.66	104	9.0	6.5	0.90	2.61	47.4	23.7	9.3
10305	0.31	144	4.80	105	9.5	7.1	0.95	2.64	48.8	20.4	10.0
10307	0.28	145	4.57	104	8.9	7.8	1.13	2.87	53.1	21.1	7.0
10308	0.27	147	4.33	108	9.1	7.0	1.08	2.60	52.0	17.6	9.2
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.278	144.8	4.604	105.2	9.12	6.86	0.990	2.644	49.70	20.88	8.86
S.D.	0.022	1.3	0.174	1.6	0.23	0.71	0.109	0.137	2.70	2.21	1.13
β-G      γ-G											
Animal No.	%	%									
	10301	16.5	5.9								
10304	15.1	4.5									
10305	15.8	5.0									
10307	14.4	4.4									
10308	17.1	4.1									
n	5	5									
Mean	15.78	4.78									
S.D.	1.08	0.70									

Biochemical findings										Species : Rat		
Sex : Male		Stage : Day 29 Dose : HBM 1000 mg/kg										
Animal No.	AST	ALT	ALP	γ-GTP	T-Bil	TBA	Glucose	T-Cho	TG	TP	UN	
	IU/L	IU/L	IU/L	IU/L	mg/dL	μmol/L	mg/dL	mg/dL	mg/dL	g/dL	mg/dL	
10401	65	29	515	0.6	0.07	6.0	141	55	17	5.0	13.3	
10402	57	26	416	0.4	0.08	14.0	157	56	29	5.4	14.3	
10404	68	25	443	0.3	0.07	3.0	152	40	20	5.1	11.1	
10405	82	30	527	0.7	0.08	4.0	146	40	20	5.1	10.9	
10406	60	26	496	0.3	0.08	5.0	159	59	43	5.4	11.1	
n	5	5	5	5	5	5	5	5	5	5	5	
Mean	66.4	27.2	479.4	0.46	0.076	6.40	151.0	50.0	25.8	5.20	12.14	
S.D.	9.7	2.2	47.8	0.18	0.005	4.39	7.5	9.2	10.6	0.19	1.56	
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	%	%	%	%	
	0.31	144	4.48	105	9.0	6.5	1.07	2.59	51.8	18.0	9.5	
10401	0.25	144	4.67	104	9.5	5.8	1.03	2.74	50.7	22.6	8.6	
10402	0.26	145	4.42	104	8.9	6.6	1.07	2.64	51.7	21.9	9.1	
10404	0.25	146	4.35	105	9.0	7.0	1.07	2.64	51.8	19.6	8.6	
10405	0.25	146	4.35	105	9.0	7.0	1.07	2.64	51.8	19.6	8.6	
10406	0.22	146	4.54	104	9.7	7.1	1.09	2.81	52.1	19.6	7.0	
n	5	5	5	5	5	5	5	5	5	5	5	
Mean	0.258	145.0	4.492	104.4	9.22	6.60	1.066	2.684	51.62	20.34	8.56	
S.D.	0.033	1.0	0.122	0.5	0.36	0.51	0.022	0.089	0.54	1.88	0.95	
β-G      γ-G												
Animal No.	%	%										
	10401	16.3	4.4									
10402	14.8	3.3										
10404	14.5	2.8										
10405	16.3	3.7										
10406	16.6	4.7										
n	5	5										
Mean	15.70	3.78										
S.D.	0.97	0.78										

Biochemical findings										Species : Rat																													
Sex : Female					Stage : Day 5 after delivery																																		
AST		ALT		ALP		γ-GTP		T-Bil		TBA		Glucose		T-Cho		TG		TP		UN																			
Animal No.	IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL	μmol/L	mg/dL	mg/dL	mg/dL	mg/dL	g/dL	mg/dL	g/dL	%	g/dL	%	g/dL	%	g/dL	%																		
50152	74	37	184	0.5	0.05	12.8	161	83	50	6.0	13.1																												
50155	91	46	173	0.4	0.06	33.4	146	55	43	6.1	15.4																												
50157	126	46	220	0.6	0.08	30.5	133	53	24	5.5	20.5																												
50160	87	43	185	0.7	0.06	10.2	142	47	28	5.6	9.7																												
50162	86	42	177	0.6	0.05	16.1	125	52	16	5.3	15.1																												
n	5	5	5	5	5	5	5	5	5	5	5																												
Mean	92.8	42.8	187.8	0.56	0.060	20.60	141.4	58.0	32.2	5.70	14.76																												
S.D.	19.6	3.7	18.7	0.11	0.012	10.62	13.6	14.3	14.0	0.34	3.93																												
Crea		Na		K		Cl		Ca		IP		A/G		Albumin		Albumin		α1-G		α2-G																			
Animal No.	mg/dL	mEq/L	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL	mg/dL	g/dL	%	g/dL	%	g/dL	%	g/dL	%	g/dL	%	g/dL	%																		
50152	0.29	143	4.87	105	10.3	6.4	1.00	2.99	49.9	18.6	11.0																												
50155	0.35	144	4.50	107	9.9	7.3	0.90	2.89	47.3	20.8	10.3																												
50157	0.36	144	4.56	105	10.5	9.0	0.80	2.44	44.4	22.5	11.7																												
50160	0.28	143	4.33	104	10.0	7.5	1.03	2.84	50.7	19.1	10.9																												
50162	0.31	143	4.82	106	9.9	8.1	0.85	2.44	46.0	23.0	10.9																												
n	5	5	5	5	5	5	5	5	5	5	5																												
Mean	0.318	143.4	4.616	105.4	10.12	7.66	0.916	2.720	47.66	20.80	10.96																												
S.D.	0.036	0.5	0.226	1.1	0.27	0.97	0.098	0.261	2.63	1.97	0.50																												
β-G		γ-G																																					
Animal No.	%	%																																					
50152	16.9	3.6																																					
50155	16.7	4.9																																					
50157	17.5	3.9																																					
50160	16.3	3.0																																					
50162	16.7	3.4																																					
n	5	5																																					
Mean	16.82	3.76																																					
S.D.	0.44	0.72																																					

Biochemical findings										Species : Rat																													
Sex : Female					Stage : Day 5 after delivery																																		
AST		ALT		ALP		γ-GTP		T-Bil		TBA		Glucose		T-Cho		TG		TP		UN																			
Animal No.	IU/L	IU/L	IU/L	IU/L	IU/L	mg/dL	μmol/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	g/dL	mg/dL	g/dL	mg/dL	g/dL	mg/dL	g/dL																		
50253	94	45	227	0.7	0.04	7.9	124	50	20	5.9	16.7																												
50254	57	32	118	0.6	0.05	13.6	155	55	32	5.8	15.9																												
50255	102	49	178	0.4	0.07	34.2	133	66	27	6.0	17.1																												
50259	120	61	200	0.5	0.05	26.8	164	66	69	5.9	22.4																												
50262	155	50	196	0.7	0.05	8.5	135	68	26	5.5	15.4																												
n	5	5	5	5	5	5	5	5	5	5	5																												
Mean	105.6	47.4	183.8	0.58	0.052	18.20	142.2	61.0	34.8	5.82	17.50																												
S.D.	35.9	10.5	40.7	0.13	0.011	11.74	16.6	8.0	19.6	0.19	2.82																												
Crea		Na		K		Cl		Ca		IP		A/G		Albumin		Albumin		α1-G		α2-G																			
Animal No.	mg/dL	mEq/L	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL	mg/dL	mg/dL	g/dL	%	g/dL	%	g/dL	%	g/dL	%	g/dL	%	g/dL	%																		
50253	0.36	143	4.71	105	10.1	7.9	0.99	2.94	49.8	19.9	10.2																												
50254	0.30	142	4.81	104	10.0	8.1	1.00	2.90	50.0	21.9	9.7																												
50255	0.34	143	4.52	105	10.1	7.5	0.84	2.74	45.6	21.4	11.4																												
50259	0.33	144	4.47	103	11.0	8.9	0.81	2.65	44.9	20.3	12.6																												
50262	0.30	144	4.85	103	9.9	9.3	0.98	2.73	49.6	17.3	12.7																												
n	5	5	5	5	5	5	5	5	5	5	5																												
Mean	0.326	143.2	4.672	104.0	10.22	8.34	0.924	2.792	47.98	20.16	11.32																												
S.D.	0.026	0.8	0.170	1.0	0.44	0.74	0.091	0.123	2.51	1.79	1.36																												
β-G		γ-G																																					
Animal No.	%	%																																					
50253	15.9	4.2																																					
50254	16.0	2.4																																					
50255	17.1	4.5																																					
50259	18.6	3.6																																					
50262	17.3	3.1																																					
n	5	5																																					
Mean	16.98	3.56																																					
S.D.	1.10	0.84																																					

Biochemical findings Sex : Female										Species : Rat	
Stage : Day 5 after delivery Dose : HBM 300 mg/kg											
Animal No.	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	TP g/dL	UN mg/dL
50351	70	47	363	1.3	0.04	13.1	159	62	164	6.0	13.6
50354	88	46	187	0.9	0.06	18.3	134	50	15	5.4	17.4
50355	61	31	131	0.7	0.04	9.6	155	45	19	5.9	14.2
50361	74	36	174	0.7	0.06	24.5	166	61	21	5.8	12.5
50362	69	31	252	0.7	0.04	12.5	122	68	31	5.7	16.7
n	5	5	5	5	5	5	5	5	5	5	5
Mean	72.4	38.2	221.4	0.86	0.048	15.60	147.2	57.2	50.0	5.76	14.88
S.D.	9.9	7.9	90.3	0.26	0.011	5.88	18.5	9.4	64.0	0.23	2.09
Crea mg/dL											
Animal No.	Na mEq/L	K mEq/L	Cl mEq/L	Ca mEq/L	IP mg/dL	A/G mg/dL	Albumin g/dL	Albumin %	α1-G %	α2-G %	
50351	0.31	142	4.64	99	10.7	7.7	0.85	2.76	46.0	20.6	10.7
50354	0.30	142	4.92	105	9.9	8.2	0.97	2.66	49.2	20.3	11.1
50355	0.28	144	4.63	104	10.4	8.4	0.91	2.81	47.6	20.7	11.4
50361	0.28	142	4.69	103	9.9	7.9	1.07	2.99	51.6	19.5	10.3
50362	0.33	142	4.75	105	9.8	7.5	1.04	2.91	51.0	22.9	9.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.300	142.4	4.726	103.2	10.14	7.94	0.968	2.826	49.08	20.80	10.58
S.D.	0.021	0.9	0.118	2.5	0.39	0.36	0.091	0.129	2.33	1.26	0.78
β-G %											
Animal No.	β-G %	γ-G %									
50351	18.6	4.1									
50354	16.6	2.8									
50355	16.3	4.0									
50361	15.5	3.1									
50362	13.7	3.0									
n	5	5									
Mean	16.14	3.40									
S.D.	1.78	0.60									

Biochemical findings										Species : Rat	
Sex : Female		Stage : Day 5 after delivery Dose : HBM 1000 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
50451	74	42	198	0.7	0.07	29.9	139	62	40	5.9	15.7
50453	74	34	190	0.6	0.06	13.1	143	48	62	5.5	15.1
50460	76	49	451	0.9	0.06	61.4	145	69	47	5.8	22.6
50461	141	62	362	0.6	0.07	28.9	173	102	56	5.7	18.7
50462	84	42	147	0.9	0.04	5.4	122	55	17	5.4	13.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	89.8	45.8	269.6	0.74	0.060	27.74	144.4	67.2	44.4	5.66	17.10
S.D.	28.9	10.5	130.3	0.15	0.012	21.52	18.4	21.0	17.5	0.21	3.62
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	%	%	%
	0.29	141	4.70	103	10.0	7.7	0.90	2.79	47.3	22.3	9.2
50451	0.30	142	5.10	104	10.0	8.3	0.94	2.66	48.4	21.3	10.5
50453	0.35	143	4.87	101	10.8	9.9	0.86	2.69	46.3	16.1	13.8
50460	0.34	145	4.25	104	11.1	8.8	0.84	2.60	45.6	20.1	13.6
50461	0.32	142	4.90	105	9.9	7.7	0.90	2.57	47.5	19.8	11.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.320	142.6	4.764	103.4	10.36	8.48	0.888	2.662	47.02	19.92	11.74
S.D.	0.025	1.5	0.321	1.5	0.55	0.92	0.039	0.086	1.09	2.36	1.98
$\beta$ -G $\gamma$ -G											
Animal No.	%	%									
	16.4	4.8									
50451	16.0	3.8									
50453	18.4	5.4									
50460	17.3	3.4									
50461	16.5	4.6									
n	5	5									
Mean	16.92	4.40									
S.D.	0.95	0.80									

Biochemical findings Sex : Female (satellite)				Stage : Day 29 Dose : HBM 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
50551	65	22	198	0.7	0.11	20.3	113	73	7	5.9	18.5
50552	62	25	184	0.6	0.08	9.5	156	61	10	5.6	13.9
50553	58	30	243	0.3	0.12	21.5	180	51	17	6.2	16.3
50554	63	22	256	0.8	0.08	5.2	138	68	15	6.1	14.9
50555	55	25	190	0.5	0.09	61.8	148	69	12	6.0	18.5
n	5	5	5	5	5	5	5	5	5	5	5
Mean	60.6	24.8	214.2	0.58	0.096	23.66	147.0	64.4	12.2	5.96	16.42
S.D.	4.0	3.3	32.9	0.19	0.018	22.43	24.5	8.6	4.0	0.23	2.08
	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	%	%	%
50551	0.39	143	4.22	103	9.9	6.4	1.15	3.16	53.5	19.2	8.3
50552	0.32	145	4.22	105	9.4	5.6	1.17	3.02	54.0	18.0	8.5
50553	0.31	140	4.32	101	10.1	7.1	1.19	3.37	54.4	19.8	7.3
50554	0.31	143	4.72	105	9.6	6.7	1.12	3.23	52.9	16.6	7.7
50555	0.35	143	4.05	102	9.7	6.4	1.27	3.35	55.9	17.7	7.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.336	142.8	4.306	103.2	9.74	6.44	1.180	3.226	54.14	18.26	7.84
S.D.	0.034	1.8	0.251	1.8	0.27	0.55	0.057	0.144	1.13	1.26	0.54
	β-G	γ-G									
Animal No.	%	%									
50551	13.7	5.3									
50552	13.8	5.7									
50553	13.8	4.7									
50554	15.2	7.6									
50555	14.8	4.2									
n	5	5									
Mean	14.26	5.50									
S.D.	0.69	1.31									

Biochemical findings Sex : Female (satellite)				Stage : Day 29 Dose : HBM 1000 mg/kg				Species : Rat			
	AST IU/L	ALT IU/L	ALP IU/L	γ-GTP IU/L	T-Bil mg/dL	TBA μmol/L	Glucose mg/dL	T-Cho mg/dL	TG mg/dL	TP g/dL	UN mg/dL
Animal No.											
50651	59	25	124	0.7	0.12	14.1	158	60	13	6.6	16.7
50652	45	20	177	0.4	0.09	7.9	156	72	20	6.3	17.3
50653	108	39	144	0.5	0.09	17.7	153	62	9	6.1	13.7
50654	61	22	181	1.0	0.06	8.2	142	63	10	5.5	15.0
50655	57	19	348	1.2	0.08	5.5	125	78	12	5.6	13.8
n	5	5	5	5	5	5	5	5	5	5	5
Mean	66.0	25.0	194.8	0.76	0.088	10.68	146.8	67.0	12.8	6.02	15.30
S.D.	24.3	8.2	88.8	0.34	0.022	5.04	13.7	7.7	4.3	0.47	1.65
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	Crea mg/dL	Na mEq/L	K mEq/L	Cl mEq/L	Ca mg/dL	IP mg/dL	A/G	Albumin g/dL	Albumin %	α1-G	α2-G
Animal No.											
50651	0.30	142	4.30	101	10.3	6.3	1.33	3.76	57.0	18.8	7.4
50652	0.34	144	4.11	103	10.1	6.4	1.13	3.35	53.1	19.4	9.0
50653	0.36	144	4.16	102	9.8	6.2	1.20	3.32	54.5	17.7	8.0
50654	0.38	144	4.60	103	9.6	6.0	1.12	2.90	52.8	13.9	9.1
50655	0.32	144	4.69	105	9.4	6.9	1.28	3.14	56.1	15.3	8.4
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.340	143.6	4.372	102.8	9.84	6.36	1.212	3.294	54.70	17.02	8.38
S.D.	0.032	0.9	0.261	1.5	0.36	0.34	0.092	0.316	1.83	2.34	0.71
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	β-G %	γ-G %									
Animal No.											
50651	12.7	4.1									
50652	13.6	4.9									
50653	14.2	5.6									
50654	17.7	6.5									
50655	13.9	6.3									
n	5	5									
Mean	14.42	5.48									
S.D.	1.92	1.00									

Biochemical findings										Species : Rat		
Sex : Male		Stage : Recovery Day 15 Dose : HBM 0 mg/kg										
Animal No.	AST	ALT	ALP	γ-GTP	T-Bil	TBA	Glucose	T-Cho	TG	TP	UN	
	IU/L	IU/L	IU/L	IU/L	mg/dL	μmol/L	mg/dL	mg/dL	mg/dL	g/dL	mg/dL	
10103	57	24	312	0.4	0.09	11.1	141	58	19	5.5	14.3	
10104	66	29	355	0.5	0.07	13.5	156	52	26	5.3	12.1	
10105	65	34	438	0.0	0.06	8.8	178	48	19	5.5	14.6	
10109	64	27	454	0.1	0.07	6.7	164	38	31	5.3	14.6	
10111	60	23	267	0.3	0.06	5.7	157	37	21	5.3	15.7	
n	5	5	5	5	5	5	5	5	5	5	5	
Mean	62.4	27.4	365.2	0.26	0.070	9.16	159.2	46.6	23.2	5.38	14.26	
S.D.	3.8	4.4	80.3	0.21	0.012	3.19	13.4	9.0	5.2	0.11	1.32	
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	%	%	%	%	
	0.31	144	4.68	104	8.6	5.4	0.93	2.65	48.2	24.6	7.8	
10103	0.25	143	4.47	105	9.1	5.4	1.01	2.67	50.3	16.4	10.0	
10104	0.38	144	4.63	107	8.6	5.4	0.97	2.71	49.2	22.7	8.8	
10105	0.29	144	4.52	104	8.4	5.9	1.01	2.66	50.2	20.5	9.5	
10109	0.33	144	4.88	104	9.1	5.4	0.89	2.50	47.2	25.1	9.1	
n	5	5	5	5	5	5	5	5	5	5	5	
Mean	0.312	143.8	4.636	104.8	8.76	5.50	0.962	2.638	49.02	21.86	9.04	
S.D.	0.048	0.4	0.160	1.3	0.32	0.22	0.052	0.080	1.33	3.55	0.83	
β-G      γ-G												
Animal No.	%	%										
	10103	13.8	5.6									
10104	17.9	5.4										
10105	14.5	4.8										
10109	15.4	4.4										
10111	14.9	3.7										
n	5	5										
Mean	15.30	4.78										
S.D.	1.57	0.77										

Biochemical findings										Species : Rat	
Sex : Male		Stage : Recovery Day 15 Dose : HBM 1000 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
10403	63	28	298	0.5	0.10	8.7	142	44	15	5.5	12.6
10407	61	26	397	0.1	0.07	13.6	141	39	10	5.5	15.8
10408	74	32	435	0.2	0.08	15.2	146	40	13	5.1	15.1
10411	71	33	369	0.3	0.05	5.7	198	48	36	5.1	16.5
10412	61	24	358	0.5	0.06	5.5	138	54	8	5.1	15.6
n	5	5	5	5	5	5	5	5	5	5	5
Mean	66.0	28.6	371.4	0.32	0.072	9.74	153.0	45.0	16.4	5.26	15.12
S.D.	6.1	3.8	50.7	0.18	0.019	4.47	25.3	6.2	11.3	0.22	1.50
	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	%	%	%
10403	0.31	145	4.35	104	9.4	6.1	0.87	2.55	46.4	24.2	8.2
10407	0.32	145	4.55	105	9.0	5.9	0.99	2.74	49.8	21.8	8.8
10408	0.33	145	4.53	106	8.8	6.5	0.97	2.51	49.2	22.1	9.3
10411	0.35	144	4.29	105	9.2	5.5	0.96	2.50	49.1	22.8	8.4
10412	0.32	145	4.56	106	9.0	5.6	0.96	2.50	49.1	16.5	10.9
n	5	5	5	5	5	5	5	5	5	5	5
Mean	0.326	144.8	4.456	105.2	9.08	5.92	0.950	2.560	48.72	21.48	9.12
S.D.	0.015	0.4	0.126	0.8	0.23	0.40	0.046	0.103	1.33	2.93	1.08
	β-G	γ-G									
Animal No.	%	%									
10403	16.2	5.0									
10407	15.0	4.6									
10408	14.8	4.6									
10411	15.1	4.6									
10412	15.9	7.6									
n	5	5									
Mean	15.40	5.28									
S.D.	0.61	1.31									

Biochemical findings Sex : Female (satellite)		Stage : Recovery Day 15 Dose : HBM 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		67	21	266	0.5	0.05	9.1	138	61	12	5.5	16.2
50557		57	26	175	0.4	0.05	5.0	139	62	9	6.3	11.3
50558		48	20	265	0.3	0.08	15.4	171	66	17	5.9	15.2
50559		52	27	235	0.5	0.09	19.3	157	64	14	6.2	14.4
50560		63	24	201	0.6	0.09	15.1	144	56	6	5.7	14.7
n		5	5	5	5	5	5	5	5	5	5	5
Mean		57.4	23.6	228.4	0.46	0.072	12.78	149.8	61.8	11.6	5.92	14.36
S.D.		7.8	3.0	40.0	0.11	0.020	5.68	14.1	3.8	4.3	0.33	1.84
		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		0.31	144	4.30	107	9.1	4.8	1.25	3.06	55.6	11.5	9.7
50557		0.33	144	5.13	106	9.8	5.0	1.11	3.32	52.7	17.3	9.5
50558		0.38	143	4.46	104	9.5	5.3	1.18	3.20	54.2	17.4	8.5
50559		0.29	144	4.10	106	9.4	5.1	1.20	3.38	54.5	15.6	9.2
50560		0.32	144	4.00	105	9.5	6.0	1.11	3.00	52.6	18.3	7.7
n		5	5	5	5	5	5	5	5	5	5	5
Mean		0.326	143.8	4.398	105.6	9.46	5.24	1.170	3.192	53.92	16.02	8.92
S.D.		0.034	0.4	0.446	1.1	0.25	0.46	0.060	0.163	1.27	2.71	0.82
		β-G	γ-G									
Animal No.		%	%									
50556		14.2	9.0									
50557		15.2	5.3									
50558		13.9	6.0									
50559		14.5	6.2									
50560		13.9	7.5									
n		5	5									
Mean		14.34	6.80									
S.D.		0.54	1.46									

Biochemical findings Sex : Female (satellite)		Stage : Recovery Day 15 Dose : HBM 1000 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
50656		56	26	210	0.9	0.06	7.5	169	91	21	6.7	14.6
50657		54	34	218	0.8	0.08	10.6	177	66	13	5.8	14.4
50658		54	24	217	1.1	0.08	11.5	129	56	21	5.8	14.7
50659		48	17	161	0.5	0.06	5.4	145	94	10	6.0	16.4
50660		42	20	148	0.6	0.08	13.8	153	56	11	6.0	14.0
n		5	5	5	5	5	5	5	5	5	5	5
Mean		50.8	24.2	190.8	0.78	0.072	9.76	154.6	72.6	15.2	6.06	14.82
S.D.		5.8	6.5	33.6	0.24	0.011	3.32	19.1	18.6	5.4	0.37	0.92
		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	%	%	%
50656		0.33	143	4.44	106	9.6	4.0	1.48	4.00	59.7	13.7	8.2
50657		0.30	144	4.61	104	9.8	5.6	1.28	3.26	56.2	15.5	9.5
50658		0.30	142	5.02	104	9.5	6.8	1.17	3.13	54.0	11.6	10.0
50659		0.40	142	4.62	104	9.5	4.6	1.17	3.24	54.0	19.2	8.4
50660		0.30	144	4.49	105	9.6	6.0	1.17	3.23	53.9	18.7	8.0
n		5	5	5	5	5	5	5	5	5	5	5
Mean		0.326	143.0	4.636	104.6	9.60	5.40	1.254	3.372	55.56	15.74	8.82
S.D.		0.043	1.0	0.228	0.9	0.12	1.11	0.135	0.355	2.51	3.24	0.88
		β-G	γ-G									
Animal No.		%	%									
50656		13.1	5.3									
50657		14.6	4.2									
50658		14.7	9.7									
50659		13.4	5.0									
50660		12.8	6.6									
n		5	5									
Mean		13.72	6.16									
S.D.		0.88	2.16									

