
プロピオン酸エチルのラットを用いた 28 日間反復投与毒性試験

最終報告書

作成日 2024年3月22日

株式会社日本バイオリサーチセンター
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2. GLP 陳述書

試験番号：430157

表 題：プロピオン酸エチルのラットを用いた 28 日間反復投与毒性試験

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）に従って実施したものである。

株式会社日本バイオリサーチセンター 羽島研究所

試験責任者



2024年 3月 22日

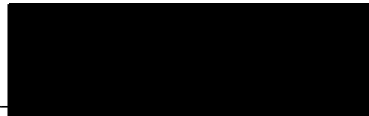
3. 最終報告書作成者署名

試験番号：430157

表題：プロピオン酸エチルのラットを用いた28日間反復投与毒性試験

株式会社日本バイオリサーチセンター 羽島研究所

試験責任者



2024年3月22日

4. 表題

プロピオン酸エチルのラットを用いた 28 日間反復投与毒性試験

5. 試験番号

430157

6. 試験委託者

厚生労働省 医薬局 医薬品審査管理課
化学物質安全対策室
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TEL : 03-5253-1111

7. 試験施設

株式会社日本バイオリサーチセンター 羽島研究所
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8. 試験目的

プロピオン酸エチルが継続的に人に摂取された場合の健康への影響を推定するために、プロピオン酸エチルを雌雄ラットに 28 日間連続経口投与し、さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性について検討した。

9. 参考としたガイドライン

「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）（最終改正：令和 2 年 11 月 5 日，薬生発 1105 第 2 号，20201015 製局第 1 号，環保企発第 2011055 号）

10. 遵守した 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）

11. 遵守した動物の福祉に関する指針等

厚生労働省通知 科発第 0601001 号「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」（平成 18 年 6 月 1 日）

「日本バイオリサーチセンター実験動物の管理および福祉に関する規定」（平成 19 年 4 月 2 日）

当試験計画は、試験施設の動物実験委員会で審査されたものである。

12. 試験責任者

株式会社日本バイオリサーチセンター 羽島研究所

13. 試験日程

試験開始日	2023年11月10日
実験開始日（投与群動物入手日）	2023年11月15日
投与群分け日	2023年11月23日
投与群投与開始日	2023年11月23日
投与群投与終了日	2023年12月20日
投与群剖検日	2023年12月21日
回復群動物入手日	2023年11月22日
回復群分け日	2023年12月1日
回復群投与開始日	2023年12月1日
回復群投与終了日	2023年12月28日
回復群剖検日	2024年1月12日
実験終了日（病理組織所見最終化日）	2024年2月20日
試験終了日	2024年3月22日

14. 試験関係資料の保存

この試験において試験施設で発生したすべての試験関係資料は、株式会社日本バイオリサーチセンター 羽島研究所の資料保存施設に保存する。保存期間は最終報告書提出日から10年間とし、その後の保存は試験委託者との別途協議の上、決定する。

15. 予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態及び試験計画書に従わなかったこと

15.1. 予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態

当試験の実施期間中に予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態はなかった。

15.2. 試験計画書に従わなかったこと

- 1) 飼育室の管理温度を 20.0～26.0℃、管理湿度を 40.0～70.0%RH としていたが、2023 年 12 月 5 日に温湿度制御機器の保守点検を実施した影響で 11 時 8 分～11 時 36 分の間に最高温度 26.4℃、10 時 49 分～10 時 50 分の間に最低湿度 39.5%RH と逸脱した。逸脱幅が僅かであることから、試験成績への影響はないと判断した。
- 2) HE 染色組織標本作製において、対照群の雄 1 例（動物番号：M01102）では薄切プレパラート上に上皮小体は認められなかった。SOP に従い、当該動物の甲状腺及び上皮小体のパラフィン包埋を再薄切して HE 染色組織標本作製したが、プレパラート上に上皮小体は認められなかった。しかし、その他の動物の上皮小体で被験物質の毒性評価は十分可能であったことから、試験成績への影響はないと判断した。なお、甲状腺の病理組織学的評価は、初回作製時におけるプレパラートの観察結果を対象とした。

その他に試験計画書に従わなかったことはなかった。

16. 試験従事者及び業務分担

■■ ■

(試験計画書の作成, 試験操作の確認, 剖検, 病理組織学的検査, 最終報告書の作成)

■■ ■■■ ■■■

(検体の投与, 一般状態観察, 体重測定, 摂餌量測定, 行動機能観察, 感覚反応検査, 握力測定, 自発運動量測定, 臍垢検査, 動物の一般飼育管理)

■■ ■■■ ■

(尿検査, 血液学的検査, 血液生化学的検査)

■■ ■■■ ■

(剖検, 器官重量の測定, 病理組織標本作製, 病理組織学的検査)

■■ ■■■ ■■■

(被験物質の管理, 投与検体の調製)

■■ ■■■ ■

(被験物質の安定性確認, 投与検体中の被験物質の安定性確認及び濃度の測定)

■■ ■

(統計処理)

17. 要約

プロピオン酸エチルが継続的に人に摂取された場合の健康への影響を推定するために、プロピオン酸エチルを雌雄ラットに 28 日間連続経口投与し、さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性について検討した。投与量は、1000 mg/kg を高用量とし、以下、300 及び 100 mg/kg を設定した。媒体にはコーン油を用い、対照群には被験物質投与群と同容量のコーン油を投与した。各群の使用動物数は対照群、300 及び 1000 mg/kg 群を雌雄各 10 例とし、各群ともそのうち半数を回復群とした。100 mg/kg 群は雌雄各 5 例とした。

1. 一般状態及び死亡状況

死亡例は、雌雄とも認められなかった。

一般状態では、雌雄いずれにも異常は認められなかった。

2. 体重及び摂餌量

体重及び摂餌量では、雌雄いずれにも被験物質に起因する変化はみられなかった。

3. 行動機能 (FOB)、感覚応答、握力及び自発運動量

自発運動量では、投与 4 週雄の 1000 mg/kg 群で投与後 60～120 分の歩行量に有意な低値がみられた。回復 2 週雄及び雌では、被験物質に起因する変化はみられなかった。

行動機能 (FOB)、感覚応答及び握力では、雌雄いずれにも被験物質に起因する変化はみられなかった。

4. 尿検査、血液学的検査及び血液生化学的検査

尿検査、血液学的検査及び血液生化学的検査では、雌雄いずれにも被験物質に起因する変化はみられなかった。

5. 剖検所見、器官重量及び病理組織学的検査

剖検所見、器官重量及び病理組織学的検査では、雌雄いずれにも被験物質に起因する変化はみられなかった。

以上のように、プロピオン酸エチルの無毒性量は、雄では 1000 mg/kg 投与により投与後 60～120 分の歩行量に有意な低値が認められたことから 300 mg/kg/day、雌では 1000 mg/kg/day と考えられる。

18. 材料及び方法

18.1. 被験物質及び対照物質（媒体）

18.1.1. 被験物質

名称 : プロピオン酸エチル

英語名称 : Ethyl propionate

CAS No. 105-37-3 (Fig. 1)

官報公示番号 (化審法) : (2)-774

ロット番号 : ██████████ (Attachment 1)

性状 : 無色澄明の液体

含量 : 99.9% (規格値 : 97.0%以上)

分子量 : 102.13

保管条件 : 室温 (1.0~30.0°C, 実測値 : 18.9~21.2°C), 遮光

保管場所 : 試験施設の被験物質保管室 (保管庫 : FMU-404I, 福島工業株式会社)

製造元 : ██████████

取扱い注意事項 : 直接手に触れない様に取り扱った。取扱い時には適切な保護具 (保護メガネ, マスク, ゴム手袋) を着用した。

18.1.2. 対照物質（媒体）

名称 : コーン油

ロット番号 : WTF5137 (Attachment 2)

使用期限 : 2025 年 9 月

保管条件 : 室温 (1.0~30.0°C, 実測値 : 21.0~25.5°C), 遮光

保管場所 : 試験施設の被験物質保管室

製造元 : 富士フイルム和光純薬株式会社

18.1.3. 被験物質の安定性確認

投与群の投与開始日前及び回復群の投与期間終了後、被験物質含量を、「投与液の濃度分析法バリデーション試験 (試験番号 : 430155)」¹⁾でバリデートされた方法 (Attachments 3-1~3-5) に従って測定した。その結果、いずれも 100.0%であった (Attachments 4-1 及び 4-2)。したがって、投与群の投与開始日前の被験物質含量に対する回復群の投与期間終了後の残存率は 100.0%であり、規定値 (100.0 ± 10.0%) の範囲内であったことから、試験期間中の被験物質の安定性が確認された。

18.1.4. 残余被験物質の取り扱い

試験施設で保存する保存サンプル (約 1 g) を除いた残余被験物質は、試験施設で廃棄した。保存サンプルの保管条件は、室温、遮光とする。

18.2. 投与検体

18.2.1. 調製

18.2.1.1. 対照物質（媒体，第1群投与検体）

コーン油をそのまま使用した。

18.2.1.2. 第2～4群投与検体

333 mg/mL（第4群投与検体）となるように，被験物質の必要量を秤量後，コーン油で希釈した。その後，各濃度に段階希釈し，褐色ガラス製容器に入れた。

18.2.2. 投与検体の濃度及び安定性の確認

投与群投与開始日前に333，100及び33 mg/mL投与検体（投与群投与開始日の投与検体と同一製法で調製した）について，「投与液の濃度分析法バリデーション試験（試験番号：430155）」¹⁾でバリデートされた方法（Attachments 3-1～3-5）に従って，調製直後及び褐色ガラス製容器に室温（1.0～30.0℃，実測値：22.3～23.1℃）・遮光下で24時間保管後（マグネチックスターラーで攪拌しながらサンプリングした）の投与検体中の被験物質濃度を確認した。その結果，調製直後の被験物質濃度は設定濃度の92.6～94.9%であり，規定値（100.0±10.0%）の範囲内であった（Attachment 5-1）。24時間保管後の残存率は調製直後の濃度に対して100.0～101.2%であり，規定値（100.0±10.0%）の範囲内であったため，上記条件下で保管中した投与検体の安定性が確認された（Attachment 6）。

投与群投与終了日に使用する333，100及び33 mg/mL投与検体について，投与検体中の被験物質濃度を確認した。その結果，被験物質濃度は設定濃度の93.7～96.5%であり，規定値（100.0±10.0%）の範囲内であった（Attachment 5-2）。

18.2.3. 調製頻度

調製は用時とした。

18.2.4. 残余投与検体の取り扱い

残余投与検体は，投与終了後に廃棄した。

18.3. 試験系

18.3.1. 動物種及び系統

動物種：ラット（SPF）

系統：CrI：CD（SD）

選択理由：毒性試験に一般的に用いられている動物種で，その系統維持が明らかである。

18.3.2. 動物の入手日、性別、週齢及び入手匹数

2023年11月15日、雄、4週齢、23匹（投与群）
2023年11月15日、雌、4週齢、23匹（投与群）
2023年11月22日、雄、4週齢、17匹（回復群）
2023年11月22日、雌、4週齢、17匹（回復群）

18.3.3. 入手翌日の体重範囲

雄：87～106 g
雌：91～104 g

18.3.4. 供給源

ジャクソン・ラボラトリー・ジャパン株式会社

18.3.5. 検疫及び馴化

入手した動物は5日間（投与群：2023年11月15日～11月20日、回復群：2023年11月22日～11月27日）の検疫期間、その後、投与群は3日間（2023年11月21日～11月23日）、回復群は4日間（2023年11月28日～12月1日）の馴化期間を設けた。この間に体重測定を3回、一般状態の観察を1日1回、行動機能（FOB）観察を1回行い、体重推移、一般状態及びFOBに異常の認められない動物を群分けに用いた（Attachments 7-1, 7-2, 8-1, 8-2, 9-1, 9-2, 10-1, 10-2, 11-1, 11-2, 12-1 及び 12-2）。

18.3.6. 群分け

各投与開始日にコンピュータプログラム（IBUKI, 株式会社日本バイオリサーチセンター）を用いて、各群の平均体重及び分散がほぼ等しくなるように群分けした。ただし、個々の動物の体重が、平均値の±20%以内になるように群分けした。投与開始日の週齢は雌雄とも5週齢であり、体重範囲は雄が153～185 g、雌が138～169 gであった。

投与群群分け日に群分け残余雄から検疫・馴化動物番号の若い順に2匹を選び、雌の回復期間終了日に実施した微生物モニタリング検査に用いた。微生物モニタリング検査において、感染を示唆するような異常はみられなかった。

分析機関：北山ラベス株式会社

微生物モニタリング検査に用いなかった群分け残余雄及び群分け残余雌は、試験系から除外した。

18.3.7. 個体識別法

動物は入手日に緑色油性インクによる尾への記入法及び緑色油性インクによる四肢への色素塗布法を併用して識別をした。群分け後も同様に識別した。各ケージには、検疫・馴化期間中は試験番号、入手年月日、検疫・馴化動物番号を記入したラベルを、群分け後は試験番号、投与量、

検疫・馴化動物番号及び動物番号を記入し、群ごとに色分けしたラベルを取り付けた。なお、FOB観察などのBlindで検査する場合は、検疫・馴化期間中のラベルを取り付けた。

18.3.8. 環境条件及び飼育管理

管理温度：20.0～26.0°C（実測値：21.8～26.4°C），管理湿度：40.0～70.0%RH（実測値：39.5～62.1%RH），明暗各12時間（照明：6時～18時），換気回数12回/時（フィルターを通した新鮮空気）に維持された飼育室（E棟3号室。ただし、検疫期間中はE棟1号室）で動物を飼育した。

検疫期間中はステンレス製懸垂式ケージ（W：240×D：380×H：200mm）を用いて1ケージあたり5匹までの雌雄別群飼育とし、馴化期間中及び群分け後は同ケージを用いて個別飼育した。

ケージ、給餌器の交換は2週間に1回以上行い、給水瓶及び受皿の交換は1週間に2回以上行った。動物飼育室の清掃・消毒は毎日行った。

18.3.9. エンリッチメント

飼育期間中、環境エンリッチメントとしてパルシート（オリエンタル酵母工業株式会社）を入れた。交換は2週間に1回以上行った。ただし、絶食時には環境エンリッチメントを使用しなかった。

18.3.10. 飼料

製造後9ヵ月以内の固型飼料（CRF-1，オリエンタル酵母工業株式会社）を給餌器に入れ、自由に摂取させた。ただし、剖検前日の夕刻から絶食した。使用した飼料のロットについて、飼料中の汚染物質濃度、細菌数及び栄養成分含量が試験施設の許容基準に適合していることを確認した。

分析機関：ユーロフィン・フード・テストング株式会社（汚染物質）及びオリエンタル酵母工業株式会社（細菌数及び栄養成分）

18.3.11. 飲料水

水道水を給水瓶を用いて自由に摂取させた。飲料水中の汚染物質濃度及び細菌数をほぼ6ヵ月ごとに分析し、試験施設の許容基準に適合していることを確認した。

分析機関：株式会社環境公害センター

18.4. 投与

18.4.1. 投与経路

投与経路：経口

選択理由：プロピオン酸エチルは、継続して経口的に人に摂取される可能性が考えられるため、経口投与を選択した。

18.4.2. 投与方法

投与方法：ディスポーザブルラット用金属製経口ゾンデ（有限会社フチガミ器械）を取り付けたディスポーザブルポリプロピレン製注射筒（テルモ株式会社）を用いて強制経口投与した。

第2～4群投与時には、注射筒を1匹毎に交換し、マグネチックスターラーで攪拌しながら注射筒に吸引した。

選択理由：被験物質を繰り返し吸引・排出することによりゴムが変性することが懸念されることから、第2～4群投与時には、注射筒を1匹毎に交換した。その他は当試験施設で用いられている通常の方法である。

18.4.3. 投与液量、投与時刻及び投与回数

投与液量：投与日に直近の体重を基準とし、3 mL/kg で算出した。

投与時刻：8時30分～14時57分までの間に行った。

投与回数：通常の毒性試験に準じて1日1回、計28回とした。

18.5. 群構成及び投与量

18.5.1. 群構成

群構成は、以下に示したように被験物質投与群として3群を設定し、その他に対照群を設けた。各群の動物数は、対照群、300及び1000 mg/kg 群を雌雄各10例、100 mg/kg 群を雌雄各5例とした。

群	試験群	投与量 (濃度)	ラベル の色	動物数 (動物番号)	
				雄	雌
第1群	対照 (コーン油)	0 mg/kg (0 mg/mL)	白色	5 ^{a)} +5 ^{b)} 10 (M01101～M01110)	5 ^{a)} +5 ^{b)} 10 (F01151～F01160)
第2群	プロピオン酸エチル	100 mg/kg (33 mg/mL)	茶色	5 ^{a)} 5 (M02201～M02205)	5 ^{a)} 5 (F02251～F02255)
第3群	プロピオン酸エチル	300 mg/kg (100 mg/mL)	青色	5 ^{a)} +5 ^{b)} 10 (M03301～M03310)	5 ^{a)} +5 ^{b)} 10 (F03351～F03360)
第4群	プロピオン酸エチル	1000 mg/kg (333 mg/mL)	紫色	5 ^{a)} +5 ^{b)} 10 (M04401～M04410)	5 ^{a)} +5 ^{b)} 10 (F04451～F04460)

a) 投与群：投与期間終了時に剖検

b) 回復群：回復期間（14日間）終了時に剖検

18.5.2. 投与量設定の理由

本試験の投与量は、雌雄ラットを用いた2週間経口投与による予備試験²⁾（試験番号：430156、投与段階：0, 30, 100, 300, 1000 mg/kg）の結果から決定した。予備試験において、死亡例及び瀕死例は、雌雄ともいずれの群にも認められなかった。統計学的には、雄の1000 mg/kg 投与で白

血球数、リンパ球数及び単球数の低値、雌の 1000 mg/kg 投与で血清中の無機リン及び脾臓の相対重量の高値がみられたが、その他に投与量に依存した変化は認められなかった。

したがって、「新規化学物質等に係る試験の方法について」において「哺乳類を用いる 28 日間反復投与毒性試験」の最高投与限度用量とされる 1000 mg/kg を当試験の高用量とし、以下公比約 3 で 300 及び 100 mg/kg 群を設けた。

なお、対照として被験物質と同一容量の媒体（コーン油）を投与する群を設けた。

18.6. 観察及び検査項目

18.6.1. 一般状態及び死亡

一般状態及び死亡の有無の観察は、投与期間中は毎日投与前・後の 2 回（ただし、剖検日は剖検前 1 回）ならびに回復期間中は毎日 1 回観察した。なお、行動機能（FOB）観察日及び自発運動量測定日は、検査終了後に投与後の一般状態を観察した。

18.6.2. 体重測定

体重は、投与 1（群分け時の体重）、8、15、22、28、29（回復 1 日）、回復 8、14 及び 15 日に測定した。

18.6.3. 摂餌量測定

摂餌量は、投与 1、8、15、22、回復 1 及び 8 日に給餌量を測定し、翌日に残量を測定し、1 日量を算出した。図表の表示は、残量の測定日とした。

18.6.4. 行動機能（FOB）観察

全例について投与開始前（検疫 5 日の検疫期間終了後：馴化 0 日）、投与群について投与 7、14、21 及び 27 日に観察した。観察時刻は、投与後 1 時間（±10 分）とし、E 棟 1 号室で Blind 方式にて実施した。

- 1) 姿勢、眼瞼閉鎖状態、常同行動（過度の毛づくろい、反復旋回運動、噛み付き行動）、間代性痙攣及び強直性痙攣はケージ内で観察した。
- 2) ケージからの出し易さ、扱い易さ、筋の緊張、被毛の状態、粘膜の状態、流涙、流涎、立毛、瞳孔及び呼吸状態は手に持って観察した。
- 3) 排尿、排便、立ち上がり及び毛づくろい回数はオープンフィールド内で 2 分間観察した。また、同時に歩行状態、眼瞼閉鎖状態、覚醒度、異常行動及び正向反射をオープンフィールド内で観察した。

18.6.5. 感覚応答検査

投与群について、投与 27 日の FOB 観察後、瞳孔反射、接近反射、触覚反射、聴覚反射及び痛覚反射を、作業台の上で検査した。

18.6.6. 握力測定

投与群について、投与 27 日の感覚応答検査終了後に CPU ゲージ (MODEL-9500, アイコーエンジニアリング株式会社) を用いて、前肢及び後肢の握力を連続 3 回測定した。3 回の測定値のうち、中央値を採用した。

18.6.7. 自発運動量測定

投与群について、投与 4 週 (雄は投与 25 日, 雌は投与 26 日) に SCANET MV-40 (有限会社メルクエスト) を使用し、歩行量及び立ち上がり回数を投与後 1 時間から投与後 2 時間まで測定し、10 分間隔で集計した。回復群については、回復 2 週 (雄は回復 10 日, 雌は回復 11 日) に 1 時間測定し、10 分間隔で集計した。

18.6.8. 尿検査

投与群は投与期間終了前 (投与 23 日), また, 回復群は回復期間終了前 (回復 12 日) に採尿ケージに入れ, 絶食・給水下で新鮮尿を採取した (投与期間終了前は当日の投与前)。引き続き給餌・給水下で 24 時間尿を採取した。ただし, 回復 12 日に爪はがれが認められた動物番号: M04406 は, 回復 13 日に新鮮尿を再採取した。得られた新鮮尿及び 24 時間尿を用いて以下の検査を行った。測定後の尿は廃棄した。

< 新鮮尿 >

項目	単位	測定方法	使用機器
色調	—	外観判定	—
pH	—	尿検査試験紙	尿化学分析装置 クリニテック アドバンタス (シーメンスヘルスケア・ダイアグノスティクス株式会社)
蛋白質	mg/dL		
ブドウ糖	mg/dL		
ケトン体	—		
ビリルビン	—		
潜血	—		
ウロビリノーゲン	E.U./dL		
沈渣 (上皮細胞, 赤血球, 白血球, 円柱, 結晶)	—	鏡検	顕微鏡 (オリンパス株式会社)

<24 時間尿 >

項目	単位	測定方法	使用機器
尿量 (UV)	mL	尿重量と尿比重 から算出	電子天秤
尿比重 (SG)	-	屈折率	デジタル臨床屈折計 SU-301 (エルマ販売株式会社)
Na K Cl	mEq/L mEq/L mEq/L	イオン選択電極法	全自動電解質分析装置 EA07 (株式会社エイアンドティー)