Necropsy findings			Stage : Day 29	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10101		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10102		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10106		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10107		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10108		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10110		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10112		
Finding absent :	Epididymis, Other organs & tissues			

Necropsy findings			Stage : Day 29	Species : Rat
Sex : Male				
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10201		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10202		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10203		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10204		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10205		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10206		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10207		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10208		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10209		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10210		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10211		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10212		
Finding absent :	Epididymis, Other organs & tissues			

Necropsy findings		Sex : Male	Stage : Day 29	Species : Rat
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10301		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10302		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10303		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10304		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10305		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10306		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10307		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10308	Infertility	
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10309		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10310		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10311		
Epididymis				
Findings :	Finding present			
Animal Comment :	right epididymis, 6 x 5, mm			
Yellowish white focus, cauda, unilateral				
Non-graded change				
Finding absent :	Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10312		
Finding absent :	Epididymis, Other organs & tissues			

Necropsy findings			Stage : Day 29	Species : Rat
Sex : Male				
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10401		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10402		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10404		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10405		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10406		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10409		
Finding absent :	Epididymis, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10410		
Finding absent :	Epididymis, Other organs & tissues			

Necropsy findings		Stage : Day 5 after delivery	Species : Rat
Sex : Female			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50151	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50152	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50153	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50154	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50155	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50156	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50157	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50158	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50159	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50160	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50161	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50162	
Finding absent :	Glandular stomach, Other organs & tissues		

Necropsy findings		Stage : Day 5 after delivery	Species : Rat
Sex : Female			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50251	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50252	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50253	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50254	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50255	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50256	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50257	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50258	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50259	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50260	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50261	
Finding absent :	Glandular stomach, Other organs & tissues		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50262	
Finding absent :	Glandular stomach, Other organs & tissues		

Necropsy findings			Stage : Day 5 after delivery	Species : Rat
Sex : Female				
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50351		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50352		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50353		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50354		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50355		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50356		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50357		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50358	Non-pregnancy	
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50359		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50360		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50361		
Glandular stomach				
Findings :	Finding present			
Animal Comment :	3 x 1, mm			
Black focus, mucosa				
Non-graded change				
Finding absent :	Other organs & tissues			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50362		
Finding absent :	Glandular stomach, Other organs & tissues			

Necropsy findings			Stage : Day 5 after delivery	Species : Rat
Sex : Female				
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50451		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50452		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50453		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50454		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50455		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50456		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50457		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50458		
Glandular stomach				
Findings :	Finding present			
Animal Comment :	4 x 1, mm			
Black focus, mucosa				
Non-graded change				
Finding absent :	Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50459		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50460		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50461		
Finding absent :	Glandular stomach, Other organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50462		
Glandular stomach				
Findings :	Finding present			
Animal Comment :	1 x 1, mm			
Black focus, mucosa				
Non-graded change				
Finding absent :	Other organs & tissues			

Necropsy findings			
Sex : Female (satellite)		Stage : Day 29	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50551	
Finding absent :	All organs & tissues		
Estrous cycle :	Diestrus		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50552	
Finding absent :	All organs & tissues		
Estrous cycle :	Proestrus		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50553	
Finding absent :	All organs & tissues		
Estrous cycle :	Proestrus		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50554	
Finding absent :	All organs & tissues		
Estrous cycle :	Diestrus		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50555	
Finding absent :	All organs & tissues		
Estrous cycle :	Diestrus		

Necropsy findings Sex : Female (satellite)			Stage : Day 29	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50651		
Finding absent :	All organs & tissues			
Estrous cycle :	Metestrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50652		
Finding absent :	All organs & tissues			
Estrous cycle :	Diestrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50653		
Finding absent :	All organs & tissues			
Estrous cycle :	Proestrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50654		
Finding absent :	All organs & tissues			
Estrous cycle :	Proestrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50655		
Finding absent :	All organs & tissues			
Estrous cycle :	Diestrus			

Necropsy findings			Stage : Recovery Day 15	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10103		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10104		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10105		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10109		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10111		
Finding absent :	All organs & tissues			

Necropsy findings			Stage : Recovery Day 15	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10403		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10407		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10408		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10411		
Finding absent :	All organs & tissues			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10412		
Finding absent :	All organs & tissues			

Necropsy findings Sex : Female (satellite)			Stage : Recovery Day 15	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50556		
Finding absent :	All organs & tissues			
Estrous cycle :	Proestrus			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50557		
Finding absent :	All organs & tissues			
Estrous cycle :	Estrus			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50558		
Finding absent :	All organs & tissues			
Estrous cycle :	Estrus			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50559		
Finding absent :	All organs & tissues			
Estrous cycle :	Proestrus			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50560		
Finding absent :	All organs & tissues			
Estrous cycle :	Proestrus			

Necropsy findings			Stage : Recovery Day 15	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50656		
Finding absent :	All organs & tissues			
Estrous cycle :	Estrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50657		
Finding absent :	All organs & tissues			
Estrous cycle :	Diestrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50658		
Finding absent :	All organs & tissues			
Estrous cycle :	Diestrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50659		
Finding absent :	All organs & tissues			
Estrous cycle :	Estrus			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50660		
Finding absent :	All organs & tissues			
Estrous cycle :	Proestrus			

Organ weight Sex : Male		Stage : Day 29 Dose : HBM 0 mg/kg						Species : Rat		
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen		
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
10101	420	11.16	2.66	3.08	0.73	1.24	0.30	705	167.86	
10102	420	10.62	2.53	2.93	0.70	1.39	0.33	600	142.86	
10106	460	11.07	2.41	3.05	0.66	1.28	0.28	801	174.13	
10107	477	13.40	2.81	3.52	0.74	1.61	0.34	791	165.83	
10108	419	10.68	2.55	2.93	0.70	1.27	0.30	736	175.66	
10110	397	9.74	2.45	2.87	0.72	1.29	0.32	591	148.87	
10112	479	11.89	2.48	3.47	0.72	1.45	0.30	658	137.37	
n	7	7	7	7	7	7	7	7	7	
Mean	438.9	11.223	2.556	3.121	0.710	1.361	0.310	697.4	158.940	
S.D.	32.6	1.160	0.138	0.266	0.026	0.132	0.021	85.1	15.613	
Thymus		Adrenal		Pituitary gland		Thyroid		Testis		
Animal No.	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
	396	94.29	50	11.90	12.3	2.93	22.1	5.26	3.31	0.79
10102	240	57.14	66	15.71	12.6	3.00	17.5	4.17	3.26	0.78
10106	219	47.61	92	20.00	14.1	3.07	17.0	3.70	3.19	0.69
10107	259	54.30	75	15.72	11.1	2.33	21.3	4.47	3.14	0.66
10108	319	76.13	60	14.32	11.2	2.67	22.2	5.30	3.10	0.74
10110	453	114.11	53	13.35	10.6	2.67	19.9	5.01	2.85	0.72
10112	274	57.20	68	14.20	13.4	2.80	24.0	5.01	3.54	0.74
n	7	7	7	7	7	7	7	7	7	7
Mean	308.6	71.540	66.3	15.029	12.19	2.781	20.57	4.703	3.199	0.731
S.D.	86.6	24.609	14.3	2.564	1.29	0.252	2.58	0.605	0.211	0.046
Epididymis		Prostate		Seminal vesicle		Brain				
Animal No.	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g
	1.33	0.32	941	224.05	2.46	0.59	2.06	0.49		
10102	1.13	0.27	603	143.57	1.93	0.46	2.17	0.52		
10106	1.25	0.27	618	134.35	2.16	0.47	2.35	0.51		
10107	1.27	0.27	552	115.72	1.74	0.36	2.09	0.44		
10108	1.14	0.27	538	128.40	2.07	0.49	2.12	0.51		
10110	1.09	0.27	458	115.37	1.56	0.39	2.11	0.53		
10112	1.33	0.28	835	174.32	2.35	0.49	2.38	0.50		
n	7	7	7	7	7	7	7	7		
Mean	1.220	0.279	649.3	147.969	2.039	0.464	2.183	0.500		
S.D.	0.099	0.019	173.8	39.101	0.322	0.075	0.129	0.029		

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

Animal No.	Organ weight Sex : Male		Stage : Day 29 Dose : HBM 100 mg/kg						Species : Rat	
	Body weight g	Liver	Kidney			Heart		Spleen		
			AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g
10201	464	11.70	2.52	3.11	0.67	1.32	0.28	749	161.42	
10202	446	10.94	2.45	3.35	0.75	1.47	0.33	755	169.28	
10203	449	11.28	2.51	3.04	0.68	1.30	0.29	722	160.80	
10204	455	10.23	2.25	3.56	0.78	1.32	0.29	626	137.58	
10205	459	13.17	2.87	2.99	0.65	1.52	0.33	1114	242.70	
10206	491	13.36	2.72	3.31	0.67	1.73	0.35	786	160.08	
10207	430	10.80	2.51	3.30	0.77	1.48	0.34	715	166.28	
10208	433	9.99	2.31	3.34	0.77	1.20	0.28	858	198.15	
10209	446	11.87	2.66	3.47	0.78	1.21	0.27	831	186.32	
10210	447	12.10	2.71	3.03	0.68	1.32	0.30	784	175.39	
10211	426	10.75	2.52	3.02	0.71	1.45	0.34	584	137.09	
10212	403	11.32	2.81	3.12	0.77	1.32	0.33	770	191.07	
n	12	12	12	12	12	12	12	12	12	
Mean	445.8	11.459	2.570	3.220	0.723	1.387	0.311	774.5	173.847	
S.D.	21.9	1.049	0.189	0.192	0.051	0.150	0.028	131.9	28.675	

Animal No.	Thymus		Adrenal		Pituitary gland		Thyroid		Testis	
	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
10201	385	82.97	101	21.77	11.1	2.39	21.3	4.59	3.41	0.73
10202	297	66.59	67	15.02	10.8	2.42	23.3	5.22	3.34	0.75
10203	313	69.71	65	14.48	12.4	2.76	24.7	5.50	3.12	0.69
10204	340	74.73	85	18.68	11.7	2.57	11.2	2.46	3.49	0.77
10205	423	92.16	59	12.85	12.9	2.81	17.3	3.77	3.26	0.71
10206	325	66.19	62	12.63	12.7	2.59	20.4	4.15	3.01	0.61
10207	472	109.77	65	15.12	11.4	2.65	22.5	5.23	3.99	0.93
10208	390	90.07	57	13.16	11.5	2.66	22.9	5.29	3.53	0.82
10209	261	58.52	62	13.90	11.3	2.53	17.1	3.83	2.87	0.64
10210	562	125.73	55	12.30	10.8	2.42	19.9	4.45	3.18	0.71
10211	242	56.81	66	15.49	9.5	2.23	22.2	5.21	3.54	0.83
10212	357	88.59	62	15.38	9.1	2.26	17.1	4.24	3.36	0.83
n	12	12	12	12	12	12	12	12	12	12
Mean	363.9	81.820	67.2	15.065	11.27	2.524	19.99	4.495	3.342	0.752
S.D.	90.6	20.830	13.0	2.732	1.15	0.184	3.76	0.880	0.292	0.090

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

Animal No.	Organ weight Sex : Male		Stage : Day 29 Dose : HBM 100 mg/kg				Species : Rat	
	Epididymis		Prostate		Seminal vesicle		Brain	
	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g
10201	1.30	0.28	888	191.38	2.44	0.53	2.22	0.48
10202	1.33	0.30	592	132.74	2.24	0.50	2.26	0.51
10203	1.24	0.28	686	152.78	2.38	0.53	2.24	0.50
10204	1.28	0.28	850	186.81	2.23	0.49	2.31	0.51
10205	1.23	0.27	680	148.15	1.96	0.43	2.27	0.49
10206	1.19	0.24	874	178.00	1.84	0.37	2.20	0.45
10207	1.49	0.35	821	190.93	2.50	0.58	2.17	0.50
10208	1.27	0.29	654	151.04	1.69	0.39	2.12	0.49
10209	1.17	0.26	526	117.94	2.05	0.46	2.21	0.50
10210	1.25	0.28	547	122.37	1.46	0.33	2.10	0.47
10211	1.26	0.30	660	154.93	2.08	0.49	2.28	0.54
10212	1.19	0.30	725	179.90	1.75	0.43	2.22	0.55
n	12	12	12	12	12	12	12	12
Mean	1.267	0.286	708.6	158.914	2.052	0.461	2.217	0.499
S.D.	0.085	0.027	125.1	26.273	0.324	0.073	0.063	0.027

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

Animal No.	Sex : Male Body weight g	Stage : Day 29 Dose : HBM 300 mg/kg						Species : Rat	
		Liver		Kidney		Heart		Spleen	
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g
10301	420	10.34	2.46	2.99	0.71	1.34	0.32	648	154.29
10302	435	10.58	2.43	3.41	0.78	1.43	0.33	744	171.03
10303	440	11.71	2.66	3.20	0.73	1.31	0.30	902	205.00
10304	468	12.84	2.74	3.43	0.73	1.47	0.31	755	161.32
10305	494	12.50	2.53	3.05	0.62	1.69	0.34	693	140.28
10306	451	11.18	2.48	3.89	0.86	1.34	0.30	800	177.38
10307	387	9.04	2.34	2.89	0.75	1.25	0.32	570	147.29
10308	432	11.13	2.58	3.03	0.70	1.39	0.32	802	185.65
10309	437	11.34	2.59	3.52	0.81	1.37	0.31	639	146.22
10310	477	11.87	2.49	4.00	0.84	1.54	0.32	808	169.39
10311	497	13.44	2.70	4.01	0.81	1.65	0.33	821	165.19
10312	448	11.20	2.50	3.36	0.75	1.30	0.29	654	145.98
n	12	12	12	12	12	12	12	12	12
Mean	448.8	11.431	2.542	3.398	0.758	1.423	0.316	736.3	164.085
S.D.	31.4	1.179	0.117	0.395	0.067	0.140	0.014	96.4	19.052

Animal No.	Thymus		Adrenal		Pituitary gland		Thyroid		Testis	
	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
10301	342	81.43	49	11.67	11.9	2.83	25.2	6.00	2.94	0.70
10302	330	75.86	52	11.95	11.3	2.60	21.5	4.94	3.79	0.87
10303	389	88.41	58	13.18	9.5	2.16	15.8	3.59	3.18	0.72
10304	351	75.00	76	16.24	13.8	2.95	26.6	5.68	3.05	0.65
10305	498	100.81	63	12.75	10.3	2.09	22.9	4.64	3.15	0.64
10306	300	66.52	66	14.63	12.8	2.84	19.7	4.37	3.33	0.74
10307	233	60.21	61	15.76	10.0	2.58	15.4	3.98	3.35	0.87
10308	363	84.03	54	12.50	11.9	2.75	19.9	4.61	3.18	0.74
10309	283	64.76	65	14.87	9.0	2.06	18.6	4.26	3.03	0.69
10310	390	81.76	53	11.11	10.8	2.26	20.4	4.28	3.37	0.71
10311	453	91.15	64	12.88	12.0	2.41	23.0	4.63	3.46	0.70
10312	336	75.00	63	14.06	11.0	2.46	25.4	5.67	3.00	0.67
n	12	12	12	12	12	12	12	12	12	12
Mean	355.7	78.745	60.3	13.467	11.19	2.499	21.20	4.721	3.236	0.725
S.D.	71.8	11.690	7.5	1.640	1.39	0.309	3.61	0.732	0.239	0.075

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

Animal No.	Organ weight Sex : Male		Stage : Day 29 Dose : HBM 300 mg/kg				Species : Rat	
	Epididymis		Prostate		Seminal vesicle		Brain	
	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g
10301	1.22	0.29	860	204.76	2.39	0.57	2.07	0.49
10302	1.39	0.32	692	159.08	2.32	0.53	2.21	0.51
10303	1.22	0.28	741	168.41	1.90	0.43	2.22	0.50
10304	1.26	0.27	500	106.84	2.13	0.46	2.16	0.46
10305	1.36	0.28	901	182.39	2.20	0.45	2.19	0.44
10306	1.36	0.30	694	153.88	2.10	0.47	2.14	0.47
10307	1.26	0.33	830	214.47	2.22	0.57	2.14	0.55
10308	1.22	0.28	729	168.75	2.31	0.53	2.24	0.52
10309	1.22	0.28	497	113.73	1.59	0.36	2.22	0.51
10310	1.27	0.27	413	86.58	1.77	0.37	2.17	0.45
10311	1.41	0.28	643	129.38	2.14	0.43	2.33	0.47
10312	1.26	0.28	708	158.04	2.20	0.49	2.22	0.50
n	12	12	12	12	12	12	12	12
Mean	1.288	0.288	684.0	153.859	2.106	0.472	2.193	0.489
S.D.	0.072	0.019	150.6	38.734	0.238	0.070	0.065	0.032

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

Organ weight Sex : Male		Stage : Day 29 Dose : HBM 1000 mg/kg						Species : Rat		
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen		
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
10401	406	9.51	2.34	3.04	0.75	1.47	0.36	671	165.27	
10402	462	12.28	2.66	3.75	0.81	1.51	0.33	845	182.90	
10404	396	9.75	2.46	3.06	0.77	1.40	0.35	588	148.48	
10405	417	9.27	2.22	3.16	0.76	1.33	0.32	776	186.09	
10406	470	12.01	2.56	3.48	0.74	1.45	0.31	771	164.04	
10409	413	9.90	2.40	3.40	0.82	1.22	0.30	607	146.97	
10410	509	14.04	2.76	3.68	0.72	1.52	0.30	970	190.57	
n	7	7	7	7	7	7	7	7	7	
Mean	439.0	10.966	2.486	3.367	0.767	1.414	0.324	746.9	169.189	
S.D.	41.8	1.820	0.188	0.289	0.036	0.108	0.024	136.3	17.773	
Thymus		Adrenal		Pituitary gland		Thyroid		Testis		
Animal No.	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
10401	391	96.31	61	15.02	11.9	2.93	21.3	5.25	3.00	0.74
10402	391	84.63	79	17.10	11.4	2.47	20.7	4.48	2.98	0.65
10404	247	62.37	64	16.16	8.8	2.22	25.0	6.31	3.03	0.77
10405	460	110.31	70	16.79	10.3	2.47	18.1	4.34	2.70	0.65
10406	452	96.17	59	12.55	13.4	2.85	21.8	4.64	3.37	0.72
10409	327	79.18	58	14.04	11.6	2.81	15.2	3.68	3.02	0.73
10410	413	81.14	64	12.57	10.2	2.00	22.7	4.46	3.14	0.62
n	7	7	7	7	7	7	7	7	7	7
Mean	383.0	87.159	65.0	14.890	11.09	2.536	20.69	4.737	3.034	0.697
S.D.	74.6	15.393	7.3	1.902	1.47	0.348	3.19	0.833	0.200	0.056
Epididymis		Prostate		Seminal vesicle		Brain				
Animal No.	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g
10401	1.22	0.30	828	203.94	2.23	0.55	2.13	0.52		
10402	1.15	0.25	810	175.32	2.02	0.44	2.07	0.45		
10404	1.27	0.32	716	180.81	2.18	0.55	2.22	0.56		
10405	1.17	0.28	707	169.54	2.09	0.50	2.20	0.53		
10406	1.22	0.26	784	166.81	2.05	0.44	2.19	0.47		
10409	1.21	0.29	539	130.51	1.84	0.45	2.08	0.50		
10410	1.28	0.25	511	100.39	2.46	0.48	2.06	0.40		
n	7	7	7	7	7	7	7	7		
Mean	1.217	0.279	699.3	161.046	2.124	0.487	2.136	0.490		
S.D.	0.048	0.027	127.5	34.523	0.194	0.048	0.068	0.054		

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

Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 0 mg/kg						Species : Rat	
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen	
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g
50151	324	10.93	3.37	2.28	0.70	1.23	0.38	675	208.33
50152	338	10.58	3.13	2.11	0.62	0.96	0.28	963	284.91
50153	303	9.77	3.22	2.32	0.77	0.98	0.32	635	209.57
50154	315	10.31	3.27	2.19	0.70	1.09	0.35	648	205.71
50155	300	9.57	3.19	1.92	0.64	0.98	0.33	685	228.33
50156	325	11.68	3.59	2.58	0.79	1.01	0.31	665	204.62
50157	346	11.09	3.21	2.48	0.72	1.13	0.33	862	249.13
50158	310	10.18	3.28	2.31	0.75	1.14	0.37	872	281.29
50159	315	9.88	3.14	2.27	0.72	1.00	0.32	690	219.05
50160	342	10.26	3.00	2.20	0.64	1.08	0.32	714	208.77
50161	264	9.44	3.58	2.05	0.78	0.94	0.36	641	242.80
50162	300	9.05	3.02	2.18	0.73	0.94	0.31	661	220.33
n	12	12	12	12	12	12	12	12	12
Mean	315.2	10.228	3.250	2.241	0.713	1.040	0.332	725.9	230.237
S.D.	22.6	0.754	0.188	0.178	0.056	0.093	0.029	109.2	28.545

		Thymus		Adrenal		Pituitary gland		Thyroid		Ovary	
Animal No.	AB mg	AB	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g
50151	271	83.64	83	25.62	19.5	6.02	19.0	5.86	127	39.20	
50152	281	83.14	70	20.71	16.8	4.97	16.7	4.94	120	35.50	
50153	244	80.53	74	24.42	17.0	5.61	20.7	6.83	113	37.29	
50154	300	95.24	84	26.67	19.7	6.25	14.8	4.70	136	43.17	
50155	244	81.33	78	26.00	16.5	5.50	14.4	4.80	92	30.67	
50156	334	102.77	79	24.31	19.9	6.12	14.3	4.40	109	33.54	
50157	283	81.79	91	26.30	17.3	5.00	17.0	4.91	106	30.64	
50158	398	128.39	76	24.52	18.5	5.97	13.6	4.39	121	39.03	
50159	370	117.46	68	21.59	20.1	6.38	13.1	4.16	103	32.70	
50160	235	68.71	85	24.85	15.9	4.65	11.6	3.39	105	30.70	
50161	314	118.94	68	25.76	17.1	6.48	20.3	7.69	101	38.26	
50162	232	77.33	97	32.33	19.0	6.33	14.1	4.70	135	45.00	
n	12	12	12	12	12	12	12	12	12	12	12
Mean	292.2	93.273	79.4	25.257	18.11	5.773	15.80	5.064	114.0	36.308	
S.D.	53.7	19.214	9.0	2.868	1.50	0.620	2.93	1.188	13.9	4.861	

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

Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 0 mg/kg		Species : Rat
Animal No.	Uterus	Brain		
	AB mg	RE mg/100g	AB g	RE g/100g
50151	854	263.58	2.06	0.64
50152	653	193.20	2.05	0.61
50153	667	220.13	2.00	0.66
50154	667	211.75	2.08	0.66
50155	697	232.33	2.03	0.68
50156	844	259.69	2.04	0.63
50157	631	182.37	2.08	0.60
50158	656	211.61	2.00	0.65
50159	646	205.08	2.05	0.65
50160	652	190.64	2.20	0.64
50161	616	233.33	1.93	0.73
50162	719	239.67	2.01	0.67
n	12	12	12	12
Mean	691.8	220.282	2.044	0.652
S.D.	78.3	26.194	0.064	0.034

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

Animal No.	Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 100 mg/kg						Species : Rat	
	Body weight g	Liver	Kidney			Heart		Spleen		
			AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g
50251	302	10.14	3.36	2.24	0.74	1.14	0.38	834	276.16	
50252	303	9.87	3.26	2.41	0.80	1.06	0.35	741	244.55	
50253	291	8.32	2.86	1.92	0.66	0.90	0.31	575	197.59	
50254	298	9.90	3.32	2.01	0.67	0.99	0.33	725	243.29	
50255	341	11.15	3.27	2.15	0.63	1.08	0.32	701	205.57	
50256	285	9.36	3.28	2.31	0.81	0.93	0.33	815	285.96	
50257	303	9.26	3.06	2.20	0.73	0.93	0.31	643	212.21	
50258	305	10.49	3.44	2.43	0.80	1.06	0.35	651	213.44	
50259	321	12.01	3.74	2.21	0.69	1.15	0.36	677	210.90	
50260	331	10.11	3.05	2.33	0.70	0.98	0.30	522	157.70	
50261	333	11.25	3.38	2.51	0.75	1.06	0.32	685	205.71	
50262	288	9.32	3.24	2.06	0.72	0.98	0.34	538	186.81	
n	12	12	12	12	12	12	12	12	12	
Mean	308.4	10.098	3.272	2.232	0.725	1.022	0.333	675.6	219.991	
S.D.	18.6	1.016	0.220	0.178	0.058	0.082	0.023	98.3	36.598	