18.6.9. 血液学的検査

投与群は最終投与の翌日、また、回復群は回復期間終了後にセコバルビタールナトリウム 5% 水溶液の腹腔内投与 (1 mL/kg) による麻酔下で腹大動脈から EDTA-2K コーティングチューブ (ベノジェクト®II 真空採血管, VP-DK052K05, テルモ株式会社) に血液を採取し、以下の検査を行った。ただし、プロトロンビン時間、活性化部分トロンボプラスチン時間及びフィブリノーゲン濃度の検査には、血液と 3.2 w/v%クエン酸ナトリウムを 9:1 の割合で混合し、遠心機 (CF9RX, 日立工機株式会社) を用いて遠心分離 [4°C, 3000 rpm (2150 × g), 15 分間] して得た血漿を用いた。なお、測定後の残余血液及び血漿は廃棄した。

項目	単位	測定方法	使用機器
赤血球数 (RBC)	10 ⁴ /μL	シーフローDC 検出法	多項目自動血球分析装置 XN-2000V (シスメックス株式会社)
ヘモグロビン量 (HGB)	g/dL	SLS ヘモグロビン法	
ヘマトクリット値 (HCT)	%	赤血球パルス波高値検出法	
血小板数 (PLT)	10 ⁴ /μL	フローサイトメトリー法	
平均赤血球容積 (MCV)	fL	RBC 及び HCT より算出	
平均赤血球色素量 (MCH)	pg	RBC 及び HGB より算出	
平均赤血球色素濃度 (MCHC)	g/dL	HCT 及び HGB より算出	
白血球数 (WBC)	10 ² /μL	フローサイトメトリー法	
白血球分類 [リンパ球 (LYMPH), 好中球 (NEUT), 好酸球 (EO), 好塩基球 (BASO), 単球 (MONO)]	%及び 10 ² /μL		
網状赤血球比率及び網状赤血球数 (RET)	%及び 10 ⁴ /μL		
プロトロンビン時間 (PT)	sec.	光散乱検出方式	全自動血液凝固測定装置 CA-620 (シスメックス株式会社)
活性化部分トロンボプラスチン時間 (APTT)	sec.		
フィブリノーゲン濃度 (Fbg)	mg/dL		

18.6.10. 血液生化学的検査

血液学的検査用の血液と同時期に、腹大動脈から採取した血液から、遠心機 (CF9RX, 日立工機株式会社) を用いて遠心分離 [4°C, 3000 rpm (2150 × g), 15 分間] して得た血清は、測定用 4 本と保存用 1 本に分けて分取した。

測定用血清 (1 本) を用いて以下の検査を行い、測定後の残余血清は廃棄した。残りの測定用血清 (3 本) 及び保存用血清は、超低温フリーザー (CLN-51UD2, 日本フリーザー株式会社) で凍結保存 (管理温度: -90~-70°C) し、最終報告書 (案) 作成後から最終報告書作成までの間に廃棄した。

項目	単位	測定方法	使用機器
AST	U/L	JSCC 標準化対応法	生化学自動分析装置 AU 480 (ベックマン・コールター株式会社)
ALT	U/L	JSCC 標準化対応法	
ALP	U/L	IFCC 標準化対応法	
総コレステロール (T-Cho)	mg/dL	CO・HMMPS 法	
トリグリセライド (TG)	mg/dL	GPO・HMMPS 法 (グリセリン消去法)	
総蛋白 (TP)	g/dL	Biuret 法	
尿素窒素 (UN)	mg/dL	ウレアーゼ・GIDH 法 (アンモニア消去法)	
クレアチニン (CRE)	mg/dL	クレアチナーゼ・HMMPS 法	
総ビリルビン (T-Bil)	mg/dL	BOD 法	
ブドウ糖 (Glu)	mg/dL	ヘキソキナーゼ・G-6-PDH 法	
無機リン (IP)	mg/dL	PNP・XDH 法	
カルシウム (Ca)	mg/dL	o-CPC 法	
ナトリウム (Na)	mEq/L	イオン選択電極法	
カリウム (K)	mEq/L	イオン選択電極法	
塩素 (Cl)	mEq/L	イオン選択電極法	
蛋白分画	%	電気泳動法	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)
A/G 比	-	蛋白分画値からの算出	
アルブミン (Alb)	g/dL	アルブミン分画値と総蛋白値から算出	-

18.6.11. 剖検

剖検日に雌の膣垢検査を行い、剖検時の性周期のステージを確認した。

18.6.9 及び 18.6.10 の項で採血した動物をさらに放血して安楽死させた後に剖検した。

18.6.12. 器官重量の測定

剖検時に、全生存例について以下の器官重量を測定した。なお、甲状腺重量は、20%中性緩衝ホルマリンで固定後（投与群は固定翌日、回復群は固定3日後）、測定した。対器官は一括秤量した。さらに、剖検前の体重を基準として器官重量の体重比（相対重量）を算出した。

脳、甲状腺（上皮小体を含む）、胸腺、心臓、肝臓、脾臓、腎臓、副腎、雄性生殖器〔精巣、精巣上体、前立腺、精囊（凝固腺を含む）〕、雌性生殖器（卵巣、子宮）。

18.6.13. 病理組織学的検査

以下の器官又は組織を20%中性緩衝ホルマリンに固定した。ただし、肺及び気管は20%中性緩衝ホルマリンを注入後、浸漬固定し、精巣及び精巣上体は改変ダビッドソン液に固定した。また、眼球はグルタルアルデヒド・ホルマリンで固定後（投与群は固定翌日、回復群は固定後2時間以降）、20%中性緩衝ホルマリンで再固定した。なお、胸骨及び大腿骨は、ギ酸ホルマリンを用いて脱灰を行った。

心臓、肺、気管、肝臓、膵臓、唾液腺（顎下腺）、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、胸腺、脾臓、腸間膜リンパ節、腋窩リンパ節、腎臓、膀胱、精巣、精巣上体、前立腺、精嚢（凝固腺を含む）、卵巣、子宮（頸部を含む）、膣、皮膚、乳腺、下垂体、副腎、甲状腺（上皮小体を含む）、脳（大脳、小脳、橋）、脊髄（頸部、胸部、腰部）、坐骨神経、眼球、ハーダー腺、大腿直筋、胸骨（骨髄を含む）、大腿骨（骨髄を含む）。

投与群の対照群及び1000 mg/kg 群について常法に従いパラフィン包埋後、HE染色組織標本作製し、病理組織学的検査を行った。なお、精巣（両側）は横断面を切り出し、PAS-ヘマトキシリン染色組織標本も作製し、病理組織学的検査を行った。

その他、剖検で異常の認められた回復群雄300 mg/kg 群の1例（動物番号：M03306）の精巣・精巣上体については、回復群雄対照群の1例（動物番号：M01106）の精巣・精巣上体とともに病理組織学的検査を行った。なお、切り出し後の器官・組織は、10%中性緩衝ホルマリンで保存した。

18.7. 人道的エンドポイント

死期の迫りが明白と考えられた動物（瀕死例）は、人道的エンドポイントを適用する計画であったが、適用例はいなかった。

18.8. 統計学的方法

体重、摂餌量、FOBにおける排尿、排便、立ち上がり及び毛づくろい回数、握力、自発運動量、尿量、尿比重、尿電解質、血液学的検査、血液生化学的検査及び器官重量（相対重量を含む）は、各群で平均値及び標準偏差を算出した。有意差検定は、対照群とプロピオン酸エチル群との間で行った。すなわち、Bartlett 検定³⁾による等分散性の検定を行い、等分散の場合にはDunnett 検定⁴⁾を用いて行った。一方、等分散と認められなかった場合は、Steel 検定⁵⁾を用いて行った。

FOB（排尿、排便、立ち上がり及び毛づくろい回数を除く）及び感覚応答検査に関する項目は、各群で平均値を算出し、Steel 検定を行った。

Dunnett 検定及びSteel 検定には、統計パッケージSASのPROBMC関数⁶⁾を使用した。

有意水準は5%とし、5%未満（ $p < 0.05$ ）と1%未満（ $p < 0.01$ ）とに分けて表示した。

病理組織学的検査において、投与群の1000 mg/kg 群で毒性が示唆され、他の投与群及び回復群についても検査を実施した器官・組織の所見については、対照群との群間比較を上記のSteel 検定

を実施し、そこで対照群との間に有意差が認められた場合は、Cochran・Armitageの傾向検定を用いて用量反応性を検定する計画であったが、対象となる所見は認められなかった。

一般状態、新鮮尿での検査項目、膿垢検査及び剖検所見については、統計学的解析を実施しなかった。

19. 試験成績

19.1. 一般状態

19.1.1. 雄 (Table 1 ; Appendices 1-1~1-4)

死亡例及び瀕死例はいずれの群にも認められなかった。

投与期間中には、いずれの群とも一般状態の異常はみられなかった。

回復期間中には、いずれの群とも一般状態の異常はみられなかった。

19.1.2. 雌 (Table 2 ; Appendices 2-1~2-4)

死亡例及び瀕死例はいずれの群にも認められなかった。

投与期間中には、いずれの群とも一般状態の異常はみられなかった。

回復期間中には、いずれの群とも一般状態の異常はみられなかった。

19.2. 体重

19.2.1. 雄 (Table 3 ; Fig. 2 ; Appendices 3-1~3-4)

投与期間中には、各被験物質群とも対照群と比べて各測定日の体重に有意差はみられなかった。

回復期間中には、各被験物質群とも対照群と比べて各測定日の体重に有意差はみられなかった。

19.2.2. 雌 (Table 4 ; Fig. 3 ; Appendices 4-1~4-4)

投与期間中には、各被験物質群とも対照群と比べて各測定日の体重に有意差はみられなかった。

回復期間中には、各被験物質群とも対照群と比べて各測定日の体重に有意差はみられなかった。

19.3. 摂餌量

19.3.1. 雄 (Table 5 ; Fig. 4 ; Appendices 5-1~5-4)

投与期間中には、各被験物質群とも対照群と比べて各測定日の摂餌量に有意差はみられなかった。

回復期間中には、各被験物質群とも対照群と比べて各測定日の摂餌量に有意差はみられなかった。

19.3.2. 雌 (Table 6 ; Fig. 5 ; Appendices 6-1~6-4)

投与期間中には、各被験物質群とも対照群と比べて各測定日の摂餌量に有意差はみられなかった。

回復期間中には、各被験物質群とも対照群と比べて各測定日の摂餌量に有意差はみられなかった。

19.4. FOB

19.4.1. 雄 (Table 7 ; Appendices 7-1~7-4)

各被験物質群とも対照群と比べて各測定日の排尿, 排便, 立ち上がり及び毛づくろい回数に有意差はみられなかった。

いずれの群とも各測定日のその他いずれの項目にも異常はみられなかった。

19.4.2. 雌 (Table 8 ; Appendices 8-1~8-4)

各被験物質群とも対照群と比べて各測定日の排尿, 排便, 立ち上がり及び毛づくろい回数に有意差はみられなかった。

いずれの群とも各測定日のその他いずれの項目にも異常はみられなかった。

19.5. 感覚応答

19.5.1. 雄 (Table 9 ; Appendices 9-1~9-4)