Animal No.	Thymus		Adrenal		Pituitary gland		Thyroid		Ovary	
	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
50251	370	122.52	83	27.48	21.1	6.99	21.3	7.05	114	37.75
50252	192	63.37	82	27.06	18.0	5.94	13.9	4.59	116	38.28
50253	309	106.19	59	20.27	13.9	4.78	7.6	2.61	87	29.90
50254	254	85.23	62	20.81	15.5	5.20	13.8	4.63	108	36.24
50255	360	105.57	72	21.11	17.6	5.16	14.1	4.13	109	31.96
50256	442	155.09	82	28.77	15.7	5.51	16.8	5.89	85	29.82
50257	289	95.38	68	22.44	19.6	6.47	17.6	5.81	113	37.29
50258	307	100.66	77	25.25	18.1	5.93	14.8	4.85	123	40.33
50259	257	80.06	91	28.35	15.9	4.95	20.9	6.51	119	37.07
50260	225	67.98	68	20.54	14.0	4.23	17.2	5.20	92	27.79
50261	312	93.69	68	20.42	15.8	4.74	17.1	5.14	111	33.33
50262	255	88.54	76	26.39	14.4	5.00	16.2	5.63	94	32.64
n	12	12	12	12	12	12	12	12	12	12
Mean	297.7	97.023	74.0	24.074	16.63	5.408	15.94	5.170	105.9	34.367
S.D.	68.9	24.644	9.5	3.438	2.27	0.792	3.60	1.161	13.0	3.993

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

Animal No.	Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 100 mg/kg		Species : Rat	
	Uterus		Brain			
	AB mg	RE mg/100g	AB g	RE g/100g		
50251	720	238.41	2.07	0.69		
50252	649	214.19	2.05	0.68		
50253	522	179.38	1.95	0.67		
50254	679	227.85	1.93	0.65		
50255	669	196.19	2.12	0.62		
50256	669	234.74	2.09	0.73		
50257	646	213.20	1.97	0.65		
50258	688	225.57	2.03	0.67		
50259	734	228.66	2.06	0.64		
50260	610	184.29	2.10	0.63		
50261	696	209.01	1.99	0.60		
50262	749	260.07	1.97	0.68		
n	12	12	12	12		
Mean	669.3	217.630	2.028	0.659		
S.D.	60.6	23.267	0.064	0.035		

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

Animal No.	Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 300 mg/kg						Species : Rat	
	Body weight g	Liver AB g	Liver		Kidney		Heart		Spleen	
			RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg
50351	329	10.60	3.22	2.12	0.64	0.96	0.29	858	260.79	
50352	315	10.27	3.26	2.54	0.81	1.01	0.32	733	232.70	
50353	321	10.64	3.31	2.61	0.81	1.08	0.34	520	161.99	
50354	311	9.26	2.98	2.31	0.74	0.95	0.31	769	247.27	
50355	303	9.47	3.13	1.98	0.65	0.99	0.33	648	213.86	
50356	273	9.74	3.57	2.25	0.82	0.99	0.36	597	218.68	
50357	330	11.05	3.35	2.61	0.79	1.07	0.32	896	271.52	
50358	321 \$	8.29 \$	2.58 \$	2.49 \$	0.78 \$	1.00 \$	0.31 \$	518 \$	161.37 \$	
50359	283	10.01	3.54	2.29	0.81	0.97	0.34	565	199.65	
50360	348	11.21	3.22	2.63	0.76	1.11	0.32	830	238.51	
50361	309	10.21	3.30	2.29	0.74	1.01	0.33	594	192.23	
50362	295	8.71	2.95	1.87	0.63	1.00	0.34	622	210.85	
n	11	11	11	11	11	11	11	11	11	11
Mean	310.6	10.106	3.257	2.318	0.745	1.013	0.327	693.8	222.550	
S.D.	21.7	0.767	0.195	0.260	0.073	0.052	0.018	129.2	31.887	

Animal No.	Thymus		Adrenal		Pituitary gland		Thyroid		Ovary	
	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
50351	209	63.53	82	24.92	12.8	3.89	12.4	3.77	99	30.09
50352	378	120.00	81	25.71	18.9	6.00	17.4	5.52	114	36.19
50353	257	80.06	88	27.41	19.2	5.98	18.6	5.79	118	36.76
50354	310	99.68	98	31.51	18.8	6.05	16.2	5.21	104	33.44
50355	270	89.11	65	21.45	16.2	5.35	13.9	4.59	83	27.39
50356	194	71.06	82	30.04	15.7	5.75	13.3	4.87	102	37.36
50357	281	85.15	85	25.76	16.8	5.09	16.0	4.85	110	33.33
50358	389 \$	121.18 \$	74 \$	23.05 \$	16.2 \$	5.05 \$	14.0 \$	4.36 \$	127 \$	39.56 \$
50359	203	71.73	89	31.45	15.3	5.41	19.4	6.86	121	42.76
50360	211	60.63	95	27.30	19.9	5.72	14.9	4.28	114	32.76
50361	287	92.88	78	25.24	11.8	3.82	12.2	3.95	100	32.36
50362	313	106.10	72	24.41	18.1	6.14	17.9	6.07	114	38.64
n	11	11	11	11	11	11	11	11	11	11
Mean	264.8	85.448	83.2	26.836	16.68	5.382	15.65	5.069	107.2	34.644
S.D.	57.3	18.472	9.5	3.122	2.65	0.822	2.51	0.940	10.9	4.259

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

Animal No. 50358 : Non-pregnancy

\$ : Excepted data from calculation

Animal No.	Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 300 mg/kg		Species : Rat	
	Uterus		Brain			
	AB mg	RE mg/100g	AB g	RE g/100g		
50351	587	178.42	2.05	0.62		
50352	606	192.38	2.01	0.64		
50353	609	189.72	2.02	0.63		
50354	667	214.47	2.09	0.67		
50355	632	208.58	2.06	0.68		
50356	583	213.55	1.97	0.72		
50357	727	220.30	2.03	0.62		
50358	535 \$	166.67 \$	2.05 \$	0.64 \$		
50359	721	254.77	2.07	0.73		
50360	642	184.48	2.15	0.62		
50361	820	265.37	2.03	0.66		
50362	604	204.75	1.98	0.67		
n	11	11	11	11		
Mean	654.4	211.526	2.042	0.660		
S.D.	73.8	27.537	0.051	0.039		

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

Animal No. 50358 : Non-pregnancy

\$ : Excepted data from calculation

Animal No.	Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 1000 mg/kg						Species : Rat	
	Body weight g	Liver AB g	Liver		Kidney		Heart		Spleen	
			RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg
50451	303	9.26	3.06	2.10	0.69	0.92	0.30	569	187.79	
50452	310	11.01	3.55	2.39	0.77	1.03	0.33	742	239.35	
50453	299	9.55	3.19	2.30	0.77	0.94	0.31	629	210.37	
50454	309	10.48	3.39	2.69	0.87	1.26	0.41	1418	458.90	
50455	339	11.07	3.27	2.66	0.78	1.13	0.33	792	233.63	
50456	336	11.88	3.54	2.87	0.85	1.02	0.30	743	221.13	
50457	316	10.69	3.38	2.41	0.76	1.06	0.34	608	192.41	
50458	276	9.56	3.46	2.13	0.77	1.08	0.39	688	249.28	
50459	332	11.59	3.49	2.76	0.83	1.07	0.32	797	240.06	
50460	305	10.29	3.37	2.83	0.93	0.96	0.31	738	241.97	
50461	312	11.56	3.71	2.19	0.70	1.00	0.32	627	200.96	
50462	342	10.34	3.02	2.27	0.66	1.09	0.32	753	220.18	
n	12	12	12	12	12	12	12	12	12	12
Mean	314.9	10.607	3.369	2.467	0.782	1.047	0.332	758.7	241.336	
S.D.	19.4	0.858	0.205	0.281	0.078	0.093	0.034	220.8	71.458	

Animal No.	Thymus		Adrenal		Pituitary gland		Thyroid		Ovary	
	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
50451	215	70.96	77	25.41	17.4	5.74	14.8	4.88	118	38.94
50452	190	61.29	91	29.35	14.9	4.81	19.3	6.23	96	30.97
50453	233	77.93	80	26.76	17.0	5.69	13.9	4.65	101	33.78
50454	236	76.38	69	22.33	15.4	4.98	20.5	6.63	131	42.39
50455	196	57.82	83	24.48	18.5	5.46	18.3	5.40	125	36.87
50456	220	65.48	75	22.32	19.0	5.65	17.1	5.09	140	41.67
50457	321	101.58	74	23.42	15.7	4.97	22.8	7.22	137	43.35
50458	182	65.94	89	32.25	12.8	4.64	16.8	6.09	121	43.84
50459	216	65.06	92	27.71	24.1	7.26	20.1	6.05	152	45.78
50460	168	55.08	88	28.85	14.2	4.66	16.7	5.48	115	37.70
50461	242	77.56	60	19.23	11.5	3.69	15.3	4.90	96	30.77
50462	301	88.01	69	20.18	17.4	5.09	9.9	2.89	122	35.67
n	12	12	12	12	12	12	12	12	12	12
Mean	226.7	71.924	78.9	25.191	16.49	5.220	17.13	5.459	121.2	38.478
S.D.	45.5	13.304	10.1	3.932	3.28	0.863	3.44	1.122	17.6	5.049

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

Organ weight Sex : Female		Stage : Day 5 after delivery Dose : HBM 1000 mg/kg		Species : Rat
Animal No.	Uterus	Brain		
	AB mg	RE mg/100g	AB g	RE g/100g
50451	717	236.63	2.11	0.70
50452	741	239.03	1.96	0.63
50453	683	228.43	1.97	0.66
50454	845	273.46	2.06	0.67
50455	718	211.80	2.11	0.62
50456	739	219.94	2.06	0.61
50457	804	254.43	2.07	0.66
50458	744	269.57	2.08	0.75
50459	872	262.65	2.19	0.66
50460	687	225.25	2.00	0.66
50461	614	196.79	2.08	0.67
50462	689	201.46	2.03	0.59
n	12	12	12	12
Mean	737.8	234.953	2.060	0.657
S.D.	72.6	25.802	0.064	0.042

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

Organ weight Sex : Female (satellite)		Stage : Day 29 Dose : HBM 0 mg/kg				Species : Rat				
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen		
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
50551	268	7.04	2.63	1.87	0.70	0.90	0.34	560	208.96	
50552	242	6.70	2.77	1.98	0.82	0.86	0.36	424	175.21	
50553	247	7.12	2.88	1.80	0.73	0.93	0.38	475	192.31	
50554	276	7.02	2.54	1.96	0.71	1.00	0.36	458	165.94	
50555	258	7.03	2.72	1.79	0.69	0.85	0.33	442	171.32	
n	5	5	5	5	5	5	5	5	5	
Mean	258.2	6.982	2.708	1.880	0.730	0.908	0.354	471.8	182.748	
S.D.	14.1	0.163	0.130	0.088	0.052	0.061	0.019	52.8	17.667	
Thymus		Adrenal		Pituitary gland		Thyroid		Ovary		
Animal No.	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	
50551	346	129.10	79	29.48	16.2	6.04	12.6	4.70	83	30.97
50552	313	129.34	67	27.69	13.8	5.70	13.8	5.70	103	42.56
50553	301	121.86	74	29.96	13.5	5.47	12.7	5.14	105	42.51
50554	375	135.87	83	30.07	15.2	5.51	17.3	6.27	111	40.22
50555	316	122.48	64	24.81	14.5	5.62	8.8	3.41	101	39.15
n	5	5	5	5	5	5	5	5	5	5
Mean	330.2	127.730	73.4	28.402	14.64	5.668	13.04	5.044	100.6	39.082
S.D.	30.0	5.761	8.0	2.224	1.09	0.227	3.04	1.088	10.5	4.768
Uterus		Brain								
Animal No.	AB mg	RE mg/100g	AB g	RE g/100g						
50551	594	221.64	1.94	0.72						
50552	1041	430.17	1.87	0.77						
50553	867	351.01	1.97	0.80						
50554	427	154.71	2.00	0.72						
50555	582	225.58	1.93	0.75						
n	5	5	5	5						
Mean	702.2	276.622	1.942	0.752						
S.D.	246.9	111.357	0.049	0.034						

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

Organ weight Sex : Female (satellite)		Stage : Day 29 Dose : HBM 1000 mg/kg						Species : Rat		
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen		
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
50651	259	7.42	2.86	2.07	0.80	1.01	0.39	535	206.56	
50652	254	6.88	2.71	1.79	0.70	0.81	0.32	432	170.08	
50653	249	6.91	2.78	1.84	0.74	0.83	0.33	534	214.46	
50654	261	7.10	2.72	1.96	0.75	0.87	0.33	661	253.26	
50655	254	6.20	2.44	1.74	0.69	0.84	0.33	482	189.76	
n	5	5	5	5	5	5	5	5	5	
Mean	255.4	6.902	2.702	1.880	0.736	0.872	0.340	528.8	206.824	
S.D.	4.7	0.447	0.158	0.134	0.044	0.080	0.028	85.3	31.048	
Thymus		Adrenal		Pituitary gland		Thyroid		Ovary		
Animal No.	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	
50651	263	101.54	78	30.12	11.5	4.44	16.0	6.18	89	34.36
50652	334	131.50	74	29.13	13.7	5.39	12.0	4.72	122	48.03
50653	158	63.45	76	30.52	12.7	5.10	7.1	2.85	80	32.13
50654	348	133.33	67	25.67	12.4	4.75	10.2	3.91	109	41.76
50655	478	188.19	73	28.74	11.5	4.53	10.8	4.25	77	30.31
n	5	5	5	5	5	5	5	5	5	5
Mean	316.2	123.602	73.6	28.836	12.36	4.842	11.22	4.382	95.4	37.318
S.D.	117.6	45.917	4.2	1.911	0.92	0.398	3.23	1.218	19.4	7.404
Uterus		Brain								
Animal No.	AB mg	RE mg/100g	AB g	RE g/100g						
50651	579	223.55	2.05	0.79						
50652	449	176.77	1.98	0.78						
50653	1125	451.81	2.02	0.81						
50654	920	352.49	1.95	0.75						
50655	460	181.10	1.93	0.76						
n	5	5	5	5						
Mean	706.6	277.144	1.986	0.778						
S.D.	301.7	120.786	0.049	0.024						

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

Organ weight Sex : Male		Stage : Recovery Day 15 Dose : HBM 0 mg/kg						Species : Rat	
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen	
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g
10103	454	10.15	2.24	3.05	0.67	1.19	0.26	667	146.92
10104	481	11.54	2.40	3.17	0.66	1.45	0.30	720	149.69
10105	465	10.91	2.35	2.95	0.63	1.37	0.29	756	162.58
10109	486	12.07	2.48	3.17	0.65	1.48	0.30	926	190.53
10111	486	11.46	2.36	3.27	0.67	1.27	0.26	736	151.44
n	5	5	5	5	5	5	5	5	5
Mean	474.4	11.226	2.366	3.122	0.656	1.352	0.282	761.0	160.232
S.D.	14.3	0.729	0.087	0.124	0.017	0.122	0.020	98.0	17.952
Thymus		Adrenal		Pituitary gland		Thyroid		Testis	
Animal No.	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB g
10103	343	75.55	46	10.13	12.6	2.78	18.1	3.99	3.60
10104	423	87.94	78	16.22	11.6	2.41	22.0	4.57	3.02
10105	375	80.65	55	11.83	10.6	2.28	21.9	4.71	3.11
10109	287	59.05	55	11.32	10.6	2.18	12.7	2.61	3.58
10111	310	63.79	61	12.55	11.8	2.43	23.3	4.79	3.19
n	5	5	5	5	5	5	5	5	5
Mean	347.6	73.396	59.0	12.410	11.44	2.416	19.60	4.134	3.300
S.D.	53.7	11.905	11.9	2.305	0.85	0.227	4.32	0.908	0.272
Epididymis		Prostate		Seminal vesicle		Brain			
Animal No.	AB g	RE g/100g	AB mg	RE mg/100g	AB g	RE g/100g	AB g	RE g/100g	
10103	1.43	0.31	1084	238.77	2.26	0.50	2.13	0.47	
10104	1.44	0.30	907	188.57	2.20	0.46	2.09	0.43	
10105	1.24	0.27	1050	225.81	2.29	0.49	2.17	0.47	
10109	1.47	0.30	762	156.79	2.34	0.48	2.09	0.43	
10111	1.45	0.30	1040	213.99	2.15	0.44	2.13	0.44	
n	5	5	5	5	5	5	5	5	
Mean	1.406	0.296	968.6	204.786	2.248	0.474	2.122	0.448	
S.D.	0.094	0.015	133.7	32.589	0.075	0.024	0.033	0.020	

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

Organ weight Sex : Male		Stage : Recovery Day 15 Dose : HBM 1000 mg/kg						Species : Rat				
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen				
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g			
10403	475	11.67	2.46	3.06	0.64	1.48	0.31	655	137.89			
10407	458	10.19	2.22	3.12	0.68	1.62	0.35	617	134.72			
10408	471	10.74	2.28	3.26	0.69	1.52	0.32	719	152.65			
10411	467	12.11	2.59	3.08	0.66	1.51	0.32	629	134.69			
10412	483	11.20	2.32	3.14	0.65	1.38	0.29	678	140.37			
n	5	5	5	5	5	5	5	5	5			
Mean	470.8	11.182	2.374	3.132	0.664	1.502	0.318	659.6	140.064			
S.D.	9.3	0.755	0.150	0.078	0.021	0.086	0.022	40.7	7.427			
Thymus												
Animal No.	AB mg		RE mg/100g		AB mg		RE mg/100g		AB g		RE g/100g	
	284	59.79	81	17.05	14.2	2.99	18.0	3.79	3.20	0.67		
10407	315	68.78	50	10.92	9.9	2.16	20.9	4.56	3.37	0.74		
10408	316	67.09	65	13.80	10.7	2.27	15.9	3.38	3.38	0.72		
10411	258	55.25	49	10.49	10.8	2.31	13.6	2.91	3.05	0.65		
10412	311	64.39	80	16.56	11.7	2.42	17.2	3.56	3.25	0.67		
n	5	5	5	5	5	5	5	5	5	5		
Mean	296.8	63.060	65.0	13.764	11.46	2.430	17.12	3.640	3.250	0.690		
S.D.	25.4	5.532	15.5	3.059	1.66	0.327	2.69	0.607	0.136	0.038		
Epididymis												
Animal No.	AB g		RE g/100g		AB mg		RE mg/100g		AB g		RE g/100g	
	1.27	0.27	755	158.95	2.43	0.51	2.29	0.48				
10407	1.23	0.27	810	176.86	1.75	0.38	2.28	0.50				
10408	1.32	0.28	816	173.25	2.40	0.51	2.30	0.49				
10411	1.26	0.27	626	134.05	2.03	0.43	2.30	0.49				
10412	1.45	0.30	1131	234.16	2.40	0.50	2.20	0.46				
n	5	5	5	5	5	5	5	5				
Mean	1.306	0.278	827.6	175.454	2.202	0.466	2.274	0.484				
S.D.	0.087	0.013	186.0	36.878	0.302	0.059	0.042	0.015				

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

Organ weight Sex : Female (satellite)		Stage : Recovery Day 15 Dose : HBM 0 mg/kg						Species : Rat		
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen		
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
50556	283	6.51	2.30	2.14	0.76	0.91	0.32	514	181.63	
50557	254	6.68	2.63	1.84	0.72	0.79	0.31	450	177.17	
50558	280	7.75	2.77	1.98	0.71	0.94	0.34	626	223.57	
50559	266	6.69	2.52	1.90	0.71	0.81	0.30	511	192.11	
50560	284	6.64	2.34	2.08	0.73	0.88	0.31	568	200.00	
n	5	5	5	5	5	5	5	5	5	
Mean	273.4	6.854	2.512	1.988	0.726	0.866	0.316	533.8	194.896	
S.D.	13.0	0.506	0.197	0.124	0.021	0.064	0.015	66.3	18.345	
Thymus		Adrenal		Pituitary gland		Thyroid		Ovary		
Animal No.	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	
50556	328	115.90	82	28.98	14.5	5.12	18.5	6.54	83	29.33
50557	260	102.36	80	31.50	14.8	5.83	11.2	4.41	103	40.55
50558	355	126.79	76	27.14	22.0	7.86	12.7	4.54	83	29.64
50559	284	106.77	87	32.71	14.3	5.38	12.0	4.51	89	33.46
50560	257	90.49	78	27.46	14.5	5.11	19.4	6.83	96	33.80
n	5	5	5	5	5	5	5	5	5	5
Mean	296.8	108.462	80.6	29.558	16.02	5.860	14.76	5.366	90.8	33.356
S.D.	43.2	13.733	4.2	2.464	3.35	1.156	3.87	1.209	8.7	4.527
Uterus		Brain								
Animal No.	AB mg	RE mg/100g	AB g	RE g/100g						
50556	794	280.57	2.02	0.71						
50557	560	220.47	1.98	0.78						
50558	748	267.14	2.03	0.73						
50559	896	336.84	2.00	0.75						
50560	1036	364.79	2.08	0.73						
n	5	5	5	5						
Mean	806.8	293.962	2.022	0.740						
S.D.	176.8	57.348	0.038	0.026						

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

Organ weight Sex : Female (satellite)		Stage : Recovery Day 15 Dose : HBM 1000 mg/kg						Species : Rat		
Animal No.	Body weight g	Liver		Kidney		Heart		Spleen		
		AB g	RE g/100g	AB g	RE g/100g	AB g	RE g/100g	AB mg	RE mg/100g	
50656	257	7.39	2.88	2.01	0.78	0.96	0.37	508	197.67	
50657	297	7.50	2.53	2.05	0.69	1.00	0.34	500	168.35	
50658	313	8.57	2.74	2.26	0.72	1.07	0.34	748	238.98	
50659	263	6.83	2.60	1.75	0.67	0.85	0.32	487	185.17	
50660	259	6.66	2.57	1.67	0.64	0.75	0.29	533	205.79	
n	5	5	5	5	5	5	5	5	5	
Mean	277.8	7.390	2.664	1.948	0.700	0.926	0.332	555.2	199.192	
S.D.	25.6	0.750	0.144	0.239	0.053	0.127	0.029	109.1	26.348	
Thymus		Adrenal		Pituitary gland		Thyroid		Ovary		
Animal No.	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	RE mg/100g	AB mg	
50656	247	96.11	87	33.85	15.8	6.15	17.6	6.85	73	28.40
50657	357	120.20	65	21.89	16.3	5.49	20.6	6.94	90	30.30
50658	536	171.25	91	29.07	15.7	5.02	14.6	4.66	119	38.02
50659	360	136.88	71	27.00	16.6	6.31	12.4	4.71	63	23.95
50660	435	167.95	57	22.01	13.2	5.10	17.5	6.76	64	24.71
n	5	5	5	5	5	5	5	5	5	5
Mean	387.0	138.478	74.2	26.764	15.52	5.614	16.54	5.984	81.8	29.076
S.D.	106.9	31.915	14.5	5.048	1.35	0.592	3.14	1.188	23.4	5.641
Uterus		Brain								
Animal No.	AB mg	RE mg/100g	AB g	RE g/100g						
50656	732	284.82	2.07	0.81						
50657	708	238.38	1.97	0.66						
50658	476	152.08	2.01	0.64						
50659	565	214.83	1.94	0.74						
50660	1190	459.46	2.01	0.78						
n	5	5	5	5						
Mean	734.2	269.914	2.000	0.726						
S.D.	275.6	116.258	0.049	0.074						