いずれの群ともいずれの項目にも異常はみられなかった。

19.5.2. 雌 (Table 10 ; Appendices 10-1~10-4)

いずれの群ともいずれの項目にも異常はみられなかった。

19.6. 握力

19.6.1. 雄 (Table 11 ; Appendices 11-1~11-4)

各被験物質群とも対照群と比べて前肢及び後肢の握力に有意差はみられなかった。

19.6.2. 雌 (Table 12 ; Appendices 12-1~12-4)

1000 及び 300 mg/kg 群では, 対照群と比べて前肢の握力の有意な高値がみられた。

100 mg/kg 群では, 対照群と比べて前肢及び後肢の握力に有意差はみられなかった。

19.7. 自発運動量

19.7.1. 投与 4 週雄 (Table 13 ; Appendices 13-1~13-4)

1000 及び 300 mg/kg 群では, 対照群と比べて投与後 110~120 分の歩行量及び立ち上がり回数に有意な低値がみられた。1000 mg/kg 群では, 投与後 60~120 分の歩行量に有意な低値がみられた。

100 mg/kg 群では, 対照群と比べて自発運動量に有意差はみられなかったが, 投与後 60~70 分, 70~80 分, 80~90 分, 90~100 分, 100~110 分及び 60~120 分の歩行量の平均値は, 対照群の平均値より高値であった。

19.7.2. 投与 4 週雌 (Table 14 ; Appendices 14-1~14-4)

1000 mg/kg 群では、対照群と比べて投与後 70~80 分の立ち上がり回数に有意な低値がみられた。

300 及び 100 mg/kg 群では、対照群と比べて自発運動量に有意差はみられなかった。

19.7.3. 回復 2 週雄 (Table 15 ; Appendices 15-1~15-3)

300 mg/kg 群では、対照群と比べて 30~40 分及び 0~60 分の歩行量及び 0~60 分の立ち上がり回数に有意な低値がみられた。

1000 mg/kg 群では、対照群と比べて自発運動量に有意差はみられなかった。

19.7.4. 回復 2 週雌 (Table 16 ; Appendices 16-1~16-3)

各被験物質群とも対照群と比べて自発運動量に有意差はみられなかった。

19.8. 尿検査

19.8.1. 投与期間終了前雄 (Table 17 ; Appendices 17-1~17-4)

各被験物質群とも、対照群と比べて尿量、尿比重及び尿電解質に有意差はみられなかった。

各被験物質群とも、色調、pH、蛋白質、ブドウ糖、ケトン体、ビリルビン、潜血、ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった。

19.8.2. 投与期間終了前雌 (Table 18 ; Appendices 18-1~18-4)

各被験物質群とも、対照群と比べて尿量、尿比重及び尿電解質に有意差はみられなかった。

各被験物質群とも、色調、pH、蛋白質、ブドウ糖、ケトン体、ビリルビン、潜血、ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった。

19.8.3. 回復期間終了前雄 (Table 19 ; Appendices 19-1~19-3)

各被験物質群とも、対照群と比べて尿量、尿比重及び尿電解質に有意差はみられなかった。

各被験物質群とも、色調、pH、蛋白質、ブドウ糖、ケトン体、ビリルビン、潜血、ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった。

19.8.4. 回復期間終了前雌 (Table 20 ; Appendices 20-1~20-3)

1000 mg/kg 群では、対照群と比べて尿量に有意な高値がみられた。

300 mg/kg 群では、対照群と比べて尿量、尿比重及び尿電解質に有意差はみられなかった。

各被験物質群とも、色調、pH、蛋白質、ブドウ糖、ケトン体、ビリルビン、潜血、ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった。

19.9. 血液学的検査

19.9.1. 投与期間終了時雄 (Table 21 ; Appendices 21-1~21-4)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.9.2. 投与期間終了時雌 (Table 22 ; Appendices 22-1~22-4)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.9.3. 回復期間終了時雄 (Table 23 ; Appendices 23-1~23-3)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.9.4. 回復期間終了時雌 (Table 24 ; Appendices 24-1~24-3)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.10. 血液生化学的検査

19.10.1. 投与期間終了時雄 (Table 25 ; Appendices 25-1~25-4)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.10.2. 投与期間終了時雌 (Table 26 ; Appendices 26-1~26-4)

1000 及び 100 mg/kg 群では、対照群と比べて Na (血清中ナトリウム濃度) の有意な低値がみられた。

300 mg/kg 群では、対照群と比べて各測定項目に有意差はみられなかった。

19.10.3. 回復期間終了時雄 (Table 27 ; Appendices 27-1~27-3)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.10.4. 回復期間終了時雌 (Table 28 ; Appendices 28-1~28-3)

各被験物質群とも、対照群と比べて各測定項目に有意差はみられなかった。

19.11. 剖検所見

19.11.1. 投与期間終了時雄 (Table 29 ; Appendices 29-1~29-4)

精巣及び精巣上体の小型化 (両側) が 1000 mg/kg 群で 1 例にみられた。300, 100 mg/kg 群及び対照群では、異常はみられなかった。

19.11.2. 投与期間終了時雌 (Table 30 ; Appendices 30-1~30-4)

いずれの群とも、異常はみられなかった。

19.11.3. 回復期間終了時雄 (Table 31 ; Appendices 31-1~31-3)

精巣及び精巣上体の小型化(両側)が 300 mg/kg 群で 1 例にみられた。1000 mg/kg 群及び対照群では、異常はみられなかった。

19.11.4. 回復期間終了時雌 (Table 32 ; Appendices 32-1~32-3)

いずれの群とも、異常はみられなかった。

19.12. 器官重量

19.12.1. 投与期間終了時雄 (Table 33 ; Appendices 33-1~33-4)

剖検日の体重は、各投与群とも対照群と比べて有意差はみられなかった。

300 及び 100 mg/kg 群では、対照群と比べて副腎の絶対重量の有意な低値がみられた。

1000 mg/kg 群では、対照群と比べて各器官の絶対重量及び相対重量に有意差はみられなかった。

19.12.2. 投与期間終了時雌 (Table 34 ; Appendices 34-1~34-4)

剖検日の体重は、各投与群とも対照群と比べて有意差はみられなかった。

各被験物質群とも、対照群と比べて各器官の絶対重量及び相対重量に有意差はみられなかった。

19.12.3. 回復期間終了時雄 (Table 35 ; Appendices 35-1~35-3)

剖検日の体重は、各投与群とも対照群と比べて有意差はみられなかった。

1000 mg/kg 群では、対照群と比べて心臓の絶対重量の有意な低値がみられた。

300 mg/kg 群では、対照群と比べて各器官の絶対重量及び相対重量に有意差はみられなかった。

19.12.4. 回復期間終了時雌 (Table 36 ; Appendices 36-1~36-3)

剖検日の体重は、各投与群とも対照群と比べて有意差はみられなかった。

各被験物質群とも、対照群と比べて各器官の絶対重量及び相対重量に有意差はみられなかった。

19.13. 病理組織学的検査

19.13.1. 投与期間終了時雄 (Table 37 ; Appendices 37-1, 37-2)

心臓：ごく軽度の限局性の単核細胞浸潤が 1000 mg/kg 群で 1 例にみられた。

空腸：ごく軽度のパイエル板の鉍質沈着が 1000 mg/kg 群で 2 例、対照群で 1 例にみられた。

腎臓：ごく軽度の片側の嚢胞が対照群で 2 例にみられた。

精巣：中等度の両側の精細管の変性/萎縮が 1000 mg/kg 群で 1 例にみられた。なお、当該例は剖検時に精巣及び精巣上体の小型化がみられた。

精巣上体：高度の両側の精子減少が 1000 mg/kg 群で 1 例にみられた。なお、当該例は剖検時に精巣及び精巣上体の小型化がみられ、精巣の病理組織学的検査で精細管の変性/萎縮がみられた。

前立腺：ごく軽度のリンパ様細胞浸潤が 1000 mg/kg 群と対照群で各 1 例にみられた。
下垂体：ごく軽度の嚢胞が 1000 mg/kg 群で 1 例にみられた。
甲状腺：ごく軽度の鰓後体の遺残及び異所性胸腺が 1000 mg/kg 群で 1 例にみられた。
眼球：ごく軽度の片側の網膜異形性が対照群で 1 例にみられた。

19.13.2. 投与期間終了時雌 (Table 38 ; Appendices 38-1, 38-2)

空腸：ごく軽度のパイエル板の鉍質沈着が 1000 mg/kg 群で 1 例，対照群で 2 例にみられた。
腎臓：ごく軽度の片側の嚢胞あるいは梗塞が対照群で各 1 例にみられた。
下垂体：ごく軽度の嚢胞が対照群で 1 例にみられた。
甲状腺：ごく軽度の鰓後体の遺残が 1000 mg/kg 群で 1 例にみられた。
眼球：ごく軽度の片側の網膜異形性が 1000 mg/kg 群で 1 例にみられた。

19.13.3. 回復期間終了時雄 (Table 39 ; Appendices 39-1, 39-2)

精巣：軽度の両側の精細管の変性／萎縮が 300 mg/kg 群で 1 例にみられた。なお，当該例は剖検時に精巣及び精巣上体の小型化がみられた。

精巣上体：高度の両側の精子減少が 300 mg/kg 群で 1 例にみられた。なお，当該例は剖検時に精巣及び精巣上体の小型化がみられ，精巣の病理組織学的検査で精細管の変性／萎縮がみられた。

20. 考察

プロピオン酸エチルを雌雄ラットに 28 日間反復経口投与し，さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性学的影響を検討した。

投与 4 週の自発運動量において，雄の 1000 mg/kg 群で投与後 60～120 分の歩行量に有意な低値がみられた。

雄の 1000 及び 300 mg/kg 群では，投与後 110～120 分の歩行量及び立ち上がり回数に有意な低値がみられたが，対照群の投与後 90～100 分の歩行量とはほぼ同値であり，投与後 90～100 分及び 100～110 分の立ち上がり回数と同値であることから，被験物質による影響とは判断しなかった。また，100 mg/kg 群の歩行量の平均値は対照群の平均値より高値で推移したが，回復 2 週の対照群より低値であることから，被験物質による影響とは判断しなかった。雌の 1000 mg/kg 群では，投与後 70～80 分の立ち上がり回数に有意な低値がみられたが，対照群の投与後 100～110 分の立ち上がり回数と同値であることから，被験物質による影響とは判断しなかった。さらに，回復 2 週において，雄の 300 mg/kg 群で 30～40 分及び 0～60 分の歩行量及び 0～60 分の立ち上がり回数に有意な低値がみられたが，投与量に関連した変化ではないことから，被験物質による影響とは判断しなかった。

死亡例は雌雄ともいずれの群にも認められなかった。

一般状態，体重，摂餌量，行動機能 (FOB) 観察，感覚応答検査，血液学的検査では，雌雄のいずれにも投与に起因する変化は認められなかった。

雌の 1000 及び 300 mg/kg 群で前肢の握力の有意な高値がみられたが，その値の差は僅かであり，

高値であることから、被験物質による毒性学的影響とは判断しなかった。

回復期間雌の 1000 mg/kg 群で尿量の有意な高値、投与期間終了時雌の 1000 及び 100 mg/kg 群で血清中ナトリウム濃度の有意な低値がみられたが、当所の背景データ内〔尿量：11.0±4.7 (mL) : Attachment 13, 血清中ナトリウム濃度：142.7±1.7 (mEq/L) : Attachment 14〕の変化であることから、被験物質による影響とは判断しなかった。