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

Histopathological findings			Stage : Day 29	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10101		
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, 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, Mammary gland			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10102		
Lung				
Findings : Finding present				
Mineralization, artery, focal				
slight				
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, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10106		
Prostate				
Findings : Finding present				
Inflammation, interstitium				
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, Mammary gland			
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10107		
Prostate				
Findings : Finding present				
Inflammation, interstitium				
Slight				
Thyroid				
Findings : Finding present				
Animal Comment: right thyroid				
Remnant, ultimobranchial body				
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, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland			

Histopathological findings		Sex : Male	Stage : Day 29	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10108		
Lung				
Findings : Finding present				
Accumulation, macrophage, alveolar				
Slight				
Kidney				
Findings : Finding present				
Animal Comment: right kidney				
Basophilic change, renal tubule				
Slight				
Pituitary gland				
Findings : Finding present				
Cyst, pars distalis				
Slight				
Thyroid				
Findings : Finding present				
Animal Comment: right thyroid				
Remnant, ultimobranchial body				
Slight				
Finding absent :	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, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland			

Test article : HBM	Dose : 0 mg/kg	Animal No. : 10110
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, 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, Mammary gland	

Test article : HBM	Dose : 0 mg/kg	Animal No. : 10112
Prostate		
Findings : Finding present		
Inflammation, interstitium		
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, Mammary gland	

Histopathological findings			Species : Rat
Sex : Male		Stage : Day 29	
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10201	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10202	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10203	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10204	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10205	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10206	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10207	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10208	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10209	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10210	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10211	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 100 mg/kg	Animal No. : 10212	
Finding absent :	Urinary bladder		

Histopathological findings			
Sex : Male		Stage : Day 29	
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10301	Species : Rat
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10302	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10303	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10304	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10305	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10306	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10307	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10308	Infertility
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10309	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10310	
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10311	
Epididymis			
Findings : Finding present			
Animal Comment: right epididymis			
Granuloma, spermatic			
Slight			
Finding absent :	Urinary bladder		
Test article : HBM	Dose : 300 mg/kg	Animal No. : 10312	
Finding absent :	Urinary bladder		

Histopathological findings			Stage : Day 29	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10401		
Lung				
Findings : Finding present				
Accumulation, macrophage, alveolar				
Slight				
Heart				
Findings : Finding present				
Inflammation, focal				
Slight				
Urinary bladder				
Findings : Finding present				
Hyperplasia, urothelium				
Slight				
Prostate				
Findings : Finding present				
Inflammation, interstitium				
Slight				
Eyeball				
Findings : Finding present				
Animal Comment: left eyeball				
Dysplasia, retina, focal				
Slight				
Finding absent :	Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Kidney, 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, Harderian gland, Skeletal muscle, Femur, Mammary gland			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10402		
Pancreas				
Findings : Finding present				
Atrophy, acinar cell, focal				
Slight				
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, 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, Mammary gland			

Histopathological findings					
Test article : HBM	Sex : Male	Dose : 1000 mg/kg	Animal No. : 10404	Stage : Day 29	Species : Rat
<b>Urinary bladder</b>					
Findings : Finding present					
Hyperplasia, urothelium					
Slight					
<b>Prostate</b>					
Findings : Finding present					
Inflammation, interstitium					
Slight					
<b>Finding absent :</b>					
Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver,					
Heart, Kidney, 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, Mammary gland					
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10405			
<b>Lung</b>					
Findings : Finding present					
Accumulation, macrophage, alveolar					
Slight					
<b>Urinary bladder</b>					
Findings : Finding present					
Hyperplasia, urothelium					
Slight					
<b>Parathyroid</b>					
Findings : Finding absent					
Animal Comment : right parathyroid : missing					
<b>Finding absent :</b>					
Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver,					
Heart, Kidney, 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, Mammary gland					

Histopathological findings			Stage : Day 29	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10406		
Heart				
Findings : Finding present				
Inflammation, focal				
Slight				
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, 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, Mammary gland			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10409		
Liver				
Findings : Finding present				
Microgranuloma				
Slight				
Pituitary gland				
Findings : Finding present				
Craniopharyngeal duct, remnant				
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, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10410		
Prostate				
Findings : Finding present				
Inflammation, interstitium				
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, Mammary gland			

Histopathological findings			Stage : Day 5 after delivery	Species : Rat
	Sex : Female			
Test article : HBM	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 : HBM	Dose : 0 mg/kg	Animal No. : 50152		
Thyroid	Findings : Finding present			
	Animal Comment: right thyroid			
	Remnant, 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 : HBM	Dose : 0 mg/kg	Animal No. : 50153		
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 : HBM	Dose : 0 mg/kg	Animal No. : 50154		
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 : HBM	Dose : 0 mg/kg	Animal No. : 50155		
Lung	Findings : Finding present			
	Accumulation, macrophage, alveolar			
	Slight			
Heart	Findings : Finding present			
	Inflammation, focal			
	Slight			
Finding absent :	Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, 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 : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50156		
Thyroid				
Findings : Finding present				
Animal Comment: right thyroid				
Remnant, 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 : HBM	Dose : 0 mg/kg	Animal No. : 50157		
Lung				
Findings : Finding present				
Accumulation, macrophage, alveolar				
Slight				
Kidney				
Findings : Finding present				
Animal Comment: right kidney				
Basophilic change, renal tubule				
Slight				
Infiltration, inflammatory cell				
Slight				
Thymus				
Findings : Finding present				
Hyperplasia, epithelial cell				
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, 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 : HBM	Dose : 0 mg/kg	Animal No. : 50158		
Pancreas				
Findings : Finding present				
Atrophy, acinar cell, focal				
Slight				
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, 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 : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50159		
Lung				
Finding absent :	Findings : Finding present Accumulation, macrophage, alveolar Slight			
	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 : HBM	Dose : 0 mg/kg	Animal No. : 50160		
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 : HBM	Dose : 0 mg/kg	Animal No. : 50161		
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 : HBM	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			Stage : Day 5 after delivery	Species : Rat
Sex : Female				
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50251		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50252		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50253		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50254		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50255		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50256		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50257		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50258		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50259		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50260		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50261		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 100 mg/kg	Animal No. : 50262		
Finding absent :	Stomach, Urinary bladder			

Histopathological findings			Stage : Day 5 after delivery	Species : Rat
Sex : Female				
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50351		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50352		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50353		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50354		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50355		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50356		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50357		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50358	Non-pregnancy	
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50359		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50360		
Finding absent :	Stomach, Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50361		
Stomach				
Findings : Finding present				
Erosion, glandular stomach, focal				
Slight				
Finding absent :	Urinary bladder			
Test article : HBM	Dose : 300 mg/kg	Animal No. : 50362		
Finding absent :	Stomach, Urinary bladder			

Histopathological findings		Stage : Day 5 after delivery	Species : Rat
Sex : Female			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50451	
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 : HBM	Dose : 1000 mg/kg	Animal No. : 50452	
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Atrophy, aHeart, 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 : HBM	Dose : 1000 mg/kg	Animal No. : 50453	
Kidney			
Findings : Finding present			
Animal Comment: right kidney			
Mineralization			
Slight			
Urinary bladder			
Findings : Finding present			
Infiltration, inflammatory cell			
Slight			
Edema, lamina propria			
Slight			
Hyperplasia, urothelium			
Slight			
Peyer's patch			
Findings : Finding present			
Mineralization			
Slight			
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Pituitary gland, Thyroid, Parathyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland		

Histopathological findings		Stage : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50454	
Urinary bladder			
Findings : Finding present			
Infiltration, inflammatory cell			
Slight			
Edema, lamina propria			
Slight			
Hyperplasia, urothelium			
Slight			
Spleen			
Findings : Finding present			
Extramedullary hematopoiesis			
Slight			
Pituitary gland			
Findings : Finding present			
Cyst, pars distalis			
Slight			
Parathyroid			
Findings : Finding absent			
Animal Comment : left parathyroid : missing			
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebrum, Cerebellum, Pons, Spinal cord, Sciatic nerve, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Thyroid, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland		

Histopathological findings		Stage : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50455	
Urinary bladder			
Findings : Finding present			
Infiltration, inflammatory cell			
Slight			
Hyperplasia, urothelium			
Slight			
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, 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 : HBM	Dose : 1000 mg/kg	Animal No. : 50456	
Heart			
Findings : Finding present			
Inflammation, focal			
Slight			
Eyeball			
Findings : Finding present			
Animal Comment: left eyeball			
Dysplasia, retina, focal			
Slight			
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, 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, Harderian gland, Skeletal muscle, Femur, Mammary gland		

Histopathological findings			Stage : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50457		
Cerebrum				
Findings : Finding present				
Mineralization				
Slight				
Thyroid				
Findings : Finding present				
Animal Comment: right and left thyroid				
Remnant, ultimobranchial body				
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, Liver, Heart, Kidney, Urinary bladder, Ovary, Uterine horn, Uterine cervix, Vagina, Cerebellum, Pons, Spinal cord, Sciatic nerve, Spleen, Thymus, Bone marrow, femur, Submandibular lymph node, Mesenteric lymph node, Peyer's patch, Pituitary gland, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland			

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Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50458
Stomach		
Findings : Finding present		
Erosion, glandular stomach, focal		
Slight		
Thyroid		
Findings : Finding present		
Animal Comment: right thyroid		
Remnant, 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	

Histopathological findings		Sex : Female	Stage : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50459		
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 : HBM	Dose : 1000 mg/kg	Animal No. : 50460		
Lung				
Findings : Finding present				
Accumulation, macrophage, alveolar				
Slight				
Heart				
Findings : Finding present				
Inflammation, focal				
Slight				
Urinary bladder				
Findings : Finding present				
Infiltration, inflammatory cell				
Slight				
Hyperplasia, urothelium				
Slight				
Thyroid				
Findings : Finding present				
Animal Comment: right and left thyroid				
Remnant, ultimobranchial body				
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, Kidney, 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, Adrenal, Eyeball, Harderian gland, Skeletal muscle, Femur, Mammary gland			

Histopathological findings		Sex : Female	Stage : Day 5 after delivery	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50461		
Lung				
Findings : Finding present				
Accumulation, macrophage, alveolar				
Slight				
Urinary bladder				
Findings : Finding present				
Infiltration, inflammatory cell				
Slight				
Edema, lamina propria				
Slight				
Hyperplasia, urothelium				
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, 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 : HBM	Dose : 1000 mg/kg	Animal No. : 50462		
Stomach				
Findings : Finding present				
Erosion, glandular stomach, focal				
Slight				
Urinary bladder				
Findings : Finding present				
Infiltration, inflammatory cell				
Slight				
Edema, lamina propria				
Slight				
Hyperplasia, urothelium				
Slight				
Finding absent :	Lung, Trachea, Submandibular gland, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Pancreas, Liver, Heart, Kidney, 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 (satellite)			Stage : Day 29	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 50551		
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 : HBM	Dose : 0 mg/kg	Animal No. : 50552		
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 : HBM	Dose : 0 mg/kg	Animal No. : 50553		
Thyroid				
Findings : Finding present				
Animal Comment: right thyroid				
Remnant, 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 : HBM	Dose : 0 mg/kg	Animal No. : 50554		
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 : HBM	Dose : 0 mg/kg	Animal No. : 50555		
Thyroid				
Findings : Finding present				
Animal Comment: right thyroid				
Remnant, 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			Stage : Day 29	Species : Rat
Sex : Female (satellite)				
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50651		
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 : HBM	Dose : 1000 mg/kg	Animal No. : 50652		
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 : HBM	Dose : 1000 mg/kg	Animal No. : 50653		
Lung	Findings : Finding present Accumulation, macrophage, alveolar Slight			
Liver	Findings : Finding present Microgranuloma Slight			
Finding absent :	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			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 50654		
Thyroid	Findings : Finding present Animal Comment: left thyroid Remnant, 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 : HBM	Dose : 1000 mg/kg	Animal No. : 50655		
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 : Male		
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10103
Finding absent :	Urinary bladder	Stage : Recovery Day 15
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10104
Finding absent :	Urinary bladder	Species : Rat
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10105
Finding absent :	Urinary bladder	
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10109
Finding absent :	Urinary bladder	
Test article : HBM	Dose : 0 mg/kg	Animal No. : 10111
Finding absent :	Urinary bladder	

Histopathological findings				
Sex : Male			Stage : Recovery Day 15	Species : Rat
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10403		
Finding absent :	Urinary bladder			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10407		
Finding absent :	Urinary bladder			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10408		
Finding absent :	Urinary bladder			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10411		
Finding absent :	Urinary bladder			
Test article : HBM	Dose : 1000 mg/kg	Animal No. : 10412		
Finding absent :	Urinary bladder			

Animal No.	Estrous cycles and copulation Generation : F0 /Before mating (day)														Dose : HBM 0 mg/kg			Species : Rat		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Length of estrous cycle (days)	Mean	Number of estrus	Animal with acyclic or irregular cycle		
	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4	4.0	3	-	
50151																				
50152	D	D	P	E	M	D	P	E	M	D	D	D	D	P	4	4	4.0	2	-	
50153	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4	4.0	3	-	
50154	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4	4.0	3	-	
50155	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4	4.0	3	-	
50156	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4	4.0	3	-	
50157	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4	4.0	3	-	
50158	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4.0	4	-	
50159	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4	4.0	3	-	
50160	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4	4.0	3	-	
50161	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4	4.0	3	-	
50162	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 Generation : F0 /Before mating (day)														Dose : HBM 100 mg/kg			Species : Rat		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Length of estrous cycle (days)			Mean	Number of estrus	Animal with acyclic or irregular cycle
	E	M	D	P	E	M	D	P	E	M	D	P	E	M	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	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50254	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4		4.0	3	-
50255	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50256	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50257	E	M	D	P	E	M	D	P	E	M	D	P	E	M	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	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50260	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4		4.0	3	-
50261	P	E	M	D	P	E	M	D	P	E	M	D	D	E	4	4	4	4.0	4	-
50262	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 Generation : F0 /Before mating (day)														Dose : HBM 300 mg/kg			Species : Rat		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Length of estrous cycle (days)		Mean	Number of estrus	Animal with acyclic or irregular cycle	
	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4				
50351																	4.0	3	-	
50352	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4	4.0	4	-
50353	D	P	E	M	D	P	E	M	D	P	E	M	D	P	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	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4		4.0	3	-
50358	P	E	M	D	P	P	E	M	D	P	E	M	D	D	5	4		4.5	3	-
50359	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4	4.0	4	-
50360	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50361	D	P	E	M	D	P	E	M	D	P	E	M	D	P	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 Generation : F0 /Before mating (day)														Dose : HBM 1000 mg/kg			Species : Rat		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Length of estrous cycle (days)		Mean	Number of estrus	Animal with acyclic or irregular cycle	
	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4				
50451																	4.0	3	-	
50452	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4	4.0	4	-
50453	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50454	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4		4.0	3	-
50455	D	P	E	E	M	D	P	E	E	M	D	P	E	E	5	5		5.0	3	-
50456	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4	4.0	4	-
50457	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4	4.0	4	-
50458	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4		4.0	3	-
50459	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4	4	4.0	4	-
50460	E	M	D	D	P	E	M	D	P	E	M	D	D	P	5	4		4.5	3	-
50461	D	P	E	M	D	P	E	M	D	P	E	M	D	P	4	4		4.0	3	-
50462	M	D	D	P	E	M	D	D	P	E	M	D	D	P	5			5.0	2	-

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														Species : Rat	
	Generation : F0							Dose : HBM 0 mg/kg								
	/1st mating (times)															
1	2	3	4	5	6	7	8	9	10	11	12	13	14			
50151	P	E														
	N	Y														
50152	E															
	Y															
50153	P	E														
	N	Y														
50154	P	E														
	N	Y														
50155	E															
	Y															
50156	P	E														
	N	Y														
50157	E															
	Y															
50158	D	P	E													
	N	N	Y													
50159	P	E														
	N	Y														
50160	E															
	Y															
50161	P	E														
	N	Y														
50162	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 : HBM 100 mg/kg									
	/1st mating (times)																
Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14			
50251	D	P	E														
	N	N	Y														
50252	M	D	P	E													
	N	N	N	Y													
50253	E																
	Y																
50254	P	E															
	N	Y															
50255	E																
	Y																
50256	E																
	Y																
50257	D	P	E														
	N	N	Y														
50258	E																
	Y																
50259	E																
	Y																
50260	P	E															
	N	Y															
50261	M	D	P	E													
	N	N	N	Y													
50262	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 : HBM 300 mg/kg									
	/1st mating (times)																
Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14			
50351	E																
	Y																
50352	D	P	E														
	N	N	Y														
50353	E																
	Y																
50354	E																
	Y																
50355	E																
	Y																
50356	P	E															
	N	Y															
50357	P	E															
	N	Y															
50358	P	E															
	N	Y															
50359	D	P	E														
	N	N	Y														
50360	E																
	Y																
50361	E																
	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 : HBM 1000 mg/kg									
	/1st mating (times)																
1	2	3	4	5	6	7	8	9	10	11	12	13	14				
50451	P	E															
	N	Y															
50452	D	P	E														
	N	N	Y														
50453	E																
	Y																
50454	P	E															
	N	Y															
50455	M	D	P	P	E												
	N	N	N	N	Y												
50456	D	P	E														
	N	N	Y														
50457	D	P	E														
	N	N	Y														
50458	P	E															
	N	Y															
50459	D	P	E														
	N	N	Y														
50460	E																
	Y																
50461	E																
	Y																
50462	E																
	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 : HBM 0 mg/kg			Species : Rat	
		Generation : F0	Sex : Male	1st mating		2nd mating		Copulation	Fertility
				Paired animal	Copulation	Fertility	Paired animal		
10101	2	50151		+	+	///	///	///	+
10102	1	50152		+	+	///	///	///	+
10103	2	50153		+	+	///	///	///	+
10104	2	50154		+	+	///	///	///	+
10105	1	50155		+	+	///	///	///	+
10106	2	50156		+	+	///	///	///	+
10107	1	50157		+	+	///	///	///	+
10108	3	50158		+	+	///	///	///	+
10109	2	50159		+	+	///	///	///	+
10110	1	50160		+	+	///	///	///	+
10111	2	50161		+	+	///	///	///	+
10112	1	50162		+	+	///	///	///	+
n	12			12	12		0	0	12
Mean	1.7								
S.D.	0.7								
No. of positives				12	12				12
%				100.0	100.0				100.0

/// : No need to input/measure

Animal No.	Day of conceiving	Reproductive performance			Dose : HBM 100 mg/kg			Species : Rat		
		Generation : F0		Sex : Male	1st mating		2nd mating		Total	
		Paired animal	Copulation	Fertility	Paired animal	Copulation	Fertility	Copulation	Fertility	
10201	3	50251	+	+	///	///	///	+	+	
10202	4	50252	+	+	///	///	///	+	+	
10203	1	50253	+	+	///	///	///	+	+	
10204	2	50254	+	+	///	///	///	+	+	
10205	1	50255	+	+	///	///	///	+	+	
10206	1	50256	+	+	///	///	///	+	+	
10207	3	50257	+	+	///	///	///	+	+	
10208	1	50258	+	+	///	///	///	+	+	
10209	1	50259	+	+	///	///	///	+	+	
10210	2	50260	+	+	///	///	///	+	+	
10211	4	50261	+	+	///	///	///	+	+	
10212	1	50262	+	+	///	///	///	+	+	
n	12		12	12		0	0	12	12	
Mean	2.0									
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 : HBM 300 mg/kg			Species : Rat		
		Generation : F0		Sex : Male	1st mating		2nd mating		Total	
		Paired animal	Copulation	Fertility	Paired animal	Copulation	Fertility	Copulation	Fertility	
10301	1	50351	+	+	///	///	///	+	+	
10302	3	50352	+	+	///	///	///	+	+	
10303	1	50353	+	+	///	///	///	+	+	
10304	1	50354	+	+	///	///	///	+	+	
10305	1	50355	+	+	///	///	///	+	+	
10306	2	50356	+	+	///	///	///	+	+	
10307	2	50357	+	+	///	///	///	+	+	
10308	2	50358	+	-	///	///	///	+	-	
10309	3	50359	+	+	///	///	///	+	+	
10310	1	50360	+	+	///	///	///	+	+	
10311	1	50361	+	+	///	///	///	+	+	
10312	1	50362	+	+	///	///	///	+	+	
n	12		12	12		0	0	12	12	
Mean	1.6									
S.D.	0.8									
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 : HBM 1000 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	3	50452	+	+	///	///	///	+	+	
10403	1	50453	+	+	///	///	///	+	+	
10404	2	50454	+	+	///	///	///	+	+	
10405	5	50455	+	+	///	///	///	+	+	
10406	3	50456	+	+	///	///	///	+	+	
10407	3	50457	+	+	///	///	///	+	+	
10408	2	50458	+	+	///	///	///	+	+	
10409	3	50459	+	+	///	///	///	+	+	
10410	1	50460	+	+	///	///	///	+	+	
10411	1	50461	+	+	///	///	///	+	+	
10412	1	50462	+	+	///	///	///	+	+	
n	12		12	12		0	0	12	12	
Mean	2.3									
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 : HBM 0 mg/kg			Species : Rat			
		Generation : F0	Sex : Female	1st mating			2nd mating			Total	
				Paired animal	Copulation	Fertility	Paired animal	Copulation	Fertility	Copulation	Fertility
50151	2	10101		+	+		///	///	///	+	+
50152	1	10102		+	+		///	///	///	+	+
50153	2	10103		+	+		///	///	///	+	+
50154	2	10104		+	+		///	///	///	+	+
50155	1	10105		+	+		///	///	///	+	+
50156	2	10106		+	+		///	///	///	+	+
50157	1	10107		+	+		///	///	///	+	+
50158	3	10108		+	+		///	///	///	+	+
50159	2	10109		+	+		///	///	///	+	+
50160	1	10110		+	+		///	///	///	+	+
50161	2	10111		+	+		///	///	///	+	+
50162	1	10112		+	+		///	///	///	+	+
n	12			12	12			0	0	12	12
Mean	1.7										
S.D.	0.7										
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 : HBM 100 mg/kg			Species : Rat		
		Generation : F0 Sex : Female			1st mating			2nd mating		
		Paired animal	Copulation	Fertility	Paired animal	Copulation	Fertility	Copulation	Fertility	
50251	3	10201	+	+	///	///	///	+	+	
50252	4	10202	+	+	///	///	///	+	+	
50253	1	10203	+	+	///	///	///	+	+	
50254	2	10204	+	+	///	///	///	+	+	
50255	1	10205	+	+	///	///	///	+	+	
50256	1	10206	+	+	///	///	///	+	+	
50257	3	10207	+	+	///	///	///	+	+	
50258	1	10208	+	+	///	///	///	+	+	
50259	1	10209	+	+	///	///	///	+	+	
50260	2	10210	+	+	///	///	///	+	+	
50261	4	10211	+	+	///	///	///	+	+	
50262	1	10212	+	+	///	///	///	+	+	
n	12		12	12		0	0	12	12	
Mean	2.0									
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 : HBM 300 mg/kg			Species : Rat		
		Generation : F0 Sex : Female			1st mating			2nd mating		
		Paired animal	Copulation	Fertility	Paired animal	Copulation	Fertility	Copulation	Fertility	
50351	1	10301	+	+	///	///	///	+	+	
50352	3	10302	+	+	///	///	///	+	+	
50353	1	10303	+	+	///	///	///	+	+	
50354	1	10304	+	+	///	///	///	+	+	
50355	1	10305	+	+	///	///	///	+	+	
50356	2	10306	+	+	///	///	///	+	+	
50357	2	10307	+	+	///	///	///	+	+	
50358	2	10308	+	-	///	///	///	+	-	
50359	3	10309	+	+	///	///	///	+	+	
50360	1	10310	+	+	///	///	///	+	+	
50361	1	10311	+	+	///	///	///	+	+	
50362	1	10312	+	+	///	///	///	+	+	
n	12		12	12		0	0	12	12	
Mean	1.6									
S.D.	0.8									
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 : HBM 1000 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	3	10402	+	+	///	///	///	+	+	
50453	1	10403	+	+	///	///	///	+	+	
50454	2	10404	+	+	///	///	///	+	+	
50455	5	10405	+	+	///	///	///	+	+	
50456	3	10406	+	+	///	///	///	+	+	
50457	3	10407	+	+	///	///	///	+	+	
50458	2	10408	+	+	///	///	///	+	+	
50459	3	10409	+	+	///	///	///	+	+	
50460	1	10410	+	+	///	///	///	+	+	
50461	1	10411	+	+	///	///	///	+	+	
50462	1	10412	+	+	///	///	///	+	+	
n	12		12	12		0	0	12	12	
Mean	2.3									
S.D.	1.2									
No. of positives			12	12				12	12	
%			100.0	100.0				100.0	100.0	