投与期間終了時の剖検で 1000 mg/kg 群雄 1 例に精巣及び精巣上体の小型化（両側）がみられ、当該例の病理組織学的検査において、精巣の精細管の変性／萎縮及び精巣上体の精子の減少が認められた。しかしながら、1 例のみの変化であり、精細管の変性／萎縮はげっ歯類の背景病変で⁷⁾、精子の減少はその結果と考えられることから、被験物質による影響とは判断しなかった。同様に、回復期間終了時の剖検で 300 mg/kg 群雄 1 例に精巣及び精巣上体の小型化（両側）がみられ、病理組織学的検査において、精巣の精細管の変性／萎縮及び精巣上体の精子の減少が認められた。

器官重量では、投与期間終了時雄の 300 及び 100 mg/kg 群で副腎の絶対重量の有意な低値、回復期間終了時雄の 1000 mg/kg 群で心臓の絶対重量の有意な低値がみられたが、当所の背景データ内〔副腎：58.8±8.4 (mg), 心臓：1.23±0.13 (g) : Attachment 15〕の変化であり、相対重量には有意差がみられなかったことから、被験物質による影響とは判断しなかった。

病理組織学的検査では、1000 mg/kg 群雄 1 例の心臓に限局性の単核細胞浸潤がみられたが、1 例のみの変化であり、げっ歯類の進行性心筋症は自然発生病変で、その初期病変である⁸⁾ことから、被験物質による影響とは判断しなかった。また、甲状腺の鰹後体の遺残及び異所性胸腺が 1000 mg/kg 群でみられたが、いずれも発生異常である⁹⁾ことから、被験物質による影響とは判断しなかった。その他の所見は、対照群でもみられ、げっ歯類で通常観察される変化であることから、被験物質による影響とは判断しなかった。

以上のように、プロピオン酸エチルの無毒性量は、雄では 1000 mg/kg 投与により投与後 60～120 分の歩行量に有意な低値が認められたことから 300 mg/kg/day、雌では 1000 mg/kg/day と考えられる。

21. 文献

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Table 1. Clinical signs in male rats

Group	Dose (mg/kg)	Number of animals and clinical signs	Days of administration																													
			1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
Ethyl propionate	100	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5		
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5		
	300	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
	1000	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

Table 1. (Continued) Clinical signs in male rats

Group	Dose (mg/kg)	Number of animals and clinical signs	Days of administration																												
			16		17		18		19		20		21		22		23		24		25		26		27		28		29		
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Control	0	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
Ethyl propionate	100	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	300	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	1000	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5

Pre: Before administration, Post: after administration.

Group	Dose (mg/kg)	Number of animals and clinical signs	Days of recovery														
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control	0	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Ethyl propionate	300	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	1000	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	

Table 2. Clinical signs in female rats

Group	Dose (mg/kg)	Number of animals and clinical signs	Days of administration																													
			1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10		
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
Ethyl propionate	100	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5		
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	300	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
	1000	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

Table 2. (Continued) Clinical signs in female rats

Group	Dose (mg/kg)	Number of animals and clinical signs	Days of administration																											
			16		17		18		19		20		21		22		23		24		25		26		27		28		29	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Ethyl propionate	100	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	300	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	1000	Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
		Normal	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

Pre: Before administration, Post: after administration.

Group	Dose (mg/kg)	Number of animals and clinical signs	Days of recovery														
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control	0	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
Ethyl propionate	300	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5		
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5		
	1000	Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5		
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5		

Table 3. Body weights of male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	10	5	10	10
Days of administration				
1	170 ± 8	166 ± 7	169 ± 9	169 ± 8
8	232 ± 11	226 ± 13	233 ± 16	229 ± 16
15	291 ± 17	287 ± 18	295 ± 24	289 ± 22
22	345 ± 21	335 ± 26	350 ± 31	344 ± 28
28	378 ± 26	364 ± 35	383 ± 40	378 ± 37
Number of animals	5	0	5	5
Days of recovery				
1	393 ± 23	-	416 ± 27	391 ± 31
8	439 ± 29	-	461 ± 30	437 ± 35
14	461 ± 27	-	490 ± 32	456 ± 32

Each value shows mean (g) ± SD.

Table 4. Body weights of female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	10	5	10	10
Days of administration				
1	153 ± 9	148 ± 7	153 ± 9	153 ± 9
8	184 ± 12	178 ± 10	182 ± 10	185 ± 12
15	209 ± 15	202 ± 12	205 ± 18	212 ± 16
22	227 ± 17	223 ± 13	227 ± 20	236 ± 20
28	246 ± 22	237 ± 14	243 ± 21	253 ± 24
Number of animals	5	0	5	5
Days of recovery				
1	250 ± 23	-	244 ± 18	259 ± 17
8	264 ± 21	-	256 ± 17	274 ± 16
14	272 ± 23	-	265 ± 23	279 ± 16

Each value shows mean (g) ± SD.

Table 5. Food consumption in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	10	5	10	10
Days of administration				
2	21 ± 2	20 ± 1	21 ± 1	22 ± 1
9	24 ± 2	26 ± 1	25 ± 3	25 ± 3
16	25 ± 2	26 ± 2	26 ± 3	26 ± 3
23	26 ± 3	26 ± 2	27 ± 4	27 ± 3
Number of animals	5	0	5	5
Days of recovery				
2	30 ± 3	-	30 ± 3	29 ± 3
9	30 ± 2	-	33 ± 4	31 ± 2

Each value shows mean (g/day) ± SD.

Table 6. Food consumption in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	10	5	10	10
Days of administration				
2	16 ± 2	16 ± 1	17 ± 2	17 ± 2
9	17 ± 3	20 ± 1	17 ± 2	18 ± 2
16	19 ± 3	16 ± 3	17 ± 1	19 ± 2
23	19 ± 3	17 ± 1	18 ± 2	19 ± 3
Number of animals	5	0	5	5
Days of recovery				
2	17 ± 4	-	18 ± 2	21 ± 4
9	21 ± 2	-	21 ± 2	22 ± 5

Each value shows mean (g/day) ± SD.

Table 7. Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Posture				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Palpebral closure				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Excessive grooming				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Repetitive circling				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Biting behavior				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Clonic convulsions				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

 Biting behavior: 1: Not observed (normal score), 2: observed.

 Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Tonic convulsions				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions, 4: saltatory convulsions,
5: asphyxial convulsions.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Ease of removal from cage				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Ease of handling				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score),

3: struggling and trying to bite observer's hand.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Muscle tone				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Fur conditions				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

(Continued)

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Mucous membranes				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Lacrimation				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

(Continued)

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Salivation				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Piloerection				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

(Continued)

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Pupil size				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Respiration				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

(Continued)

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Frequency of urination				
Days of administration				
Pre	1.0 ± 1.0	0.6 ± 0.5	0.4 ± 0.5	0.6 ± 0.9
7	0.6 ± 0.5	0.8 ± 0.4	0.4 ± 0.5	1.0 ± 0.7
14	0.8 ± 0.4	0.6 ± 0.5	0.2 ± 0.4	0.8 ± 0.8
21	0.6 ± 0.5	0.2 ± 0.4	0.2 ± 0.4	0.6 ± 0.5
27	0.4 ± 0.5	0.6 ± 0.9	0.2 ± 0.4	0.2 ± 0.4
Frequency of defecation				
Days of administration				
Pre	1.2 ± 0.8	1.0 ± 1.0	2.0 ± 1.6	0.6 ± 1.3
7	1.8 ± 1.9	2.0 ± 1.2	2.8 ± 2.7	1.2 ± 1.3
14	1.4 ± 0.9	2.2 ± 0.8	2.6 ± 1.5	0.8 ± 1.3
21	1.4 ± 1.3	2.0 ± 2.1	1.8 ± 2.5	1.6 ± 0.5
27	0.8 ± 1.3	1.2 ± 1.6	2.2 ± 2.9	0.6 ± 1.3

Each value shows mean ± SD.

Pre: Before administration period.

(Continued)

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Frequency of rearing				
Days of administration				
Pre	8.0 ± 5.4	5.2 ± 3.9	7.4 ± 3.6	4.4 ± 1.7
7	4.2 ± 1.6	2.8 ± 1.9	3.2 ± 3.0	1.4 ± 0.9
14	1.0 ± 1.7	2.6 ± 2.7	1.4 ± 1.7	0.4 ± 0.5
21	1.6 ± 1.5	3.4 ± 3.6	4.0 ± 5.4	0.2 ± 0.4
27	9.2 ± 7.3	5.4 ± 3.2	6.6 ± 4.0	4.8 ± 4.3
Frequency of grooming				
Days of administration				
Pre	0.0 ± 0.0	0.2 ± 0.4	0.2 ± 0.4	0.0 ± 0.0
7	0.6 ± 1.3	0.0 ± 0.0	0.0 ± 0.0	0.2 ± 0.4
14	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
21	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
27	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0

Each value shows mean ± SD.

Pre: Before administration period.

(Continued)

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Gait				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Palpebral closure				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Consciousness				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Behavioral abnormalities				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

Table 7. (Continued) Detailed clinical signs by FOB in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Righting reflex				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score), 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Table 8. Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Posture				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Palpebral closure				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Excessive grooming				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Repetitive circling				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Biting behavior				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Clonic convulsions				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

 Biting behavior: 1: Not observed (normal score), 2: observed.

 Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals in cages				
Tonic convulsions				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions, 4: saltatory convulsions,
5: asphyxial convulsions.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Ease of removal from cage				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Ease of handling				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score),

3: struggling and trying to bite observer's hand.

(Continued)

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Muscle tone				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Fur conditions				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

(Continued)

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Mucous membranes				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Lacrimation				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Salivation				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Piloerection				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

(Continued)

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Observation of animals on observer's palm				
Pupil size				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Respiration				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

(Continued)

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Frequency of urination				
Days of administration				
Pre	1.0 ± 1.2	0.8 ± 0.8	0.8 ± 0.8	0.4 ± 0.5
7	0.2 ± 0.4	0.2 ± 0.4	0.0 ± 0.0	0.2 ± 0.4
14	0.0 ± 0.0	0.4 ± 0.5	0.2 ± 0.4	0.0 ± 0.0
21	0.2 ± 0.4	0.0 ± 0.0	0.2 ± 0.4	0.0 ± 0.0
27	0.2 ± 0.4	0.4 ± 0.5	0.0 ± 0.0	0.0 ± 0.0
Frequency of defecation				
Days of administration				
Pre	0.6 ± 0.9	0.2 ± 0.4	0.4 ± 0.9	0.0 ± 0.0
7	0.8 ± 1.8	0.8 ± 1.8	0.6 ± 1.3	0.2 ± 0.4
14	0.0 ± 0.0	1.0 ± 2.2	0.0 ± 0.0	0.0 ± 0.0
21	0.0 ± 0.0	0.6 ± 1.3	0.0 ± 0.0	0.0 ± 0.0
27	0.0 ± 0.0	1.0 ± 2.2	1.0 ± 2.2	0.2 ± 0.4

Each value shows mean ± SD.