/// : No need to input/measure

Dam No.	Gestation period (day)	Delivery data				Dose : HBM 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	17(8/9)	94.1	16	11	5	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50152	22	16(8/8)	75.0	12	5	7	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50153	22	13(7/6)	84.6	11	6	5	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50154	22	16(9/7)	93.8	15	2	13	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50155	22	13(7/6)	100.0	13	10	3	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50156	22	17(10/7)	100.0	17	11	6	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50157	22	17(10/7)	94.1	16	14	2	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50158	22	18(9/9)	88.9	16	7	9	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50159	22	13(7/6)	100.0	13	7	6	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50160	22	14(11/3)	92.9	13	7	6	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50161	22	15(9/6)	93.3	14	10	4	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50162	22	16(11/5)	100.0	16	12	4	16	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
Mean		22.00	15.4	93.06	14.3	8.5	5.8	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
S.D.		0.00	1.8	7.45	1.9	3.4	2.9	1.9	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 Generation : F0				Dose : HBM 100 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	18(12/6)	94.4	18	8	9	17	0	0	0	0	0	0	0	1	1	0	0	1	1	0	0	
50252	22	14(6/8)	100.0	14	9	5	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50253	22	13(9/4)	100.0	13	8	5	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50254	22	15(8/7)	93.3	14	7	7	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50255	22	14(3/11)	92.9	13	4	9	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50256	23	7(1/6)	100.0	7	0	7	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50257	23	15(11/4)	100.0	15	8	7	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50258	23	15(11/4)	100.0	15	11	4	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50259	22	19(11/8)	89.5	17	10	7	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50260	22	13(7/6)	92.3	12	5	7	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50261	22	19(7/12)	84.2	16	6	10	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
50262	22	15(7/8)	100.0	15	10	5	15	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	
Mean		22.25	14.8	95.55	14.1	7.2	6.8	14.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.1	0.0	0.0	0.1	
S.D.		0.45	3.2	5.29	2.8	3.1	1.9	2.7	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.3	0.0	0.0	0.3	0.0	0.0	0.3	

( / ) : Number of implantation Right/Left, M : Male, F : Female, U : Unable to be sexed

Dam No.	Gestation period (day)	Delivery data				Dose : HBM 300 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)	71.4	10	5	5	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50352	22	15(5/10)	86.7	13	3	10	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50353	23	14(8/6)	78.6	11	5	6	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50354	22	15(7/8)	100.0	15	8	7	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50355	22	14(7/7)	92.9	13	5	8	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50356	22	16(5/11)	93.8	15	7	8	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50357	22	16(8/8)	81.3	13	8	5	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50359	22	14(5/9)	92.9	13	6	7	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50360	23	16(10/6)	87.5	14	5	9	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50361	22	17(8/9)	100.0	17	11	6	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50362	22	14(7/7)	71.4	10	6	4	10	0	0	0	0	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	11	11	11	11
Mean		22.18	15.0	86.95	13.1	6.3	6.8	13.1	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.		0.40	1.1	10.22	2.2	2.1	1.8	2.2	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 Generation : F0				Dose : HBM 1000 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
50451	22	13(8/5)	92.3	12	9	3	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50452	23	16(8/8)	87.5	14	8	6	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50453	22	17(11/6)	94.1	16	7	9	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50454	22	18(6/12)	72.2	13	6	7	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50455	23	17(8/9)	94.1	16	8	8	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50456	22	15(11/4)	86.7	13	5	8	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50457	22	15(7/8)	100.0	15	8	7	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50458	22	16(9/7)	87.5	15	7	7	14	0	1	0	1	0	0	0	0	0	0	0	0	1	0	1	1
50459	22	19(10/9)	94.7	18	12	6	18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50460	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
50461	22	18(13/5)	94.4	17	9	8	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
50462	22	16(9/7)	93.8	15	9	6	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		22.17	16.3	90.93	14.9	7.8	7.0	14.8	0.0	0.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1
S.D.		0.39	1.6	7.00	1.7	1.9	1.7	1.7	0.0	0.3	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.3

( / ) : Number of implantation Right/Left, M : Male, F : Female, U : Unable to be sexed

Delivery data			
Generation : F0		Dose : HBM 0 mg/kg	Species : Rat
Dam No.	Number of corpora lutea	Implantation index (%)	
50151	17(8/9)	100.0	
50152	17(9/8)	94.1	
50153	13(7/6)	100.0	
50154	16(9/7)	100.0	
50155	15(8/7)	86.7	
50156	17(10/7)	100.0	
50157	17(10/7)	100.0	
50158	18(9/9)	100.0	
50159	14(8/6)	92.9	
50160	15(11/4)	93.3	
50161	16(9/7)	93.8	
50162	16(11/5)	100.0	
n	12	12	
Mean	15.9	96.73	
S.D.	1.4	4.45	

( / ) : Right/Left

Delivery data			
Generation : F0		Dose : HBM 100 mg/kg	Species : Rat
Dam No.	Number of corpora lutea	Implantation index (%)	
50251	18(12/6)	100.0	
50252	16(7/9)	87.5	
50253	14(9/5)	92.9	
50254	15(8/7)	100.0	
50255	14(3/11)	100.0	
50256	8(2/6)	87.5	
50257	18(11/7)	83.3	
50258	16(11/5)	93.8	
50259	19(11/8)	100.0	
50260	13(7/6)	100.0	
50261	20(7/13)	95.0	
50262	16(8/8)	93.8	
n	12	12	
Mean	15.6	94.48	
S.D.	3.2	5.87	

( / ) : Right/Left

Delivery data		Dose : HBM 300 mg/kg	Species : Rat
Generation : F0	Number of corpora lutea	Implantation index (%)	
Dam No.			
50351	15(10/5)	93.3	
50352	15(5/10)	100.0	
50353	14(8/6)	100.0	
50354	16(7/9)	93.8	
50355	14(7/7)	100.0	
50356	16(5/11)	100.0	
50357	17(9/8)	94.1	
50359	14(5/9)	100.0	
50360	16(10/6)	100.0	
50361	17(8/9)	100.0	
50362	14(7/7)	100.0	
n	11	11	
Mean	15.3	98.29	
S.D.	1.2	2.93	

( / ) : Right/Left

Delivery data			
Generation : F0		Dose : HBM 1000 mg/kg	Species : Rat
Dam No.	Number of corpora lutea	Implantation index (%)	
50451	13(8/5)	100.0	
50452	16(8/8)	100.0	
50453	17(11/6)	100.0	
50454	18(6/12)	100.0	
50455	17(8/9)	100.0	
50456	15(11/4)	100.0	
50457	15(7/8)	100.0	
50458	16(9/7)	100.0	
50459	19(10/9)	100.0	
50460	17(12/5)	94.1	
50461	18(13/5)	100.0	
50462	16(9/7)	100.0	
n	12	12	
Mean	16.4	99.51	
S.D.	1.6	1.70	

( / ) : Right/Left

Delivery data (External examination of offspring)		Unit : Number of anomalous offspring (incidence %)	Day after birth : 0
Generation : F0		Dose : HBM 0 mg/kg	Species : Rat
Dam No.	Number of offspring examined	/Findings	
50151	16	No anomaly	
50152	12	No anomaly	
50153	11	No anomaly	
50154	15	No anomaly	
50155	13	No anomaly	
50156	17	No anomaly	
50157	16	No anomaly	
50158	16	No anomaly	
50159	13	No anomaly	
50160	13	No anomaly	
50161	14	No anomaly	
50162	16	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 : HBM 100 mg/kg	Species : Rat
Dam No.	Number of offspring examined	/Findings		
50251	17	No anomaly		
50252	14	No anomaly		
50253	13	No anomaly		
50254	14	No anomaly		
50255	13	No anomaly		
50256	7	No anomaly		
50257	15	No anomaly		
50258	15	No anomaly		
50259	17	No anomaly		
50260	12	No anomaly		
50261	16	No anomaly		
50262	15	No anomaly		
Total	168			
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 : HBM 300 mg/kg	Species : Rat
Dam No.	Number of offspring examined	/Findings	
50351	10	No anomaly	
50352	13	No anomaly	
50353	11	No anomaly	
50354	15	No anomaly	
50355	13	No anomaly	
50356	15	No anomaly	
50357	13	No anomaly	
50359	13	No anomaly	
50360	14	No anomaly	
50361	17	No anomaly	
50362	10	No anomaly	
Total	144		
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 : HBM 1000 mg/kg	Species : Rat
Dam No.	Number of offspring examined	/Findings	
50451	12	No anomaly	
50452	14	No anomaly	
50453	16	No anomaly	
50454	13	No anomaly	
50455	16	No anomaly	
50456	13	No anomaly	
50457	15	No anomaly	
50458	14	No anomaly	
50459	18	No anomaly	
50460	15	No anomaly	
50461	17	No anomaly	
50462	15	No anomaly	
Total	178		
n	12		
Mean			
S.D.			

Mean : Average of incidence (%)

		Clinical sign of offspring Generation : F0					Time : 1
		Dose : HBM 0 mg/kg					Species : Rat
Dam No.	Number of offspring	/Day after birth					
		0	1	2	3	4	
50151	Alive : Male	11	11	11	11	11	
	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	11/5	11/5	11/5	11/5	11/5	
50152	Alive : Male	5	5	5	5	5	
	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	5/7	5/7	5/7	5/7	5/7	
50153	Alive : Male	6	6	6	6	5	
	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	1/0/0	
	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	5/5	
50154	Alive : Male	2	2	2	2	2	
	Female	13	13	13	13	13	
	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	2/13	2/13	2/13	2/13	2/13	
50155	Alive : Male	10	10	10	10	10	
	Female	3	3	3	3	3	
	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	10/3	10/3	10/3	10/3	10/3	
50156	Alive : Male	11	11	11	11	11	
	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	11/6	11/6	11/6	11/6	11/6	

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

		Clinical sign of offspring Generation : F0					Time : 1
		Dose : HBM 0 mg/kg					Species : Rat
Dam No.	Number of offspring	/Day after birth					
		0	1	2	3	4	
50157	Alive : Male	14	14	14	14	14	
	Female	2	2	2	2	2	
	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	14/2	14/2	14/2	14/2	14/2	
50158	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	
50159	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	
50160	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	
50161	Alive : Male	10	10	10	10	10	
	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	10/4	10/4	10/4	10/4	10/4	
50162	Alive : Male	12	12	12	12	12	
	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	12/4	12/4	12/4	12/4	12/4	

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

		Clinical sign of offspring Generation : F0					Time : 1	
		Dose : HBM 100 mg/kg					Species : Rat	
Dam No.	Number of offspring	/Day after birth						
		0	1	2	3	4		
50251	Alive : Male	7	7	7	7	7		
	Female	9	9	9	9	8		
	Dead : Dead	1 <sup>a</sup> /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	7/9	7/9	7/9	7/9	7/8		
50252	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		
50253	Alive : Male	8	8	8	8	8		
	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	8/5	8/5	8/5	8/5	8/5		
50254	Alive : Male	7	7	7	7	7		
	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	7/7	7/7	7/7	7/7	7/7		
50255	Alive : Male	4	4	4	4	4		
	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	4/9	4/9	4/9	4/9	4/9		
50256	Alive : Male	0	0	0	0	0		
	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	0/7	0/7	0/7	0/7	0/7		

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

a : One live male pup died of an accident after measurement of its body weight on the Day 0 after birth.

		Clinical sign of offspring Generation : F0					Time : 1
		Dose : HBM 100 mg/kg					Species : Rat
Dam No.	Number of offspring	/Day after birth					
		0	1	2	3	4	
50257	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	
50258	Alive : Male	11	11	11	11	11	
	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	11/4	11/4	11/4	11/4	11/4	
50259	Alive : Male	10	10	10	10	10	
	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	10/7	10/7	10/7	10/7	10/7	
50260	Alive : Male	5	5	5	5	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	1/0/0	
	Cannibalism	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	
	Signs						
	No abnormality	5/7	5/7	5/7	5/7	4/7	
50261	Alive : Male	6	6	6	6	6	
	Female	10	10	10	9	9	
	Dead : Dead	0/0/0	0/0/0	0/0/0	0/1/0	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	6/9	6/9	
50262	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	

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

		Clinical sign of offspring Generation : F0					Time : 1
Dam No.	Number of offspring	Dose : HBM 300 mg/kg					Species : Rat
		/Day after birth	0	1	2	3	4
50351	Alive : Male		5	5	5	5	5
	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		5/5	5/5	5/5	5/5	5/5
	Alive : Male		3	3	3	3	3
	Female		10	10	10	10	10
	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		3/10	3/10	3/10	3/10	3/10
	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	
	Signs						
50353	No abnormality		5/6	5/6	5/6	5/6	5/6
	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		5	5	5	5	5
	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		5/6	5/6	5/6	5/6	5/6
	Alive : Male		8/7	8/7	8/7	8/7	8/7
	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	
50355	Signs						
	No abnormality		5/8	5/8	5/8	5/8	5/8
	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		5/8	5/8	5/8	5/8	5/8
50356	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		5/8	5/8	5/8	5/8	5/8
	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	

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

		Clinical sign of offspring Generation : F0					Time : 1	
Dam No.	Number of offspring	Dose : HBM 300 mg/kg					Species : Rat	
		0	1	2	3	4		
50357	Alive : Male	8	8	8	8	8		
	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	8/5	8/5	8/5	8/5	8/5		
	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		
50359	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	5	5	5	5	5		
	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							
50360	No abnormality	5/9	5/9	5/9	5/9	5/9		
	Alive : Male	11	11	11	11	11		
	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	11/6	11/6	11/6	11/6	11/6		
	Alive : Male	6	6	6	6	6		
	Female	4	4	4	4	4		
50361	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	11/6	11/6	11/6	11/6	11/6		
	Alive : Male	6	6	6	6	6		
	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		
50362	Signs							
	No abnormality	6/4	6/4	6/4	6/4	6/4		

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

		Clinical sign of offspring Generation : F0					Time : 1
Dam No.	Number of offspring	Dose : HBM 1000 mg/kg					Species : Rat
		/Day after birth	0	1	2	3	4
50451	Alive : Male		9	9	9	9	9
	Female		3	3	3	3	3
	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		9/3	9/3	9/3	9/3	9/3
	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	
50452	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		8/6	8/6	8/6	8/6	8/6
	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						
50453	No abnormality		7/9	7/9	7/9	7/9	7/9
	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	
	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		8	8	8	8	8
	Female		8	8	8	8	8
50454	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
	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	
50455	Signs						
	No abnormality		5/8	5/8	5/8	5/8	5/8
	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	
	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		5	5	5	5	5
50456	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
	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	

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

		Clinical sign of offspring Generation : F0					Time : 1	
		Number of offspring	Dose : HBM 1000 mg/kg					Species : Rat
Dam No.			/Day after birth	0	1	2	3	
50457	Alive :	Male		8	8	8	8	8
		Female		7	7	7	7	7
		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	
		Male		7	7	7	7	7
		Female		7	7	7	7	7
		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	
50458	Alive :	Cannibalism	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	
		Signs						
		No abnormality	7/7	7/7	7/7	7/7	7/7	
		Male		7	7	7	7	7
		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	7/7	7/7	7/7	7/7	7/7	
50459	Alive :	Male		12	12	12	12	12
		Female		6	6	6	6	6
		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	Signs						
		No abnormality	12/6	12/6	12/6	12/6	12/6	
		Male		6	6	6	6	6
		Female		9	9	9	9	9
		Dead	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	
50460	Alive :	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	
		Male		6	6	6	6	6
	Dead :	Female		9	9	9	9	9
		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						
50461	Alive :	No abnormality	6/9	6/9	6/9	6/9	6/9	
		Male		9	9	9	9	9
		Female		8	8	8	8	8
		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	
	Signs	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	
		Male		9	9	9	9	9
		Female		6	6	6	6	6
50462	Alive :	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	
	Dead :	Male		9	9	9	9	9
		Female		6	6	6	6	6
		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	

( / ) : Number of offspring Male/Female/Unable to be sexed

F0 lactation)1 : Daily examination

Litter size and viability index of offspring						Species : Rat
Generation : F0			Dose : HBM 0 mg/kg			
Dam No.	Sex	/Day after birth	0 All pups Male/Female	0 Live pups Male/Female	0 Viability index (%)	
50151	Total		16 (11/5)	16 (11/5)	100.0	16 (11/5)
50152	Total		12 (5/7)	12 (5/7)	100.0	12 (5/7)
50153	Total		11 (6/5)	11 (6/5)	100.0	10 (5/5)
50154	Total		15 (2/13)	15 (2/13)	100.0	15 (2/13)
50155	Total		13 (10/3)	13 (10/3)	100.0	13 (10/3)
50156	Total		17 (11/6)	17 (11/6)	100.0	17 (11/6)
50157	Total		16 (14/2)	16 (14/2)	100.0	16 (14/2)
50158	Total		16 (7/9)	16 (7/9)	100.0	16 (7/9)
50159	Total		13 (7/6)	13 (7/6)	100.0	13 (7/6)
50160	Total		13 (7/6)	13 (7/6)	100.0	13 (7/6)
50161	Total		14 (10/4)	14 (10/4)	100.0	14 (10/4)
50162	Total		16 (12/4)	16 (12/4)	100.0	16 (12/4)
Total			172	172	171	
Male/Female			102/70	102/70	101/70	
n			12	12	12	
Mean				100.00	99.24	
S.D.				0.00	2.63	

Litter size and viability index of offspring  
Generation : F0

Dose : HBM 100 mg/kg

Species : Rat

Dam No.	Sex	/Day after birth		Viability index (%)	Live pups Male/Female	Viability index (%)
		0 All pups Male/Female	0 Live pups Male/Female			
50251	Total	18 <sup>a</sup> (8/9)	17 <sup>b</sup> (8/9)	94.4	15 (7/8)	93.8 <sup>c</sup>
50252	Total	14 (9/5)	14 (9/5)	100.0	14 (9/5)	100.0
50253	Total	13 (8/5)	13 (8/5)	100.0	13 (8/5)	100.0
50254	Total	14 (7/7)	14 (7/7)	100.0	14 (7/7)	100.0
50255	Total	13 (4/9)	13 (4/9)	100.0	13 (4/9)	100.0
50256	Total	7 (0/7)	7 (0/7)	100.0	7 (0/7)	100.0
50257	Total	15 (8/7)	15 (8/7)	100.0	15 (8/7)	100.0
50258	Total	15 (11/4)	15 (11/4)	100.0	15 (11/4)	100.0
50259	Total	17 (10/7)	17 (10/7)	100.0	17 (10/7)	100.0
50260	Total	12 (5/7)	12 (5/7)	100.0	11 (4/7)	91.7
50261	Total	16 (6/10)	16 (6/10)	100.0	15 (6/9)	93.8
50262	Total	15 (10/5)	15 (10/5)	100.0	15 (10/5)	100.0
Total		169	168	164		
Male/Female		86/82	86/82	84/80		
n		12	12	12	12	
Mean			99.53		98.28	
S.D.			1.62		3.16	

a : Including 1 dead pup, who's sex was indistinguishable because of maternal cannibalism.

b : Includong 1 live male pup that died of an accident.

c : One male pup that died of an accident on Day 0 is excluded from calculation.

Litter size and viability index of offspring  
Generation : F0  
Dose : HBM 300 mg/kg  
Species : Rat

Dam No.	Sex	/Day after birth		Viability index (%)	Live pups Male/Female	Viability index (%)
		0 All pups Male/Female	0 Live pups Male/Female			
50351	Total	10 (5/5)	10 (5/5)	100.0	10 (5/5)	100.0
50352	Total	13 (3/10)	13 (3/10)	100.0	13 (3/10)	100.0
50353	Total	11 (5/6)	11 (5/6)	100.0	11 (5/6)	100.0
50354	Total	15 (8/7)	15 (8/7)	100.0	15 (8/7)	100.0
50355	Total	13 (5/8)	13 (5/8)	100.0	13 (5/8)	100.0
50356	Total	15 (7/8)	15 (7/8)	100.0	15 (7/8)	100.0
50357	Total	13 (8/5)	13 (8/5)	100.0	13 (8/5)	100.0
50359	Total	13 (6/7)	13 (6/7)	100.0	13 (6/7)	100.0
50360	Total	14 (5/9)	14 (5/9)	100.0	14 (5/9)	100.0
50361	Total	17 (11/6)	17 (11/6)	100.0	17 (11/6)	100.0
50362	Total	10 (6/4)	10 (6/4)	100.0	10 (6/4)	100.0
Total		144	144	144		
Male/Female		69/75	69/75	69/75		
n		11	11	11		
Mean				100.00		
S.D.				0.00		

Litter size and viability index of offspring						Species : Rat	
Generation : F0			Dose : HBM 1000 mg/kg				
Dam No.	Sex	/Day after birth	0 All pups Male/Female	0 Live pups Male/Female	0 Viability index (%)		
50451	Total		12 (9/3)	12 (9/3)	100.0	12 (9/3)	
50452	Total		14 (8/6)	14 (8/6)	100.0	14 (8/6)	
50453	Total		16 (7/9)	16 (7/9)	100.0	16 (7/9)	
50454	Total		13 (6/7)	13 (6/7)	100.0	13 (6/7)	
50455	Total		16 (8/8)	16 (8/8)	100.0	16 (8/8)	
50456	Total		13 (5/8)	13 (5/8)	100.0	13 (5/8)	
50457	Total		15 (8/7)	15 (8/7)	100.0	15 (8/7)	
50458	Total		15 (7/8)	14 (7/7)	93.3	14 (7/7)	
50459	Total		18 (12/6)	18 (12/6)	100.0	18 (12/6)	
50460	Total		15 (6/9)	15 (6/9)	100.0	15 (6/9)	
50461	Total		17 (9/8)	17 (9/8)	100.0	17 (9/8)	
50462	Total		15 (9/6)	15 (9/6)	100.0	15 (9/6)	
Total			179	178	178		
Male/Female			94/85	94/84	94/84		
n			12	12	12		
Mean				99.44	100.00		
S.D.				1.93	0.00		

Body weight of offspring Generation : F0 /Day after birth				Dose : HBM 0 mg/kg	Unit : g	Species : Rat
Dam No.	Sex	0	4			
		n	B.W.	n	B.W.	
50151	Male	11	6.18	11	10.44	
	Female	5	5.74	5	10.26	
50152	Male	5	7.48	5	11.32	
	Female	7	6.86	7	11.03	
50153	Male	6	6.32	5	10.90	
	Female	5	5.80	5	9.96	
50154	Male	2	6.80	2	11.95	
	Female	13	6.08	13	10.35	
50155	Male	10	6.61	10	10.63	
	Female	3	5.67	3	9.53	
50156	Male	11	6.58	11	10.22	
	Female	6	6.32	6	9.90	
50157	Male	14	6.79	14	10.54	
	Female	2	5.95	2	9.20	
50158	Male	7	6.44	7	10.26	
	Female	9	6.22	9	9.82	
50159	Male	7	6.36	7	11.70	
	Female	6	5.98	6	10.95	
50160	Male	7	6.50	7	11.33	
	Female	6	6.23	6	10.93	
50161	Male	10	6.62	10	10.57	
	Female	4	6.20	4	9.90	
50162	Male	12	6.33	12	9.78	
	Female	4	6.03	4	9.35	
n	Male	102		101		
	Female	70		70		
Mean	Male		6.584		10.803	
	Female		6.090		10.098	
S.D.	Male		0.340		0.650	
	Female		0.318		0.621	

Body weight of offspring Generation : F0 /Day after birth				Dose : HBM 100 mg/kg	Unit : g	Species : Rat
Dam No.	Sex	0	4			
		n	B.W.	n	B.W.	
50251	Male	8	6.43	7	10.96	
	Female	9	5.94	8	10.06	
50252	Male	9	6.57	9	11.33	
	Female	5	6.30	5	10.88	
50253	Male	8	6.44	8	10.59	
	Female	5	6.22	5	10.14	
50254	Male	7	6.47	7	11.40	
	Female	7	6.17	7	10.70	
50255	Male	4	7.50	4	12.28	
	Female	9	6.92	9	11.50	
50256	Male	0	-	0	-	
	Female	7	8.76	7	15.83	
50257	Male	8	7.09	8	11.01	
	Female	7	6.79	7	10.47	
50258	Male	11	7.93	11	12.42	
	Female	4	7.50	4	11.53	
50259	Male	10	6.54	10	10.49	
	Female	7	6.29	7	9.76	
50260	Male	5	6.56	4	11.03	
	Female	7	6.09	7	9.80	
50261	Male	6	5.58	6	9.68	
	Female	10	5.79	9	10.26	
50262	Male	10	6.48	10	10.21	
	Female	5	5.86	5	9.50	
n	Male	86		84		
	Female	82		80		
Mean	Male		6.690		11.036	
	Female		6.553		10.869	
S.D.	Male		0.621		0.819	
	Female		0.853		1.691	

- : Not applicable

Body weight of offspring Generation : F0 /Day after birth				Dose : HBM 300 mg/kg	Unit : g	Species : Rat
Dam No.	Sex	0	4			
		n	B.W.	n	B.W.	
50351	Male	5	6.52	5	12.08	
	Female	5	5.88	5	11.28	
50352	Male	3	7.10	3	11.73	
	Female	10	6.48	10	10.86	
50353	Male	5	8.52	5	13.70	
	Female	6	7.87	6	12.50	
50354	Male	8	6.64	8	11.11	
	Female	7	6.63	7	10.94	
50355	Male	5	7.40	5	12.06	
	Female	8	6.85	8	11.14	
50356	Male	7	6.41	7	10.66	
	Female	8	6.44	8	10.76	
50357	Male	8	7.15	8	11.79	
	Female	5	6.84	5	11.26	
50359	Male	6	6.90	6	11.93	
	Female	7	6.23	7	10.13	
50360	Male	5	8.36	5	12.92	
	Female	9	7.47	9	12.60	
50361	Male	11	6.62	11	9.40	
	Female	6	6.23	6	8.20	
50362	Male	6	6.97	6	11.62	
	Female	4	6.30	4	10.63	
n	Male	69		69		
	Female	75		75		
Mean	Male		7.145		11.727	
	Female		6.656		10.936	
S.D.	Male		0.706		1.120	
	Female		0.581		1.172	

Body weight of offspring Generation : F0 /Day after birth				Dose : HBM 1000 mg/kg	Unit : g	Species : Rat
Dam No.	Sex	0	4			
		n	B.W.	n	B.W.	
50451	Male	9	7.11	9	11.84	
	Female	3	6.70	3	11.27	
50452	Male	8	7.31	8	11.93	
	Female	6	7.32	6	11.90	
50453	Male	7	6.09	7	9.57	
	Female	9	6.03	9	9.38	
50454	Male	6	6.17	6	9.82	
	Female	7	5.81	7	9.31	
50455	Male	8	8.04	8	12.60	
	Female	8	7.29	8	11.05	
50456	Male	5	6.94	5	11.40	
	Female	8	6.46	8	11.03	
50457	Male	8	6.35	8	9.63	
	Female	7	6.04	7	9.14	
50458	Male	7	6.60	7	10.13	
	Female	7	6.16	7	9.79	
50459	Male	12	6.35	12	10.17	
	Female	6	5.93	6	9.58	
50460	Male	6	6.25	6	9.68	
	Female	9	6.01	9	9.57	
50461	Male	9	6.40	9	9.83	
	Female	8	6.26	8	9.70	
50462	Male	9	6.24	9	9.74	
	Female	6	5.82	6	9.02	
n	Male	94		94		
	Female	84		84		
Mean	Male	6.654		10.528		
	Female	6.319		10.062		
S.D.	Male	0.586		1.090		
	Female	0.527		0.972		

Necropsy findings of offspring					
Generation : F0		Dose : HBM 0 mg/kg		Species : Rat	
Dam No.	Number of live offspring examined on Day 4	/Findings	Number of dead offspring examined on Day 0-4	/Findings	
50151	16	Absent	0		
50152	12	Absent	0		
50153	10	1, Multifocal yellowish white foci of liver; 9, Absent	0		
50154	15	Absent	0		
50155	13	Absent	0		
50156	17	Absent	0		
50157	16	Absent	0		
50158	16	Absent	0		
50159	13	Absent	0		
50160	13	Absent	0		
50161	14	Absent	0		
50162	16	Absent	0		
Total	171		0		
n	12		0		

Necropsy findings of offspring			Species : Rat
Generation : F0	Dose : HBM 100 mg/kg		
Dam No.	Number of live offspring examined on Day 4	/Findings	Number of dead offspring examined on Day 0-4
50251	15	Absent	2
50252	14	Absent	0
50253	13	Absent	0
50254	14	Absent	0
50255	13	Absent	0
50256	7	Absent	0
50257	15	Absent	0
50258	15	Absent	0
50259	17	Absent	0
50260	11	Absent	0
50261	15	Absent	1
50262	15	Absent	0
Total	164		3
n	12		2

a : Showed partial loss of the body because of maternal cannibalism

b : Died of an accident

Necropsy findings of offspring					
Generation : F0			Dose : HBM 300 mg/kg		Species : Rat
Dam No.	Number of live offspring examined on Day 4	/Findings	Number of dead offspring examined on Day 0-4	/Findings	
50351	10	Absent	0		
50352	13	Absent	0		
50353	11	Absent	0		
50354	15	Absent	0		
50355	13	Absent	0		
50356	15	Absent	0		
50357	13	Absent	0		
50359	13	Absent	0		
50360	14	Absent	0		
50361	17	Absent	0		
50362	10	Absent	0		
Total	144		0		
n	11		0		

Necropsy findings of offspring			Dose : HBM 1000 mg/kg			Species : Rat	
Generation : F0	Number of live offspring examined on Day 4	/Findings	Number of dead offspring examined on Day 0-4	/Findings			
Dam No.							
50451	12	Absent	0				
50452	14	Absent	0				
50453	16	Absent	0				
50454	13	Absent	0				
50455	16	Absent	0				
50456	13	Absent	0				
50457	15	Absent	0				
50458	14	Absent	1	Absent (Day 0)			
50459	18	Absent	0				
50460	15	Absent	0				
50461	17	Absent	0				
50462	15	Absent	0				
Total	178		1				
n	12		1				



## 試験成績書

2017年07月26日

東京化成工業株式会社 品質保  
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 : Methyl 2-Hydroxyisobutyrate			
製品コード : H0256 CAS番号 : 2110-78-3	等級 : GR	製品ロット : H3XDK	判定 : 合格

項目	結果	規格値
純度(GC)	99.9 %	99.5 %以上
比重 (20/20)	1.0342	1.0330 ~ 1.0350
屈折率 n20/D	1.4116	1.4100 ~ 1.4130

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。  
規格の内容は予告なく変更する場合があります。本書面に掲載されている内容が最新です。製品に貼付されているラベルの内容と異なる場合がありますが、製品自体の品質は最新の規格を満たしています。

## 最終報告書

試験名

投与液中の $\alpha$ -ヒドロキシソラク酸メチルの安定性試験および濃度確認試験

著者

久永 晃資

試験終了日

2018年1月9日

試験施設

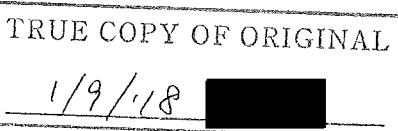
株式会社日曹分析センター 小田原事業所  
〒250-0216 神奈川県小田原市高田 345

試験委託者

株式会社化合物安全性研究所 安全性研究部  
〒004-0839 北海道札幌市清田区真栄 363 番地 24

試験番号

NCAS 17-211



## GLP 適合陳述書

試験番号 : NCAS 17-211

試験名 : 投与液中の  $\alpha$ -ヒドロキシソラク酸メチルの安定性試験および濃度確認試験

この試験は、以下の GLP に従って実施した。

「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)

この試験はここに述べられた方法により行われ、この最終報告書は試験実施により得られた生データを正確に反映したものである。

試験責任者 :

[REDACTED] 2018 年 1 月 9 日  
[REDACTED]

株式会社日曹分析センター 小田原事業所

## 信頼性保証書

試験番号： NCAS 17-211

試験名： 投与液中の $\alpha$ -ヒドロキシイソラク酸メチルの安定性試験および濃度確認試験

上記試験の信頼性保証の監査または査察を適用 GLP および信頼性保証部門 (QAU) の SOP に基づいて実施した。監査または査察の結果は、以下の日付で試験責任者および運営管理者に報告した。

監査または査察項目	日付 (月/日/年)		
	監査または 査察日	報告日	
		試験責任者	運営管理者
試験計画書	9/8/2017	9/12/2017	9/12/2017
試験計画書変更届 1	9/15/2017	9/15/2017	9/15/2017
試験計画書変更届 2	10/5/2017	10/6/2017	10/6/2017
実験操作			
・ 赤外吸収スペクトル測定	9/15/2017	9/20/2017	9/20/2017
・ 模擬投与液の調製	9/19,28,29/2017	9/29/2017	9/29/2017
・ 投与液の受領	10/5/2017	10/6/2017	10/6/2017
・ 被験溶液の調製	9/19/2017	9/20/2017	9/20/2017
・ 標準溶液の調製	9/19/2017	9/20/2017	9/20/2017
・ HPLC 測定	9/19/2017	9/20/2017	9/20/2017
生データおよび関連試験資料	12/25-27/2017	12/27/2017	12/27/2017
報告書草案	12/25-27/2017	12/27/2017	12/27/2017
最終報告書	1/9/2018	1/9/2018	1/9/2018

QAU は、この試験が試験計画書および SOP に従って行われ、報告された方法や手段が実際に使われたものであり、結果は記録されたデータを正確に反映していることを確認した。

QAU 責任者



2018 年 1 月 9 日

(株) 日曹分析センター

## 試験情報

試験番号 : NCAS 17-211

試験名 : 投与液中の  $\alpha$ -ヒドロキシイソラク酸メチルの安定性試験および濃度確認試験

報告書番号 : NCAS 17-211

試験委託者 : 株式会社化合物安全性研究所 安全性研究部

〒004-0839 北海道札幌市清田区真栄 363 番地 24

試験施設 : 株式会社日曹分析センター 小田原事業所

〒250-0216 神奈川県小田原市高田 345

TEL 080-6899-8378 FAX 0465-42-3586

試験責任者 :



試験従事者 :



試験開始日 : 2017年9月8日

実験開始日 : 2017年9月15日

実験終了日 : 2017年11月28日

試験終了日 : 2018年1月9日

適用ガイドライン : なし

関連する試験 : 試験番号 SR17144 :  $\alpha$ -ヒドロキシイソラク酸メチル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 NCAS 17-210NG : 投与液中の  $\alpha$ -ヒドロキシイソラク酸メチルの分析法検討および分析法確認試験

試資料保管 : 本試験に関する全ての文書は、当試験施設の資料室に該当通知後 10 年間保管する。その後の保管場所については、試験委託者と協議して決定する。被験物質(保管用サンプル)は該当の通知後、10 年間または品質低下を起こさない期間のいずれか短い期間保管する。

SOP および試験計画書からの逸脱 :

本試験において、SOP および試験計画書からの逸脱はなかった。

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 :

本試験において、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。

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## 概要

株式会社化合物安全性研究所からの委託により、投与液中の  $\alpha$ -ヒドロキシソラク酸メチル(略称:HBM)の安定性試験および濃度確認試験を実施した。

2017年9月15日にFT-JR(ATR法)を用いて測定対象物質のIRスペクトルを測定し、公知スペクトル(Spectral Database for Organic Compounds)と比較した。両者のIRスペクトルは一致しており、測定対象物質の同一性を確認した。

投与液中の  $\alpha$ -ヒドロキシソラク酸メチルの安定性を確認するため、10 mg/mLおよび200 mg/mL模擬投与液を2017年9月19日に試験施設で調製し、HPLCを用いて調製直後の測定対象物質濃度を確認した。これら模擬投与液を遮光条件下での冷蔵9日間保存後、さらに室温24時間保存した。2017年9月29日にHPLCを用いて保存後の測定対象物質濃度を確認した。調製直後および保存後の模擬投与液中の測定対象物質濃度を比較して、残存率を算出した結果、10 mg/mL 模擬投与液の残存率は99.3%、200 mg/mL 模擬投与液の残存率は101.6%であり、判定基準(100%±15%以内)を満たした。

以上の結果、投与液中の  $\alpha$ -ヒドロキシソラク酸メチルは調製後、遮光条件下で冷蔵保存9日間後、さらに室温保存24時間後まで安定であることを確認した。

試験委託者より2017年10月5日および2017年11月1日に受領した投与液中の測定対象物質の濃度確認試験を、HPLCを用いて行った。投与液中の測定対象物質濃度の平均値および相対標準偏差は、判定基準(設定濃度±15%以内および15%以内)を満たした(下表参照)。

以上の結果、投与液中の  $\alpha$ -ヒドロキシソラク酸メチルが設定濃度に調製されていることを確認した。

試験委託者が実施する毒性試験(委託者試験番号SR17144)における最終投与日以降の2017年11月28日に、測定対象物質のIRスペクトルを測定し、2017年9月15日に測定したIRスペクトルと比較した。両者のIRスペクトルは一致しており、実験期間中の測定対象物質が安定であったことを確認した。

Received date	Nominal concentration (mg/mL)	Determined concentration		Criteria	
		Mean (mg/mL)	RSD* (%)	Mean conc. (mg/mL)	RSD* (%)
October 5, 2017	20	20.25	0.29	20±3	≤15
	60	59.95	0.96	60±9	≤15
	200	198.1	0.22	200±30	≤15
November 1, 2017	20	20.03	0.19	20±3	≤15
	60	59.19	0.13	60±9	≤15
	200	196.4	0.33	200±30	≤15

\* relative standard deviations

## 緒言

株式会社化合物安全性研究所からの委託により、投与液中の $\alpha$ -ヒドロキシソラク酸メチルの安定性試験・濃度確認および $\alpha$ -ヒドロキシソラク酸メチルの同一性確認・安定性確認を実施した。

## 実験材料および方法

### 1. 測定対象物質

化合物名 :  $\alpha$ -ヒドロキシソラク酸メチル  
 別名 : methyl 2-hydroxy-2-methylpropionate  
 略称 : HBM  
 CAS No. : 2110-78-3  
 分子式 : C<sub>5</sub>H<sub>10</sub>O<sub>3</sub>  
 分子量 : 118.13  
 純度 : 99.9% (GC)  
 ロット番号 : H3XDK  
 入手先 : 株式会社化合物安全性研究所  
 入手日 : 2017年9月15日  
 NCAS 検索番号 : STD-1552  
 保管状態 : 褐色ガラス瓶中に気密、冷蔵(1~10°C)

### 2. 試薬および機器

精製水 : 日本薬局方精製水、日医工株式会社  
 メタノール : HPLC 用、和光純薬工業(株)  
 超純水 : Milli-Q 水・純水(Elix 水)製造システム(Milli-Q Integral 3、日本ミリポア(株))で精製した  
 Milli-Q 水  
 天秤 : XP205、メトラー・トレド(株)  
 冷蔵庫 : FKEX-5000、日本フリーザー(株)  
 室温保管庫 : SH-170FINC、コクヨ  
 サーモレコーダー : TR-71U、(株)ティアンドディ  
 フーリエ変換赤外分光光度計 : Spectrum One、PerkinElmer(株)  
 高速液体クロマトグラフ (HPLC) :  
 送液装置 : LC-10ADvp、(株)島津製作所  
 検出器 : SPD-10AVvp、(株)島津製作所  
 恒温槽 : CTO-10Avp、(株)島津製作所  
 オートインジェクタ : SIL-10ADvp、(株)島津製作所  
 データ処理装置 : CLASS-VP、(株)島津製作所

### 3. 投与液

2017年10月5日および2017年11月1日に、毒性試験施設で調製した20、60および200 mg/mL の投与液を受領した。受領した試料は即日分析した。残余試料は冷蔵保存し、実験終了後に試験委託者の了解を得て廃

棄した。

#### 4. 実験操作

##### 4.1. 測定対象物質の同一性

FT-IR (ATR 法) を用いて測定対象物質の IR スペクトルを測定し、公知スペクトル (Spectral Database for Organic Compounds) との比較により同一性を確認した。

2017 年 9 月 15 日に、次の条件で IR スペクトルを測定した。測定は室温で実施した。

##### <FT-IR 測定条件>

測定法： ATR 法

測定波数： 4000～400 cm<sup>-1</sup>

分解能： 4 cm<sup>-1</sup>

積算回数： 1 回

##### 4.2. 測定対象物質の安定性

試験委託者が実施する毒性試験（委託者試験番号 SR17144）における最終投与日以降に、FT-IR (ATR 法) を用いて測定対象物質の IR スペクトルを測定し、4.1 項にて測定したスペクトルと比較した。スペクトルが一致した場合、実験期間中の測定対象物質は安定であったと判断した。

2017 年 11 月 28 日に、4.1 項に記載の条件で IR スペクトルを測定した。測定は室温で実施した。

##### 4.3. HPLC 条件

カラム： Halo C18、2.7 μm、4.6 mm i.d. × 150 mm、Advanced materials technology

移動相： メタノール + 超純水 = 50 + 50 (v/v)

流速： 0.3 mL/min

カラム温度： 40°C

検出波長： 225 nm

注入量： 10 μL

##### 4.4. 標準溶液の調製

測定対象物質の約 100 mg を 50 mL 容メスフラスコに秤量し、HPLC 移動相を加えて溶解および定容し、標準原液 No. ST2000 を調製した。この液を次表に従い HPLC 移動相で希釈して標準溶液 No. SS40～SS600 を調製した。標準原液 No. および標準溶液 No. には調製月日(mmd)を付して識別した。濃度の有効数字は 4 衔とした。

Standard solution No.	Source solution		Dilution volume (mL)	Nominal concentration (mg/L)
	No.	Volume (mL)		
SS40 (mmd)	SS200 (mmd)	2	10	40
SS50 (mmd)	SS200 (mmd)	2.5	10	50
SS200 (mmd)	ST2000 (mmd)	2	20	200
SS500 (mmd)	ST2000 (mmd)	5	20	500
SS600 (mmd)	ST2000 (mmd)	3	10	600

#### 4.5. 検量線

標準溶液のHPLC測定を4.3項に示す条件で行い、得られたクロマトグラム上の測定対象物質のピーク面積を得た。得られたピーク面積を縦軸に、測定対象物質濃度(mg/L)を横軸としてグラフを作成するとともに、回帰直線の傾き、y切片及び相関係数(r)を算出した。計算にはMicrosoft Office Excel 2010 (SP2 MSO)を用いた。

#### 4.6. 投与液中の $\alpha$ -ヒドロキシイソラク酸メチルの濃度測定

3項の投与液を以下のように希釀して被験溶液を調製した。別に、精製水1mLにメタノール1mLを加え、HPLC移動相を加えて50mLとして対照溶液とした(n=1)。

##### 20 mg/mL 投与液

20 mg/mL投与液1mLにメタノール1mLを加え、HPLC移動相を加えて50mLとして被験溶液とした。(n=2、50倍希釀)

##### 60 mg/mL 投与液

60 mg/mL投与液1mLにメタノール1mLを加え、HPLC移動相を加えて20mLとした。この液2mLにHPLC移動相を加えて20mLとして被験溶液とした。(n=2、200倍希釀)

##### 200 mg/mL 投与液

200 mg/mL投与液1mLにメタノール1mLを加え、HPLC移動相を加えて20mLとした。この液1mLにHPLC移動相を加えて20mLとして被験溶液とした。(n=2、400倍希釀)

被験溶液および対照溶液を4.3項に示すHPLC条件で分析し、得られたクロマトグラム上の測定対象物質のピーク面積を得た。予め作成した検量線より、被験溶液中の測定対象物質濃度を算出した。濃度の有効数字は4桁とした。次式を用いて投与液中の測定対象物質濃度を求めた。また、投与液中の測定対象物質濃度の平均値及び相対標準偏差を求めた。判定基準は、平均値が設定濃度±15%以内および相対標準偏差が15%以内とした。

Received date	Dosing solution		Dilution factor	Test solution (mg/L)	
	Nominal conc. (mg/mL)	No.		Nominal conc. (mg/L)	No.
October 5, 2017	20	P1-1	50	400	P1-1-1, P1-1-2
	60	P2-1	200	300	P2-1-1, P2-1-2
	200	P3-1	400	500	P3-1-1, P3-1-2
November 1, 2017	20	P1-2	50	400	P1-2-1, P1-2-2
	60	P2-2	200	300	P2-2-1, P2-2-2
	200	P3-2	400	500	P3-2-1, P3-2-2

$$\text{投与液中の測定対象物質濃度} = \frac{\text{被験溶液中の測定対象物質濃度 (mg/L)} \times \text{希釀倍率}}{1000}$$

#### 4.7. 投与液中の $\alpha$ -ヒドロキシイソラク酸メチルの安定性確認

測定対象物質の103.19 mgおよび1005.92 mgを10mLおよび5mL容メスフラスコに秤量し、精製水を加えて溶解および定容し、10 mg/mLおよび200 mg/mL模擬投与液No. DS1およびNo. DS2を調製した。

模擬投与液を以下のように希釀して被験溶液を調製した。別に、精製水1mLにメタノール1mLを加え、HPLC

移動相を加えて 20 mL として対照溶液 No. CS-1 とした(n=1)。

#### 10 mg/mL 投与液

10 mg/mL 模擬投与液 1 mL にメタノール 1 mL を加え、HPLC 移動相を加えて 20 mL として被験溶液とした。  
(n=2、20 倍希釈)

#### 200 mg/mL 投与液

200 mg/mL 模擬投与液 1 mL にメタノール 1 mL を加え、HPLC 移動相を加えて 20 mL とした。この液 1 mL に HPLC 移動相を加えて 20 mL として被験溶液とした。 (n=2、400 倍希釈)

被験溶液および対照溶液を 4.3 項に示す HPLC 条件で分析し、得られたクロマトグラム上の測定対象物質のピーク面積を得た。予め作成した検量線より、被験溶液中の測定対象物質濃度を算出した。濃度の有効数字は 4 衔とした。次式を用いて調製直後の模擬投与液中の測定対象物質濃度を求めた。

$$\text{模擬投与液中の測定対象物質濃度 (mg/mL)} = \frac{\text{被験溶液中の測定対象物質濃度 (mg/L)} \times \text{希釈倍率}}{1000}$$

10 mg/mL および 200 mg/mL 模擬投与液を遮光条件下で冷蔵 9 日間保存後、さらに室温 24 時間保存した。保存後の模擬投与液中の測定対象物質濃度を上記と同様に算出し、次式を用いて残存率を求めた。判定基準は残存率 100% ± 15% 以内とした。

$$\text{残存率 (\%)} = \frac{\text{保存後の測定対象物質平均濃度}}{\text{調製直後の測定対象物質平均濃度}} \times 100$$

## 結果および考察

投与液中の α-ヒドロキシイソラク酸メチル（略称：HBM）の安定性試験・濃度確認および α-ヒドロキシイソラク酸メチルの同一性確認・安定性確認を実施した結果を以下に示す。

#### 測定対象物質の同一性

2017 年 9 月 15 日に測定した測定対象物質の IR スペクトルを Fig. 1 に示す。公知スペクトル (Spectral Database for Organic Compounds) を Fig. 2 に示す。両者のスペクトルは一致しており、同一性を確認した。

#### 測定対象物質の安定性

試験委託者が実施する毒性試験（委託者試験番号 SR17144）における最終投与日以降である 2017 年 11 月 28 日に測定した測定対象物質の IR スペクトルを Fig. 3 に示す。2017 年 9 月 15 日に測定した IR スペクトル (Fig. 1) と比較した結果、両者の IR スペクトルは一致しており、実験期間中の測定対象物質が安定であったことを確認した。

#### 投与液中の $\alpha$ -ヒドロキシイソラク酸メチルの安定性確認

標準溶液の測定結果を Table 1 に示す。模擬投与液中の測定対象物質の濃度測定結果を Table 2 に示す。検量線の一例を Fig. 4 に示す。HPLC 移動相のクロマトグラム例を Fig. 5 に示す。標準溶液のクロマトグラム例を Fig. 6～Fig. 10 に示す。対照溶液のクロマトグラム例を Fig. 11 に示す。被験溶液のクロマトグラム例を Fig. 12～Fig. 15 に示す。

模擬投与液を遮光条件下での冷蔵（3.1～3.8 °C）9 日間保存後、さらに室温（22.5～22.9 °C）24 時間保存した結果、10 mg/mL 模擬投与液の残存率は 99.3%、200 mg/mL 模擬投与液の残存率は 101.6% であり、判定基準（100%±15%以内）を満たした。