Pre: Before administration period.

(Continued)

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control		Ethyl propionate			
Dose (mg/kg)	0		100	300	1000	
Number of animals	5		5	5	5	
Open-field test						
Frequency of rearing						
Days of administration						
Pre	7.0 ± 2.3		7.2 ± 5.4		3.8 ± 1.9	6.2 ± 2.3
7	2.8 ± 4.2		5.0 ± 2.8		3.4 ± 2.6	2.6 ± 1.5
14	6.0 ± 9.6		6.4 ± 6.3		4.0 ± 2.6	3.4 ± 2.9
21	9.4 ± 8.3		6.6 ± 4.0		7.8 ± 6.3	7.0 ± 2.7
27	10.2 ± 3.3		9.4 ± 7.4		8.0 ± 3.5	5.2 ± 4.5
Frequency of grooming						
Days of administration						
Pre	0.0 ± 0.0		0.0 ± 0.0		0.0 ± 0.0	0.2 ± 0.4
7	0.0 ± 0.0		0.0 ± 0.0		0.0 ± 0.0	0.0 ± 0.0
14	0.0 ± 0.0		0.0 ± 0.0		0.2 ± 0.4	0.0 ± 0.0
21	0.0 ± 0.0		0.0 ± 0.0		0.0 ± 0.0	0.0 ± 0.0
27	0.0 ± 0.0		0.0 ± 0.0		0.0 ± 0.0	0.0 ± 0.0

Each value shows mean ± SD.

(Continued)

Pre: Before administration period.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Gait				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Palpebral closure				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Consciousness				
Days of administration				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
27	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Behavioral abnormalities				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

(Continued)

Pre: Before administration period.

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

Table 8. (Continued) Detailed clinical signs by FOB in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Open-field test				
Righting reflex				
Days of administration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
27	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Each value shows mean (range).

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score), 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Table 9. Sensory response in male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Pupillary reflex	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Approaching behavior	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Response to touch	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Auditory reflex	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pain reflex	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)

Each value shows mean (range).

Findings were graded as follows;

- Pupillary reflex: 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior: 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch: 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex: 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Table 10. Sensory response in female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Pupillary reflex	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Approaching behavior	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Response to touch	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Auditory reflex	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pain reflex	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)

Each value shows mean (range).

Findings were graded as follows;

- Pupillary reflex: 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior: 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch: 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex: 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Table 11. Grip strength of male rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Grip strength (kg)				
Forelimb	0.582 ± 0.087	0.599 ± 0.040	0.613 ± 0.088	0.630 ± 0.058
Hindlimb	0.165 ± 0.020	0.166 ± 0.049	0.158 ± 0.019	0.165 ± 0.032

Each value shows mean ± SD.

Table 12. Grip strength of female rats

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Grip strength (kg)				
Forelimb	0.416 ± 0.007	0.479 ± 0.051	0.438 ± 0.024 #	0.465 ± 0.040 #
Hindlimb	0.128 ± 0.020	0.135 ± 0.022	0.123 ± 0.014	0.146 ± 0.016

Each value shows mean ± SD.

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

Table 13. Spontaneous motor activity of male rats (administration period)

Group	Control		Ethyl propionate					
Dose (mg/kg)	0		100		300		1000	
Number of animals	5		5		5		5	
Ambulatory counts								
Minutes after administration								
60-70	122	± 160	275	± 375	166	± 239	26	± 35
70-80	45	± 48	168	± 297	13	± 12	27	± 33
80-90	49	± 48	168	± 371	70	± 102	16	± 13
90-100	18	± 30	254	± 546	13	± 14	8	± 12
100-110	30	± 58	229	± 466	28	± 36	19	± 19
110-120	221	± 198	132	± 159	12	± 10 #	22	± 28 #
Total	486	± 284	1226	± 2036	302	± 259	119	± 47 #
Rearing counts								
Minutes after administration								
60-70	1	± 1	6	± 8	1	± 3	0	± 0
70-80	1	± 1	2	± 5	0	± 1	0	± 0
80-90	0	± 0	4	± 9	1	± 1	0	± 0
90-100	0	± 0	8	± 14	1	± 1	0	± 0
100-110	0	± 0	4	± 8	0	± 0	1	± 1
110-120	4	± 4	3	± 5	0	± 0 #	0	± 0 #
Total	5	± 5	27	± 46	3	± 4	1	± 1

Each value shows mean ± SD.

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

Table 14. Spontaneous motor activity of female rats (administration period)

Group	Control		Ethyl propionate					
Dose (mg/kg)	0		100		300		1000	
Number of animals	5		5		5		5	
Ambulatory counts								
Minutes after administration								
60-70	486	± 936	368	± 505	1592	± 2098	157	± 191
70-80	616	± 1127	781	± 1135	575	± 830	25	± 14
80-90	827	± 1041	32	± 59	505	± 1115	44	± 32
90-100	158	± 221	758	± 1159	254	± 495	33	± 29
100-110	37	± 44	171	± 253	201	± 431	520	± 1131
110-120	122	± 260	10	± 12	487	± 1065	31	± 23
Total	2246	± 1321	2119	± 2041	3614	± 5784	810	± 1108
Rearing counts								
Minutes after administration								
60-70	3	± 5	1	± 2	15	± 22	0	± 0
70-80	2	± 3	10	± 21	6	± 11	0	± 0 #
80-90	7	± 9	3	± 6	7	± 15	0	± 0
90-100	2	± 4	5	± 6	2	± 4	0	± 0
100-110	0	± 0	1	± 2	2	± 4	4	± 10
110-120	1	± 1	0	± 0	5	± 11	0	± 0
Total	14	± 12	20	± 27	37	± 66	5	± 10

Each value shows mean ± SD.

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

Table 15. Spontaneous motor activity of male rats (recovery period)

Group	Control		Ethyl propionate			
Dose (mg/kg)	0		300	1000		
Number of animals	5		5	5		
Ambulatory counts						
Minutes						
0-10	981 ±	1171	333 ±	384	300 ±	315
10-20	706 ±	935	56 ±	41	446 ±	526
20-30	445 ±	566	64 ±	83	146 ±	178
30-40	486 ±	632	19 ±	35 #	64 ±	91
40-50	156 ±	245	203 ±	189	152 ±	183
50-60	611 ±	817	198 ±	364	70 ±	78
Total	3385 ±	2277	872 ±	866 *	1178 ±	804
Rearing counts						
Minutes						
0-10	30 ±	31	14 ±	21	9 ±	9
10-20	23 ±	31	1 ±	1	14 ±	15
20-30	8 ±	8	0 ±	0	3 ±	5
30-40	8 ±	16	0 ±	0	1 ±	3
40-50	5 ±	12	4 ±	2	5 ±	9
50-60	23 ±	35	4 ±	8	2 ±	3
Total	97 ±	68	23 ±	27 *	35 ±	34

Each value shows mean ± SD.

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

Table 16. Spontaneous motor activity of female rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
Ambulatory counts			
Minutes			
0-10	1274 ± 1598	529 ± 1008	702 ± 942
10-20	864 ± 1190	918 ± 1302	822 ± 796
20-30	350 ± 347	829 ± 1219	175 ± 365
30-40	138 ± 258	96 ± 111	345 ± 748
40-50	482 ± 1027	246 ± 518	36 ± 34
50-60	735 ± 1625	309 ± 581	18 ± 25
Total	3843 ± 2908	2926 ± 2190	2098 ± 2267
Rearing counts			
Minutes			
0-10	12 ± 16	7 ± 11	5 ± 7
10-20	11 ± 19	12 ± 17	12 ± 15
20-30	5 ± 8	13 ± 20	1 ± 3
30-40	1 ± 2	0 ± 1	3 ± 7
40-50	7 ± 15	1 ± 3	0 ± 1
50-60	17 ± 37	2 ± 4	0 ± 0
Total	52 ± 54	35 ± 26	22 ± 25

Each value shows mean ± SD.

Table 17. Urinalysis in male rats (administration period)

Group	Control		Ethyl propionate			
	0		100	300		1000
Dose (mg/kg)	0		100	300		1000
Number of animals	5		5	5		5
Volume (mL): Mean \pm SD	14.0 \pm 6.6		16.6 \pm 8.6	12.2 \pm 2.9		13.2 \pm 2.8
Specific gravity: Mean \pm SD	1.046 \pm 0.019		1.043 \pm 0.023	1.037 \pm 0.018		1.044 \pm 0.018
Color						
Light yellow	5		5	5		5
pH						
8.0	0		0	0		1
8.5	5		5	5		4
Protein						
Trace	0		2	0		2
30 mg/dL	4		2	4		2
100 mg/dL	1		1	1		1
Glucose						
Negative	5		5	5		5
Ketone						
Trace	2		2	2		3
Slight	3		3	3		2
Bilirubin						
Negative	5		5	5		5
Occult blood						
Negative	4		5	5		5
Trace	1		0	0		0
Urobilinogen						
0.1 E.U./dL	4		3	4		4
1.0 E.U./dL	1		2	1		1

(Continued)

Table 17. (Continued) Urinalysis in male rats (administration period)

Group	Control		Ethyl propionate			
	0		100	300		1000
Dose (mg/kg)	0		100	300		1000
Number of animals	5		5	5		5
Urinary sediments						
Epithelial cells						
<1 cells/HPF	4		5	3		4
1 - 4 cells/HPF	1		0	2		1
Erythrocytes						
<1 cells/HPF	5		5	5		5
Leukocytes						
<1 cells/HPF	5		5	5		5
Casts						
Not observed	5		5	5		5
Crystals						
Not observed	5		4	4		5
Observed	0		1	1		0
Na (mEq/L): Mean ± SD	109.3 ± 45.3		107.9 ± 65.1	57.7 ± 62.2		103.8 ± 63.2
K (mEq/L): Mean ± SD	245.3 ± 108.4		228.8 ± 125.3	173.9 ± 104.8		218.6 ± 99.0
Cl (mEq/L): Mean ± SD	168.5 ± 82.9		152.6 ± 95.4	92.7 ± 72.8		149.8 ± 84.8
Na (mEq/day): Mean ± SD	1.35 ± 0.40		1.36 ± 0.40	0.64 ± 0.65		1.31 ± 0.78
K (mEq/day): Mean ± SD	2.96 ± 0.67		2.96 ± 0.56	1.95 ± 0.94		2.76 ± 1.12
Cl (mEq/day): Mean ± SD	2.02 ± 0.56		1.90 ± 0.57	1.04 ± 0.72		1.90 ± 1.01

Table 18. Urinalysis in female rats (administration period)