以上の結果、投与液中の $\alpha$ -ヒドロキシイソラク酸メチルは調製後、遮光条件下で冷蔵保存 9 日間後、さらに室温保存 24 時間まで安定であることを確認した。

#### 投与液中の $\alpha$ -ヒドロキシイソラク酸メチルの濃度測定

投与液中の測定対象物質の濃度測定結果を Table 3 に示す。被験溶液のクロマトグラム例を Fig. 16～Fig. 18 に示す。

投与液中の測定対象物質濃度の平均値および相対標準偏差は、判定基準（設定濃度±15%以内および 15%以内）を満たした。

以上の結果、投与液中の $\alpha$ -ヒドロキシイソラク酸メチルが設定濃度に調製されていることを確認した。

## 結論

本試験において、FT-IR(ATR 法)を用いて $\alpha$ -ヒドロキシイソラク酸メチルの同一性および安定性を確認した。また、HPLC を用いて投与液中の $\alpha$ -ヒドロキシイソラク酸メチルが設定濃度に調製されていること、および安定性（遮光条件下における冷蔵保存 9 日間後、さらに室温保存 24 時間安定）を確認した。

Table 1 Result of the standard solutions

Experiment	Standard solution No.	Concentration (mg/L)	Peak area	Regression equation Correlation coefficient
Stability of the HBM concentration in the dosing solution	SS40 (0919)	41.40	23796	Regression equation: $y = 601.12 x - 1702.5$ Correlation coefficient: 1.000 (analyzed date: September 19, 2017)
	SS50 (0919)	51.75	29259	
	SS200 (0919)	207.0	123621	
	SS500 (0919)	517.5	303196	
	SS600 (0919)	621.0	376423	
	SS40 (0929)	40.64	23712	Regression equation: $y = 612.35 x - 1491.6$ Correlation coefficient: 1.000 (analyzed date: September 29, 2017)
	SS50 (0929)	50.80	30149	
	SS200 (0929)	203.2	122002	
	SS500 (0929)	508.0	308616	
	SS600 (0929)	609.6	372850	
Determination of the HBM concentration in the dosing solution	SS40 (1005)	42.40	25003	Regression equation: $y = 606.64 x - 325.68$ Correlation coefficient: 1.000 (analyzed date: October 5, 2017)
	SS50 (1005)	53.00	31725	
	SS200 (1005)	212.0	128655	
	SS500 (1005)	530.0	322461	
	SS600 (1005)	636.0	384353	
	SS40 (1101)	40.66	22358	Regression equation: $y = 564.35 x + 278.38$ Correlation coefficient: 1.000 (analyzed date: November 1, 2017)
	SS50 (1101)	50.83	29361	
	SS200 (1101)	203.3	115509	
	SS500 (1101)	508.3	287811	
	SS600 (1101)	609.9	343769	

Table 2 Result of the stability of the test article (HBM) concentration in the dosing solution

Test solution No.	Storage	Prepared conc. (mg/mL)	Dilution factor	Peak area	Detected conc. (mg/L)	Determined conc. (mg/mL)		Residual rate (%)
						Individual	Mean	
DS1-1-1	Before	10.32	20	310763	519.8	10.40	10.56	99.3
DS1-1-2				320899	536.7	10.73		
DS1-2-1				319888	524.8	10.50	10.49	
DS1-2-2				319533	524.2	10.48		
DS2-1-1	Before	201.2	400	300103	502.1	200.8	198.8	101.6
DS2-1-2				294009	491.9	196.8		
DS2-2-1				308474	506.2	202.5	202.0	
DS2-2-2				306867	503.6	201.4		

$$\text{Residual rate (\%)} = \frac{\text{HBM concentration after storage}}{\text{HBM concentration before storage}} \times 100$$

Table 3 Result of the determination of the test article (HBM) concentration in the dosing solution

Test solution No.	Nominal conc. (mg/mL)	Dilution factor	Peak area	Detected conc. (mg/L)	Determined conc. (mg/mL)			Criteria	
					Individual	Mean (mg/mL)	RSD (%)	Mean (mg/mL)	RSD (%)
P1-1-1	20	50	244836	404.1	20.21	20.25	0.29	$20 \pm 3$	$\leq 15$
P1-1-2			245854	405.8	20.29				
P2-1-1	60	200	182749	301.8	60.36	59.95	0.96	$60 \pm 9$	$\leq 15$
P2-1-2			180279	297.7	59.54				
P3-1-1	200	400	299722	494.6	197.8	198.1	0.22	$200 \pm 30$	$\leq 15$
P3-1-2			300655	496.1	198.5				
P1-2-1	20	50	226057	400.1	20.00	20.03	0.19	$20 \pm 3$	$\leq 15$
P1-2-2			226650	401.1	20.06				
P2-2-1	60	200	167460	296.2	59.25	59.19	0.13	$60 \pm 9$	$\leq 15$
P2-2-2			167147	295.7	59.14				
P3-2-1	200	400	276694	489.8	195.9	196.4	0.33	$200 \pm 30$	$\leq 15$
P3-2-2			277982	492.1	196.8				

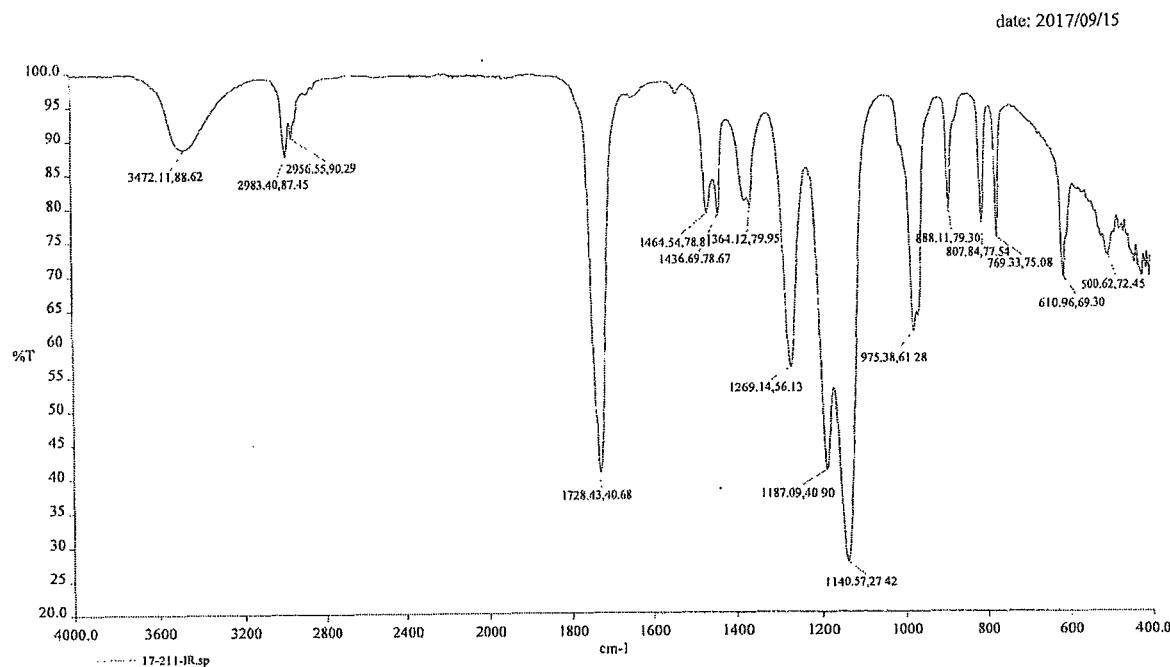


Fig. 1 IR spectrum of the test article for the identity test (analyzed date: September 15, 2017).

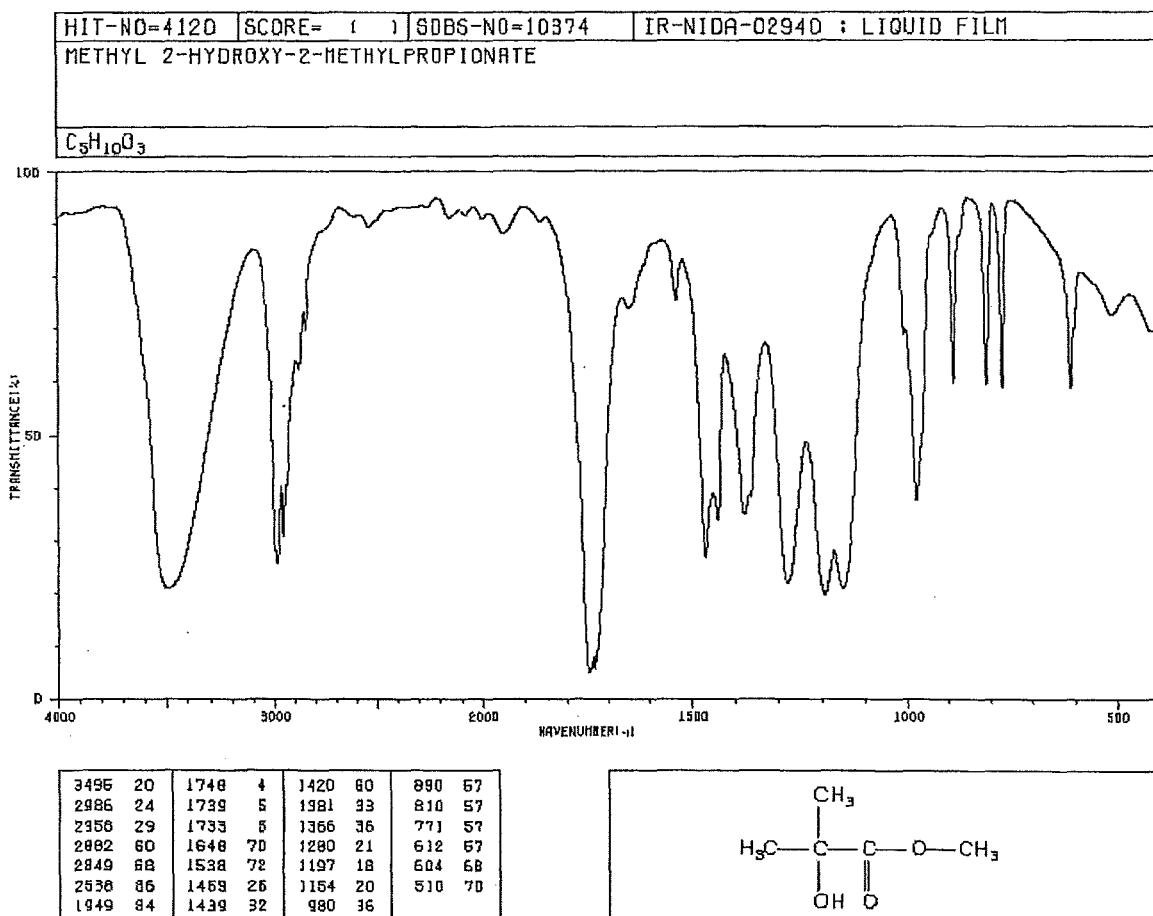


Fig. 2 Common IR spectrum of the test article provided by the Spectral Database for Organic Compounds.

SDBSWeb : <http://sdbs.db.aist.go.jp> (National Institute of Advanced Industrial Science and Technology, download: 2017/09/15)

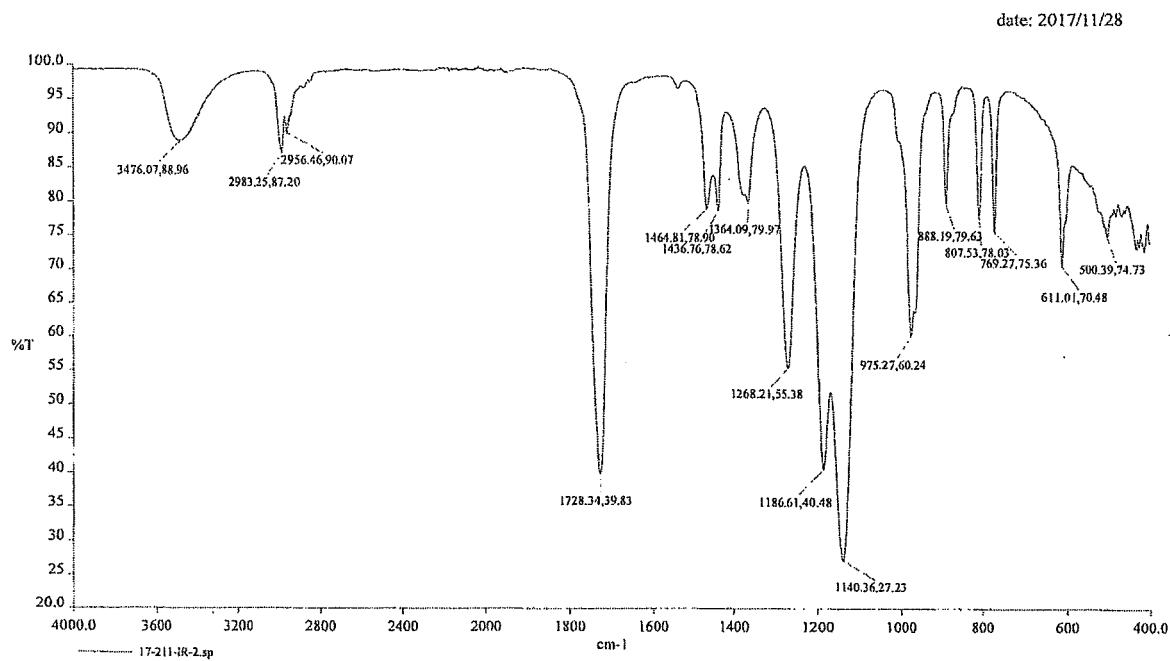


Fig. 3 IR spectrum of the test article for the stability test (analyzed date: November 28, 2017).

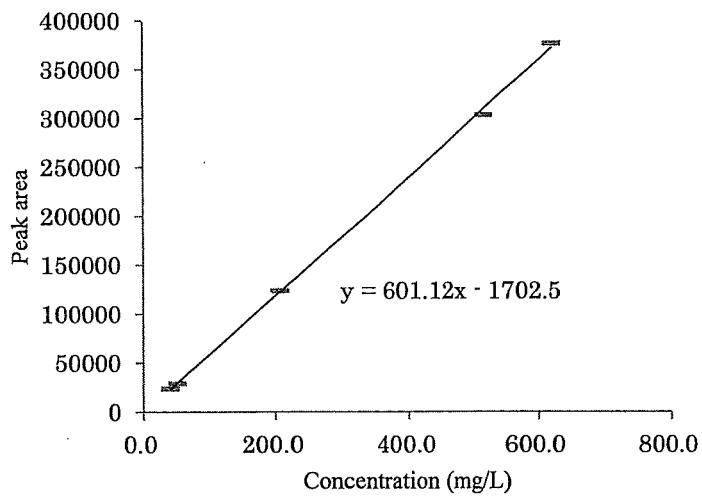
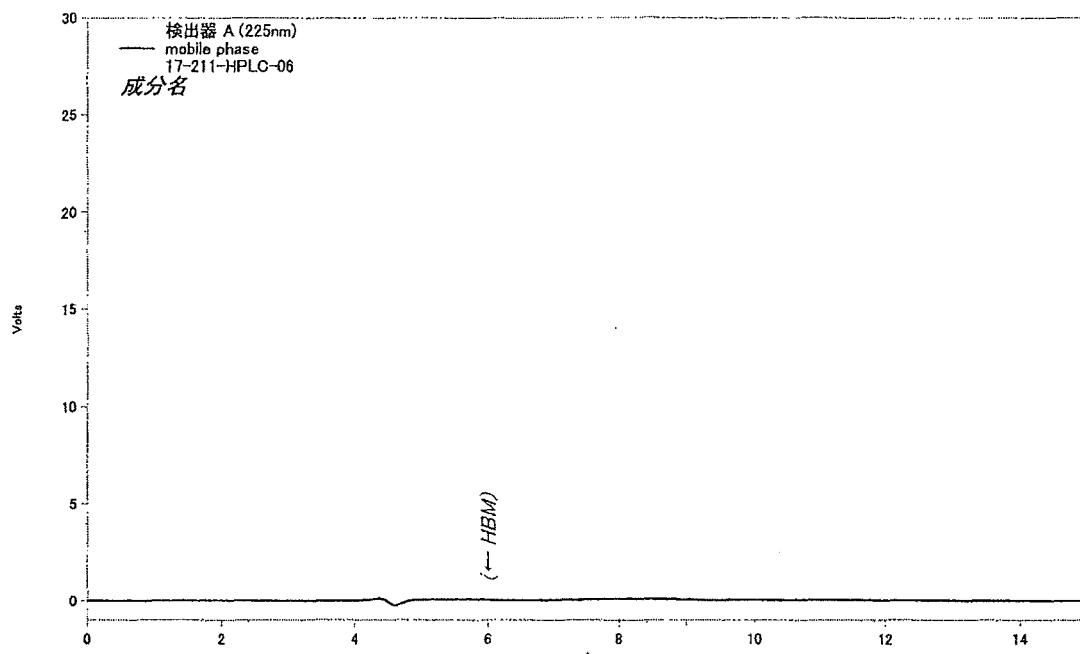
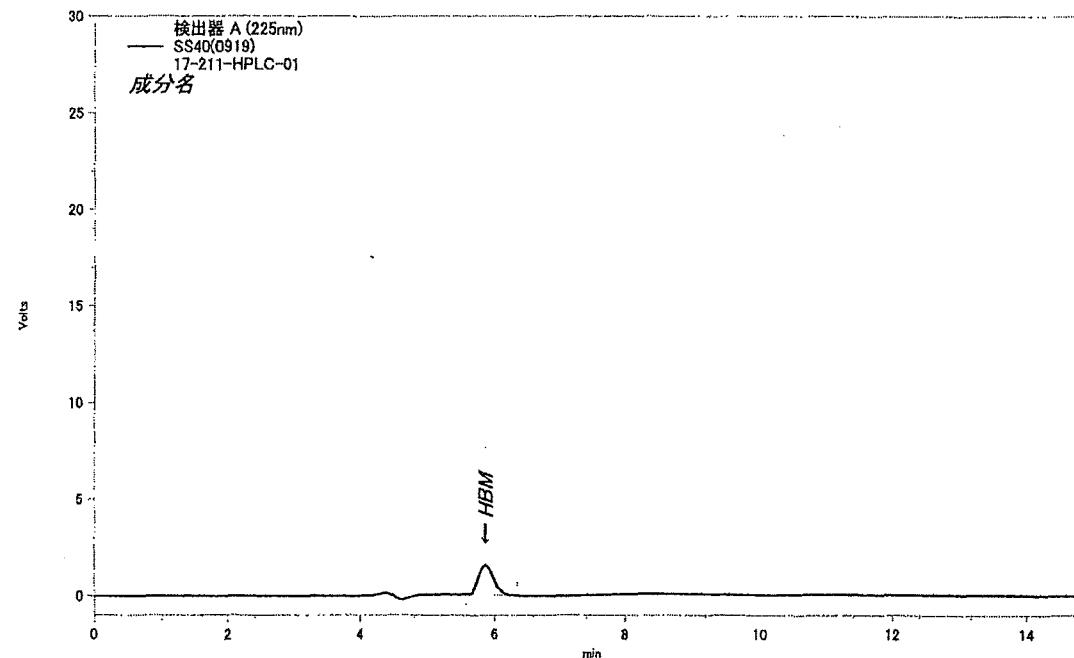


Fig. 4 Typical calibration plot and regression line (analyzed date: September 19, 2017).



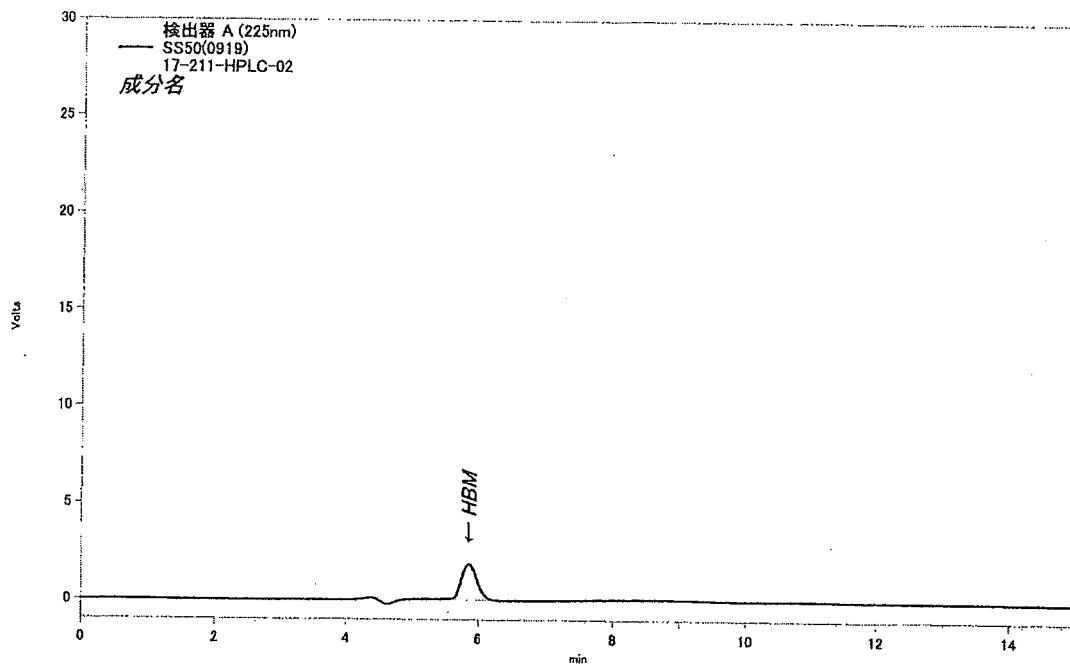
検出器 A (225nm)	Peak No.	Retention time	Peak area
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Fig. 5 Typical chromatogram of the mobile phase.



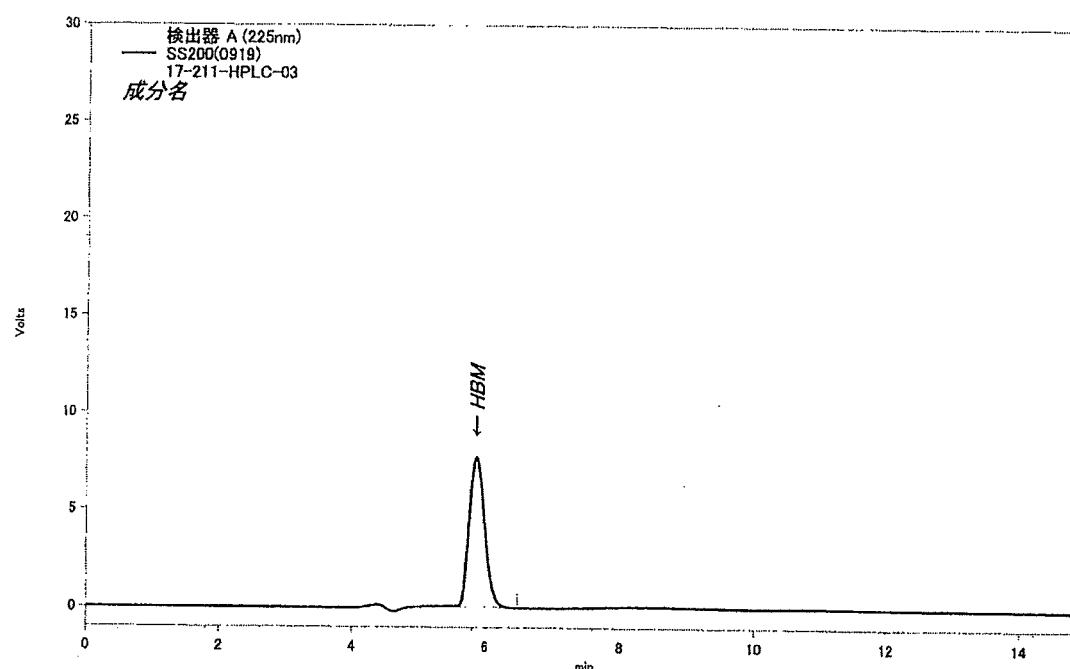
検出器 A (225nm)	Peak No.	Retention time	Peak area
	1	5.857	23796

Fig. 6 Typical chromatogram of the standard solution No. SS40(0919).