Group	Control		Ethyl propionate			
	0		100	300		1000
Dose (mg/kg)	0		100	300		1000
Number of animals	5		5	5		5
Volume (mL): Mean \pm SD	8.1 \pm 2.3	7.4 \pm 3.7	10.4 \pm 1.8	11.0 \pm 5.7		
Specific gravity: Mean \pm SD	1.053 \pm 0.008	1.050 \pm 0.023	1.045 \pm 0.011	1.047 \pm 0.017		
Color	5		5	5		
Light yellow	5		5	5		
pH	0		1	0		
7.5	0		1	0		
8.0	1		0	2		
8.5	2		4	3		
\geq 9.0	2		0	0		
Protein	1		3	4		
Negative	1		3	4		
Trace	1		1	0		
30 mg/dL	3		0	1		
100 mg/dL	0		1	0		
Glucose	5		5	5		
Negative	5		5	5		
Ketone	3		4	4		
Negative	3		4	4		
Trace	2		0	1		
Slight	0		1	0		
Bilirubin	5		5	5		
Negative	5		5	5		
Occult blood	5		5	5		
Negative	5		5	5		
Urobilinogen	2		4	4		
0.1 E.U./dL	2		4	4		
1.0 E.U./dL	3		1	1		

(Continued)

Table 18. (Continued) Urinalysis in female rats (administration period)

Group	Control		Ethyl propionate			
	0		100	300		1000
Dose (mg/kg)	0		100	300		1000
Number of animals	5		5	5		5
Urinary sediments						
Epithelial cells						
<1 cells/HPF	4		4	5		4
1 - 4 cells/HPF	1		1	0		1
Erythrocytes						
<1 cells/HPF	5		5	5		5
Leukocytes						
<1 cells/HPF	5		5	5		5
Casts						
Not observed	5		5	5		5
Crystals						
Not observed	4		5	4		5
Observed	1		0	1		0
Na (mEq/L): Mean ± SD	111.6 ± 23.0		114.1 ± 59.4	94.7 ± 42.9		78.4 ± 48.2
K (mEq/L): Mean ± SD	252.1 ± 46.8		209.2 ± 122.3	216.1 ± 69.2		204.2 ± 77.1
Cl (mEq/L): Mean ± SD	168.8 ± 33.2		138.5 ± 77.1	148.6 ± 59.2		124.7 ± 58.2
Na (mEq/day): Mean ± SD	0.87 ± 0.17		0.68 ± 0.27	0.99 ± 0.50		0.84 ± 0.49
K (mEq/day): Mean ± SD	2.01 ± 0.55		1.26 ± 0.46	2.24 ± 0.83		2.08 ± 0.91
Cl (mEq/day): Mean ± SD	1.33 ± 0.30		0.83 ± 0.33	1.53 ± 0.68		1.25 ± 0.56

Table 19. Urinalysis in male rats (recovery period)

Group	Control		Ethyl propionate	
	0		300	1000
Dose (mg/kg)	0		300	1000
Number of animals	5		5	5
Volume (mL): Mean \pm SD	17.5 \pm 4.5	15.5 \pm 2.0	16.2 \pm 8.7	
Specific gravity: Mean \pm SD	1.044 \pm 0.013	1.053 \pm 0.009	1.046 \pm 0.016	
Color				
Light yellow	5	5	5	
pH				
6.0	0	0	1	
8.0	2	3	0	
8.5	3	2	4	
Protein				
Trace	3	3	2	
30 mg/dL	2	2	2	
100 mg/dL	0	0	1	
Glucose				
Negative	5	5	5	
Ketone				
Trace	3	3	2	
Slight	2	2	3	
Bilirubin				
Negative	5	5	5	
Occult blood				
Negative	5	4	5	
Trace	0	1	0	
Urobilinogen				
0.1 E.U./dL	5	5	5	

(Continued)

Table 19. (Continued) Urinalysis in male rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
Urinary sediments			
Epithelial cells			
<1 cell/HPF	5	5	5
Erythrocytes			
<1 cell/HPF	5	5	5
Leukocytes			
<1 cell/HPF	5	5	5
Casts			
Not observed	5	5	5
Crystals			
Not observed	5	5	5
Na (mEq/L): Mean \pm SD	85.1 \pm 42.1	109.7 \pm 32.5	82.0 \pm 43.2
K (mEq/L): Mean \pm SD	210.9 \pm 73.6	252.8 \pm 40.4	209.7 \pm 85.5
Cl (mEq/L): Mean \pm SD	114.7 \pm 62.1	148.5 \pm 36.3	112.8 \pm 62.4
Na (mEq/day): Mean \pm SD	1.40 \pm 0.52	1.68 \pm 0.46	1.16 \pm 0.49
K (mEq/day): Mean \pm SD	3.52 \pm 0.83	3.88 \pm 0.51	2.92 \pm 0.64
Cl (mEq/day): Mean \pm SD	1.89 \pm 0.82	2.27 \pm 0.49	1.56 \pm 0.64

Table 20. Urinalysis in female rats (recovery period)

Group	Control		Ethyl propionate	
Dose (mg/kg)	0		300	1000
Number of animals	5		5	5
Volume (mL): Mean \pm SD	8.0 \pm 1.7		8.9 \pm 3.7	12.7 \pm 2.1 *
Specific gravity: Mean \pm SD	1.048 \pm 0.013		1.055 \pm 0.021	1.036 \pm 0.010
Color				
Light yellow	5		5	5
pH				
7.0	0		1	0
8.0	1		0	1
8.5	4		3	4
\geq 9.0	0		1	0
Protein				
Negative	2		3	4
Trace	0		1	1
30 mg/dL	3		1	0
Glucose				
Negative	5		5	5
Ketone				
Negative	3		5	5
Trace	2		0	0
Bilirubin				
Negative	5		5	5
Occult blood				
Negative	5		5	3
Trace	0		0	2
Urobilinogen				
0.1 E.U./dL	2		5	5
1.0 E.U./dL	3		0	0

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

(Continued)

Table 20. (Continued) Urinalysis in female rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
Urinary sediments			
Epithelial cells			
<1 cell/HPF	5	5	5
Erythrocytes			
<1 cell/HPF	5	5	5
Leukocytes			
<1 cell/HPF	5	5	5
Casts			
Not observed	5	5	5
Crystals			
Not observed	5	5	5
Na (mEq/L): Mean ± SD	76.8 ± 44.2	94.0 ± 55.8	53.2 ± 38.5
K (mEq/L): Mean ± SD	199.5 ± 90.8	242.1 ± 118.2	136.7 ± 73.1
Cl (mEq/L): Mean ± SD	106.4 ± 61.5	138.0 ± 78.9	80.6 ± 52.7
Na (mEq/day): Mean ± SD	0.59 ± 0.33	0.71 ± 0.43	0.72 ± 0.59
K (mEq/day): Mean ± SD	1.51 ± 0.60	1.92 ± 1.02	1.84 ± 1.22
Cl (mEq/day): Mean ± SD	0.79 ± 0.41	1.06 ± 0.68	1.09 ± 0.81

Table 21. Hematological findings in male rats (administration period)

Group	Control	Ethyl propionate			
Dose (mg/kg)	0	100	300	1000	
Number of animals	5	5	5	5	5
RBC (10 ⁴ /μL)	770 ± 39	765 ± 19	778 ± 24	780 ± 34	
HGB (g/dL)	15.0 ± 0.5	15.2 ± 0.5	15.4 ± 0.7	15.5 ± 0.6	
HCT (%)	43.2 ± 1.4	43.6 ± 1.1	44.2 ± 2.2	44.0 ± 1.6	
MCV (fL)	56.2 ± 1.1	57.0 ± 0.9	56.8 ± 1.1	56.4 ± 0.9	
MCH (pg)	19.4 ± 0.4	19.9 ± 0.4	19.7 ± 0.4	19.8 ± 0.3	
MCHC (g/dL)	34.6 ± 0.2	34.9 ± 0.3	34.8 ± 0.4	35.2 ± 0.6	
PLT (10 ⁴ /μL)	113.9 ± 10.4	120.2 ± 10.0	113.8 ± 6.5	116.8 ± 9.0	
RET (10 ⁴ /μL)	25.47 ± 2.21	21.57 ± 4.01	23.36 ± 2.31	24.68 ± 2.42	
RET (%)	3.31 ± 0.34	2.83 ± 0.57	3.00 ± 0.28	3.17 ± 0.42	
PT (sec.)	16.9 ± 2.2	15.0 ± 3.5	14.6 ± 2.1	14.6 ± 3.1	
APTT (sec.)	22.6 ± 1.8	20.5 ± 1.9	22.0 ± 1.4	20.6 ± 2.0	
Fbg (mg/dL)	246.8 ± 18.1	247.2 ± 24.8	241.9 ± 11.4	258.9 ± 17.5	
WBC (10 ² /μL)	81.1 ± 27.7	63.1 ± 8.1	66.7 ± 7.0	61.1 ± 14.2	
Differential leukocyte (10 ² /μL)					
Lymphocyte	65.6 ± 28.4	50.1 ± 5.5	54.7 ± 6.6	48.3 ± 13.7	
Neutrophil	12.4 ± 3.4	10.3 ± 2.0	9.1 ± 3.1	10.0 ± 3.0	
Eosinophil	0.6 ± 0.3	0.8 ± 0.5	0.9 ± 0.3	0.8 ± 0.2	
Basophil	0.1 ± 0.0	0.1 ± 0.1	0.1 ± 0.0	0.1 ± 0.1	
Monocyte	2.3 ± 0.8	1.7 ± 0.5	1.8 ± 0.7	1.9 ± 0.6	
Differential leukocyte (%)					
Lymphocyte	79.4 ± 6.0	79.6 ± 1.9	82.1 ± 4.0	78.7 ± 7.0	
Neutrophil	16.7 ± 6.0	16.3 ± 1.6	13.8 ± 4.7	16.7 ± 5.7	
Eosinophil	0.8 ± 0.3	1.3 ± 0.7	1.4 ± 0.3	1.4 ± 0.5	
Basophil	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.2 ± 0.1	
Monocyte	2.9 ± 0.7	2.7 ± 0.5	2.7 ± 0.9	3.1 ± 1.0	

Each value shows mean ± SD.

Table 22. Hematological findings in female rats (administration period)

Group	Control	Ethyl propionate			
Dose (mg/kg)	0	100	300	1000	
Number of animals	5	5	5	5	5
RBC (10 ⁴ /μL)	765 ± 21	734 ± 36	733 ± 51	749 ± 31	
HGB (g/dL)	15.2 ± 0.4	14.5 ± 0.3	14.7 ± 0.7	15.0 ± 0.6	
HCT (%)	43.0 ± 0.7	40.9 ± 1.3	41.3 ± 2.0	42.3 ± 2.0	
MCV (fL)	56.3 ± 1.2	55.7 ± 1.3	56.5 ± 1.4	56.5 ± 1.1	
MCH (pg)	19.9 ± 0.6	19.7 ± 0.6	20.1 ± 0.5	20.0 ± 0.4	
MCHC (g/dL)	35.4 ± 0.5	35.5 ± 0.7	35.5 ± 0.2	35.4 ± 0.4	
PLT (10 ⁴ /μL)	112.0 ± 7.6	121.4 ± 14.5	127.1 ± 17.7	113.7 ± 8.4	
RET (10 ⁴ /μL)	19.40 ± 3.50	16.34 ± 3.15	20.50 ± 3.46	19.74 ± 4.01	
RET (%)	2.54 ± 0.48	2.24 ± 0.50	2.82 ± 0.56	2.62 ± 0.45	
PT (sec.)	9.6 ± 0.4	9.6 ± 0.3	9.6 ± 0.2	9.4 ± 0.2	
APTT (sec.)	17.4 ± 0.6	17.5 ± 0.6	17.5 ± 0.5	17.6 ± 1.0	
Fbg (mg/dL)	197.4 ± 6.5	170.3 ± 16.7	197.7 ± 19.8	200.9 ± 30.1	
WBC (10 ² /μL)	56.5 ± 13.0	53.7 ± 11.6	48.1 ± 19.8	48.5 ± 5.5	
Differential leukocyte (10 ² /μL)					
Lymphocyte	50.0 ± 12.2	45.3 ± 9.6	42.2 ± 18.7	40.7 ± 4.2	
Neutrophil	4.7 ± 0.6	6.2 ± 3.5	4.2 ± 1.7	6.1 ± 1.6	
Eosinophil	0.5 ± 0.2	0.7 ± 0.3	0.4 ± 0.3	0.5 ± 0.1	
Basophil	0.1 ± 0.0	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.0	
Monocyte	1.3 ± 0.5	1.4 ± 0.5	1.2 ± 0.5	1.1 ± 0.5	
Differential leukocyte (%)					
Lymphocyte	88.3 ± 2.2	84.6 ± 5.4	86.3 ± 4.7	83.9 ± 3.1	
Neutrophil	8.5 ± 1.4	11.4 ± 5.4	10.0 ± 4.9	12.5 ± 2.5	
Eosinophil	0.9 ± 0.4	1.2 ± 0.3	0.9 ± 0.4	1.1 ± 0.2	
Basophil	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.2 ± 0.1	
Monocyte	2.2 ± 0.7	2.7 ± 0.7	2.6 ± 0.5	2.3 ± 0.8	

Each value shows mean ± SD.