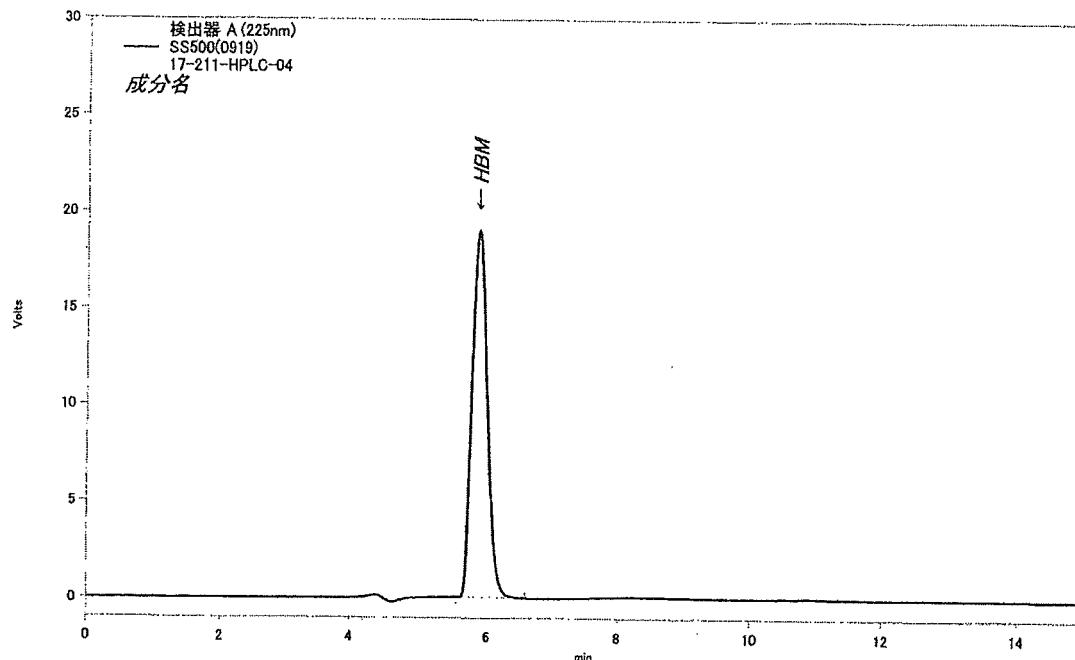
検出器 A (225nm)

Fig. 7 Typical chromatogram of the standard solution No. SS50(0919).



検出器 A (225nm)

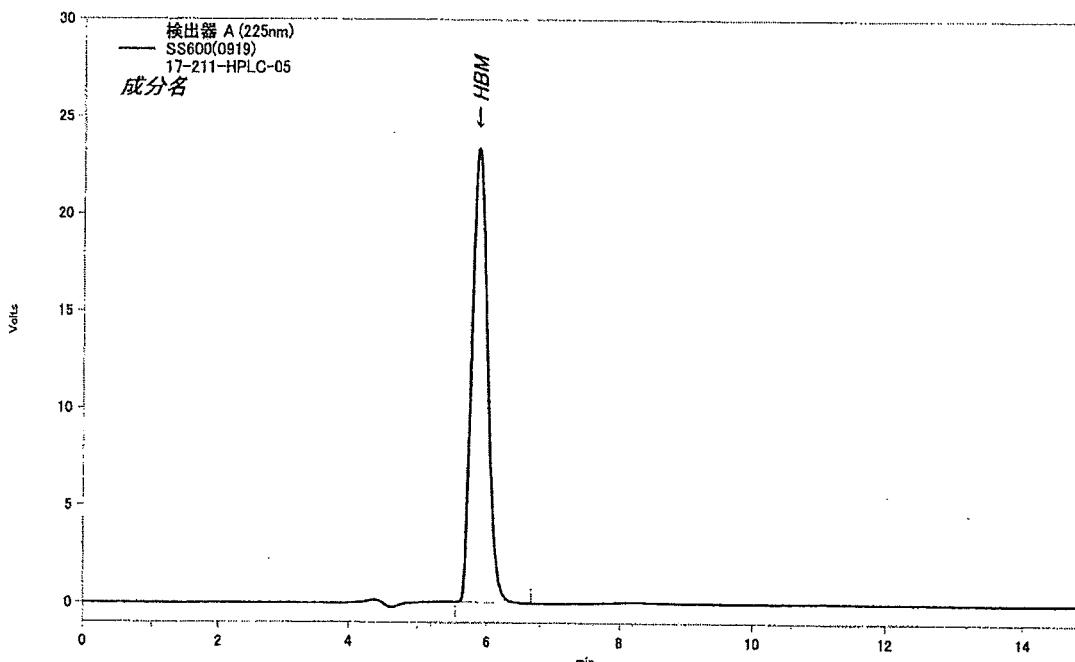
Fig. 8 Typical chromatogram of the standard solution No. S200(0919).



検出器 A (225nm)

Peak No.	Retention time	Peak area
1	5.855	303196

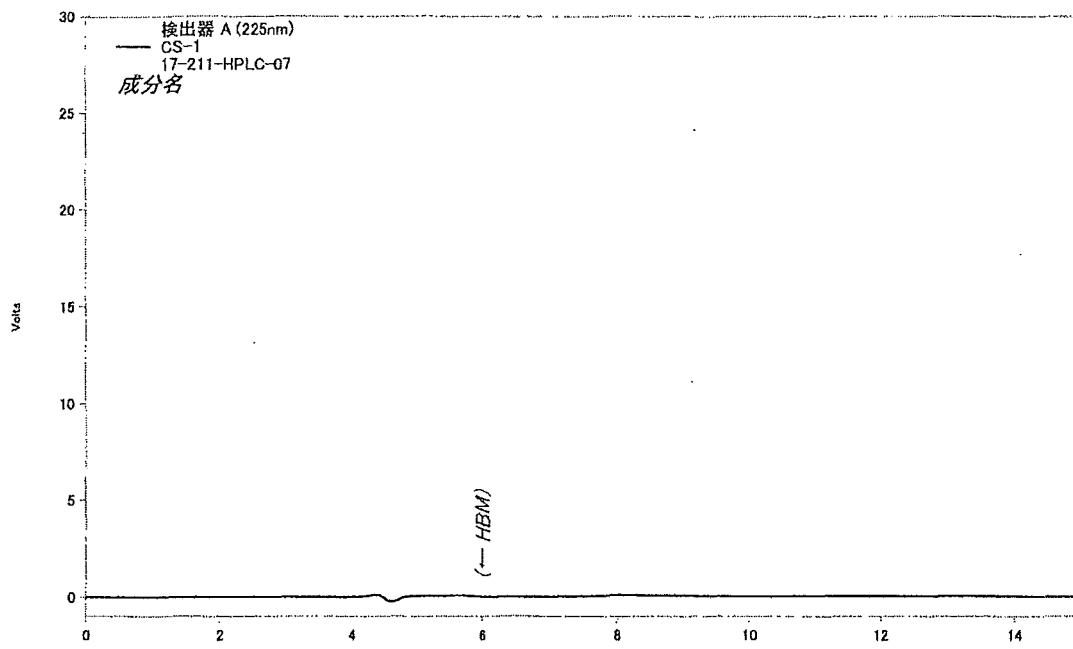
Fig. 9 Typical chromatogram of the standard solution No. SS500(0919).



検出器 A (225nm)

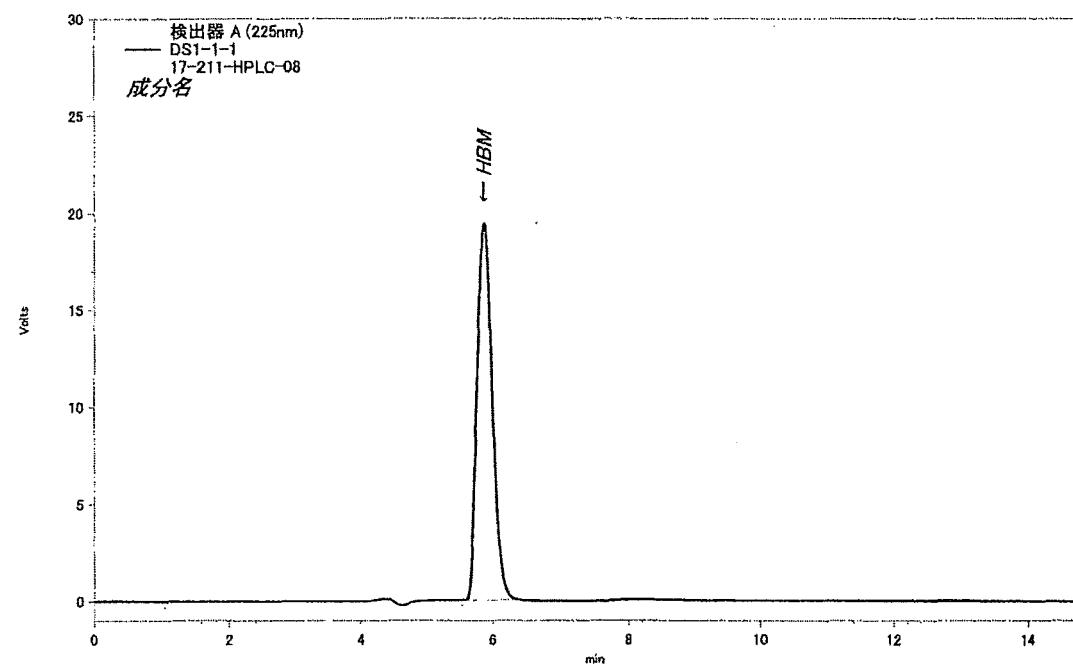
Peak No.	Retention time	Peak area
1	5.852	376423

Fig. 10 Typical chromatogram of the standard solution No. SS600(0919).



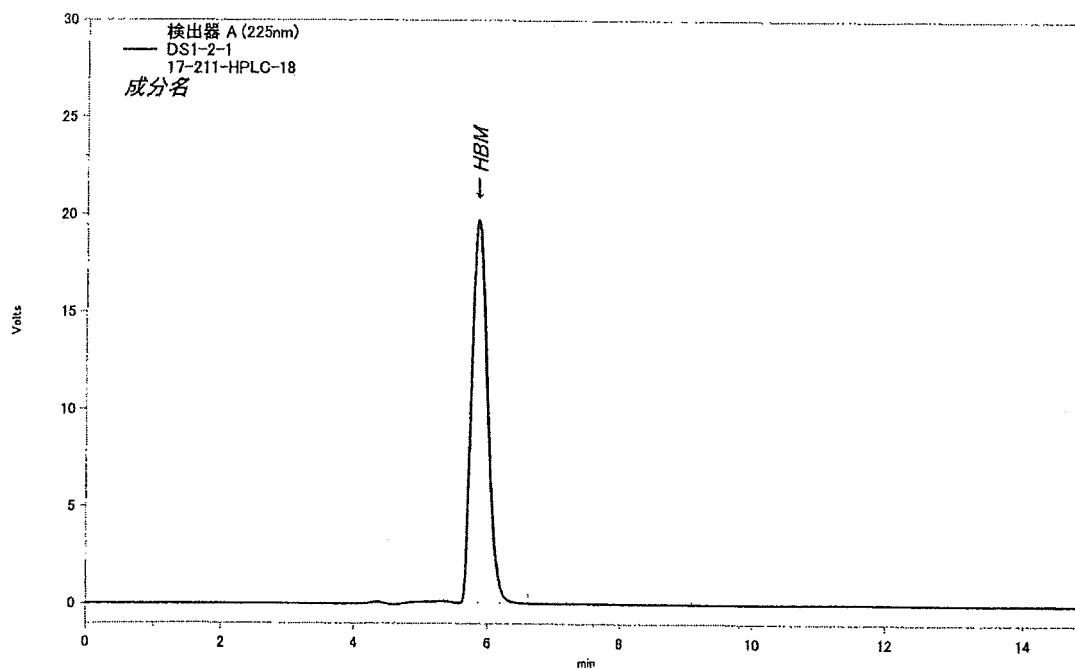
検出器 A (225nm)	Peak No.	Retention time	Peak area
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Fig. 11 Typical chromatogram of the control solution No. CS-1.



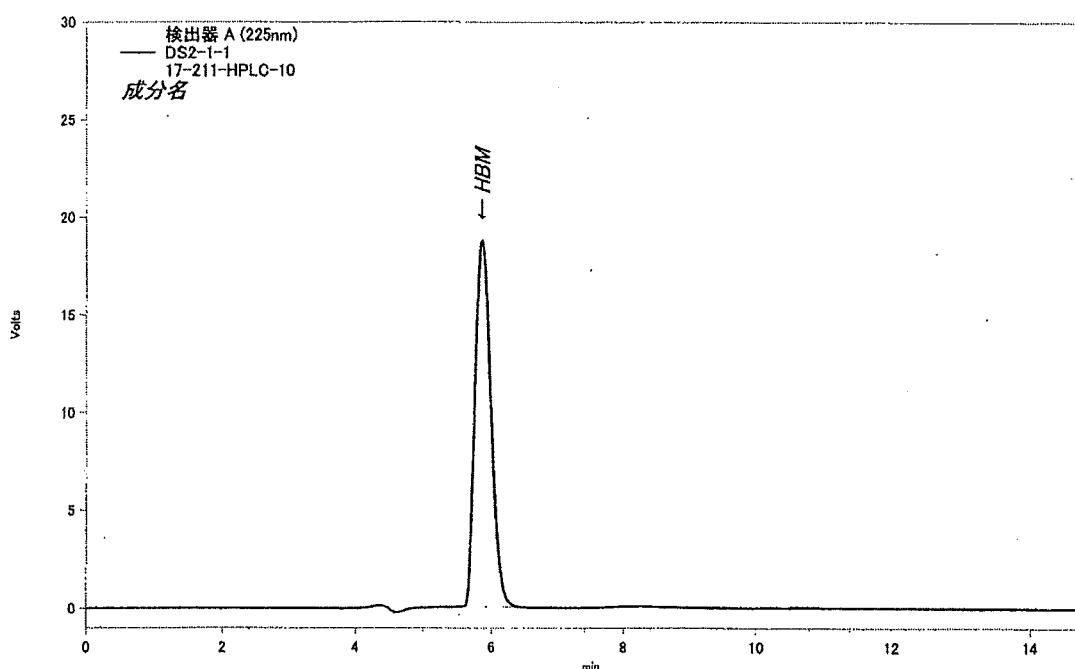
検出器 A (225nm)	Peak No.	Retention time	Peak area
	1	5.852	310763

Fig. 12 Typical chromatogram of the test solution No. DS1-1-1.



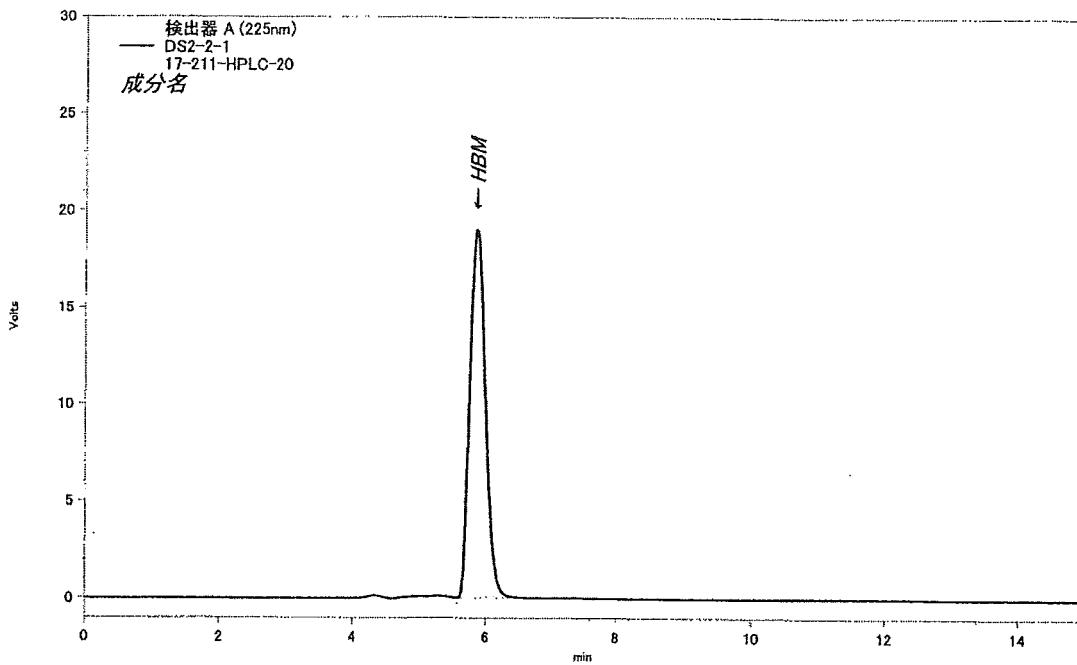
Peak No.	Retention time	Peak area
1	5.849	319888

Fig. 13 Typical chromatogram of the test solution No. DS1-2-1.



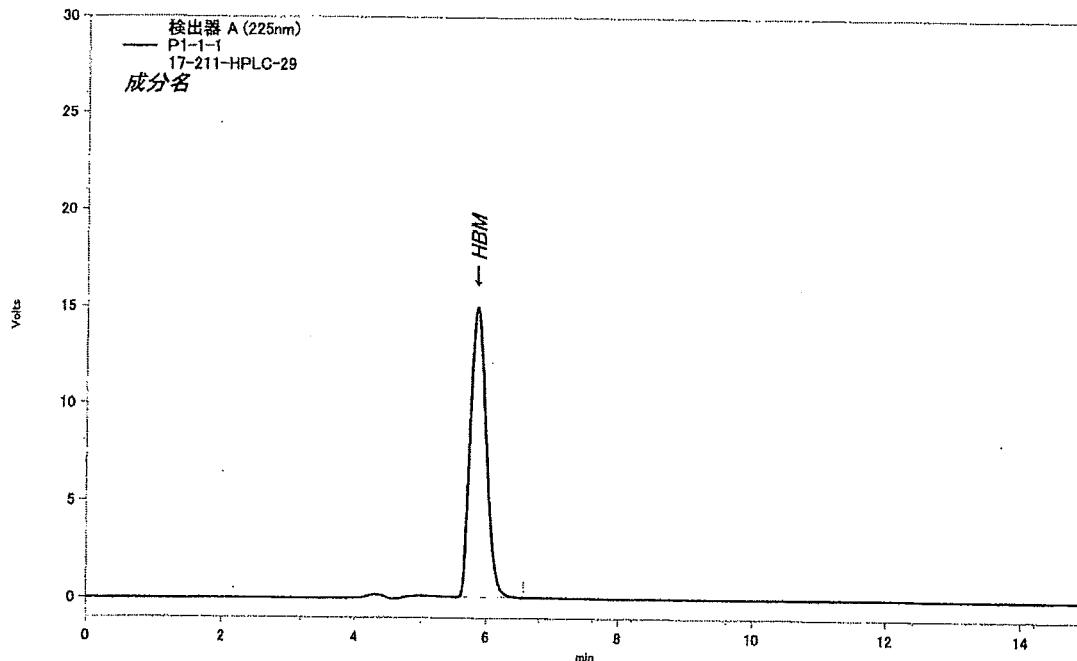
Peak No.	Retention time	Peak area
1	5.853	300103

Fig. 14 Typical chromatogram of the test solution No. DS2-1-1.



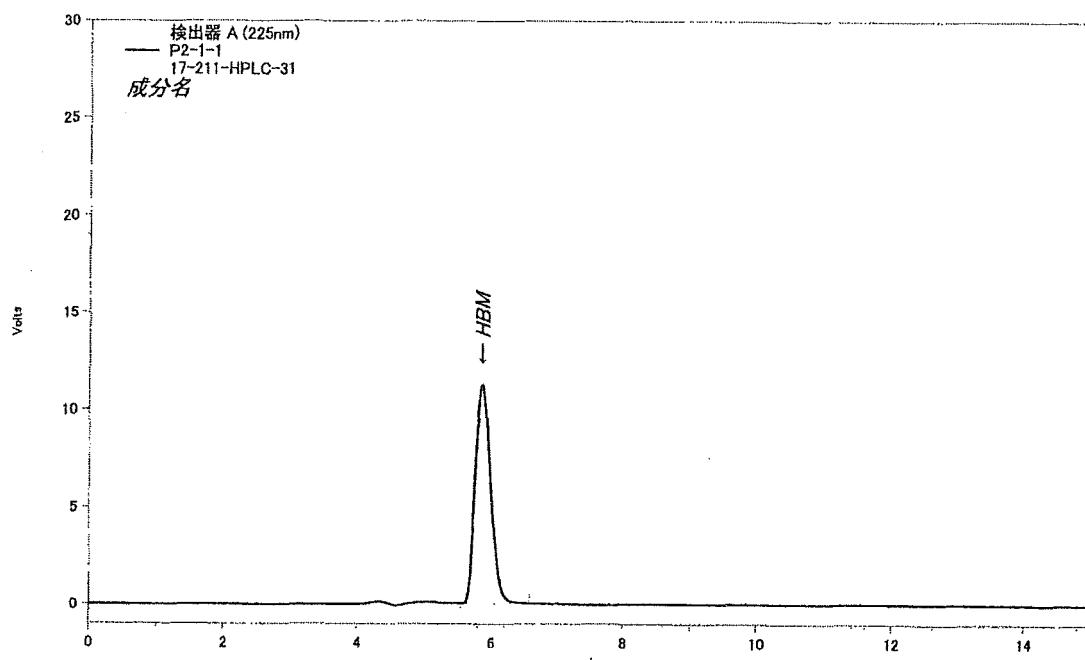
検出器 A (225nm)		Peak No.	Retention time	Peak area
1			5.849	308474

Fig. 15 Typical chromatogram of the test solution No. DS2-2-1.



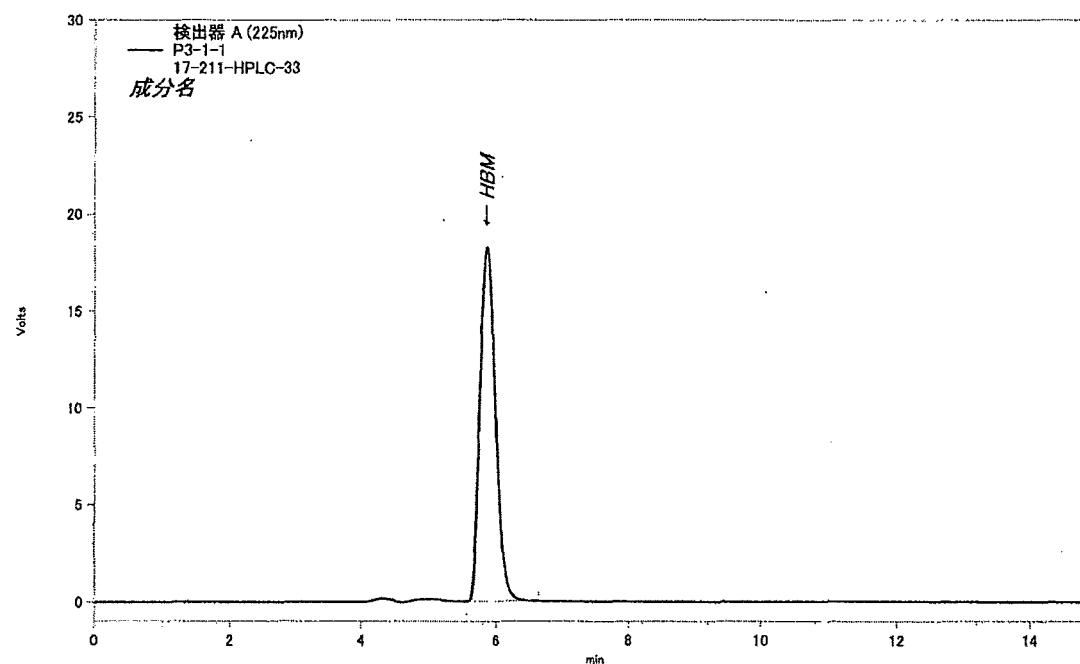
検出器 A (225nm)		Peak No.	Retention time	Peak area
1			5.850	244836

Fig. 16 Typical chromatogram of the test solution No. P1-1-1.



検出器 A (225nm)			
Peak No.	Retention time	Peak area	
1	5.853	182749	

Fig. 17 Typical chromatogram of the test solution No. P2-1-1.



検出器 A (225nm)			
Peak No.	Retention time	Peak area	
1	5.849	299722	

Fig. 18 Typical chromatogram of the test solution No. P3-1-1.