Table 23. Hematological findings in male rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
RBC (10 ⁴ /μL)	815 ± 43	828 ± 14	840 ± 36
HGB (g/dL)	15.4 ± 0.4	15.5 ± 0.4	15.7 ± 0.6
HCT (%)	44.2 ± 0.9	44.5 ± 1.0	45.2 ± 2.1
MCV (fL)	54.3 ± 1.8	53.7 ± 1.4	53.8 ± 1.6
MCH (pg)	18.9 ± 0.8	18.7 ± 0.6	18.7 ± 0.6
MCHC (g/dL)	34.8 ± 0.8	34.8 ± 0.3	34.7 ± 0.5
PLT (10 ⁴ /μL)	103.8 ± 8.7	111.4 ± 5.9	109.6 ± 17.7
RET (10 ⁴ /μL)	21.88 ± 2.06	22.55 ± 1.72	24.80 ± 3.09
RET (%)	2.70 ± 0.35	2.72 ± 0.19	2.96 ± 0.39
PT (sec.)	14.3 ± 2.0	15.4 ± 2.4	14.7 ± 3.5
APTT (sec.)	21.8 ± 1.6	22.7 ± 2.2	21.2 ± 1.0
Fbg (mg/dL)	228.8 ± 14.8	228.4 ± 19.9	233.7 ± 9.8
WBC (10 ² /μL)	70.4 ± 24.6	78.8 ± 20.4	68.6 ± 21.6
Differential leukocyte (10 ² /μL)			
Lymphocyte	59.6 ± 23.1	63.9 ± 21.4	54.6 ± 21.9
Neutrophil	8.4 ± 2.3	11.9 ± 2.8	11.4 ± 3.4
Eosinophil	0.8 ± 0.3	1.0 ± 0.4	0.8 ± 0.2
Basophil	0.2 ± 0.1	0.2 ± 0.1	0.1 ± 0.1
Monocyte	1.5 ± 0.3	1.8 ± 0.3	1.6 ± 0.4
Differential leukocyte (%)			
Lymphocyte	83.9 ± 4.4	79.8 ± 7.8	78.0 ± 9.3
Neutrophil	12.6 ± 4.0	16.3 ± 7.2	18.1 ± 8.1
Eosinophil	1.1 ± 0.4	1.3 ± 0.4	1.2 ± 0.5
Basophil	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.0
Monocyte	2.1 ± 0.3	2.3 ± 0.6	2.5 ± 1.1

Each value shows mean ± SD.

Table 24. Hematological findings in female rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
RBC (10 ⁴ /μL)	773 ± 34	791 ± 41	785 ± 51
HGB (g/dL)	14.8 ± 0.5	14.8 ± 0.8	15.0 ± 0.6
HCT (%)	42.0 ± 1.8	42.4 ± 2.2	42.6 ± 1.8
MCV (fL)	54.3 ± 1.7	53.7 ± 0.9	54.4 ± 1.4
MCH (pg)	19.1 ± 0.3	18.7 ± 0.4	19.2 ± 0.5
MCHC (g/dL)	35.2 ± 0.6	34.8 ± 0.7	35.2 ± 0.8
PLT (10 ⁴ /μL)	114.1 ± 8.4	113.4 ± 8.7	105.1 ± 8.0
RET (10 ⁴ /μL)	18.16 ± 3.34	20.13 ± 3.23	17.27 ± 2.67
RET (%)	2.35 ± 0.44	2.55 ± 0.44	2.21 ± 0.35
PT (sec.)	9.6 ± 0.3	9.7 ± 0.3	9.4 ± 0.3
APTT (sec.)	17.6 ± 0.8	17.8 ± 1.0	17.5 ± 0.5
Fbg (mg/dL)	191.0 ± 11.6	184.7 ± 13.8	190.3 ± 11.1
WBC (10 ² /μL)	31.3 ± 11.8	29.5 ± 10.4	44.3 ± 15.9
Differential leukocyte (10 ² /μL)			
Lymphocyte	22.5 ± 7.2	21.4 ± 8.8	31.1 ± 9.1
Neutrophil	7.6 ± 4.3	6.7 ± 1.5	11.5 ± 6.5
Eosinophil	0.6 ± 0.2	0.6 ± 0.2	0.7 ± 0.2
Basophil	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.0
Monocyte	0.6 ± 0.3	0.7 ± 0.4	0.9 ± 0.3
Differential leukocyte (%)			
Lymphocyte	72.8 ± 4.8	71.7 ± 4.8	71.6 ± 5.5
Neutrophil	23.3 ± 4.5	23.8 ± 5.0	24.5 ± 6.2
Eosinophil	1.9 ± 0.5	2.0 ± 0.5	1.7 ± 0.5
Basophil	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.2
Monocyte	1.9 ± 0.4	2.3 ± 0.5	2.0 ± 0.5

Each value shows mean ± SD.

Table 25. Blood chemical findings in male rats (administration period)

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
AST (U/L)	89.0 ± 14.2	91.1 ± 17.0	88.8 ± 17.5	92.9 ± 26.6
ALT (U/L)	30.8 ± 5.5	27.3 ± 4.6	27.1 ± 5.3	25.1 ± 3.1
ALP (U/L)	222.4 ± 31.1	196.6 ± 42.7	207.1 ± 33.8	219.3 ± 26.8
TP (g/dL)	5.40 ± 0.16	5.21 ± 0.22	5.46 ± 0.21	5.32 ± 0.17
Alb (g/dL)	2.60 ± 0.16	2.42 ± 0.19	2.60 ± 0.11	2.43 ± 0.17
Protein fraction (%)				
alb	48.2 ± 3.2	46.4 ± 2.7	47.6 ± 2.7	45.5 ± 1.9
α ₁ -glb	21.2 ± 3.1	22.4 ± 1.2	22.7 ± 1.7	23.6 ± 2.5
α ₂ -glb	8.6 ± 0.7	9.3 ± 1.1	8.7 ± 1.0	8.7 ± 0.7
β-glb	17.3 ± 0.5	17.2 ± 1.0	16.7 ± 1.2	17.2 ± 1.6
γ-glb	4.7 ± 1.4	4.6 ± 0.7	4.3 ± 0.7	5.0 ± 1.1
A/G	0.94 ± 0.12	0.87 ± 0.09	0.91 ± 0.10	0.84 ± 0.06
T-Bil (mg/dL)	0.11 ± 0.01	0.11 ± 0.00	0.12 ± 0.01	0.12 ± 0.01
UN (mg/dL)	12.2 ± 1.4	11.9 ± 1.8	13.5 ± 3.5	12.3 ± 0.7
CRE (mg/dL)	0.32 ± 0.02	0.29 ± 0.01	0.32 ± 0.04	0.30 ± 0.02
Glu (mg/dL)	128.1 ± 18.2	123.4 ± 8.3	122.0 ± 10.1	115.9 ± 6.4
T-Cho (mg/dL)	54.6 ± 12.3	50.0 ± 3.0	52.4 ± 9.6	59.3 ± 9.2
TG (mg/dL)	52.9 ± 36.3	36.4 ± 10.6	35.5 ± 15.0	54.0 ± 15.7
Na (mEq/L)	144.3 ± 0.5	144.1 ± 0.9	144.8 ± 0.6	144.1 ± 1.2
K (mEq/L)	3.92 ± 0.25	4.04 ± 0.19	4.07 ± 0.15	4.04 ± 0.32
Cl (mEq/L)	107.2 ± 0.7	106.7 ± 0.4	106.6 ± 1.0	106.4 ± 0.8
Ca (mg/dL)	9.7 ± 0.2	9.7 ± 0.3	9.8 ± 0.1	9.8 ± 0.3
IP (mg/dL)	8.9 ± 0.9	8.7 ± 0.8	9.2 ± 0.6	9.3 ± 0.5

Each value shows mean ± SD.

Table 26. Blood chemical findings in female rats (administration period)

Group		Control	Ethyl propionate			
Dose (mg/kg)		0	100	300	1000	
Number of animals		5	5	5	5	5
AST	(U/L)	91.2 ± 14.7	82.0 ± 9.6	93.0 ± 18.6	78.7 ± 13.7	
ALT	(U/L)	17.4 ± 3.3	18.5 ± 3.1	17.2 ± 2.9	16.3 ± 2.9	
ALP	(U/L)	130.7 ± 35.5	94.5 ± 26.0	130.8 ± 21.5	133.3 ± 34.6	
TP	(g/dL)	5.57 ± 0.24	5.69 ± 0.37	5.56 ± 0.43	5.78 ± 0.21	
Alb	(g/dL)	2.85 ± 0.12	2.91 ± 0.20	2.82 ± 0.21	2.95 ± 0.13	
Protein fraction (%)						
alb		51.2 ± 0.8	51.1 ± 1.1	50.9 ± 2.6	51.2 ± 2.9	
α ₁ -glb		19.3 ± 2.1	19.4 ± 2.4	20.5 ± 0.9	20.5 ± 1.2	
α ₂ -glb		8.2 ± 0.5	8.5 ± 0.5	8.4 ± 0.6	8.0 ± 1.2	
β-glb		16.5 ± 0.6	15.6 ± 1.3	15.7 ± 1.6	16.7 ± 1.2	
γ-glb		4.8 ± 1.3	5.4 ± 1.3	4.5 ± 0.5	3.6 ± 1.0	
A/G		1.05 ± 0.03	1.05 ± 0.05	1.04 ± 0.11	1.05 ± 0.12	
T-Bil	(mg/dL)	0.12 ± 0.01	0.13 ± 0.01	0.11 ± 0.01	0.12 ± 0.01	
UN	(mg/dL)	13.3 ± 1.7	11.8 ± 1.6	12.3 ± 1.2	12.9 ± 2.7	
CRE	(mg/dL)	0.39 ± 0.05	0.33 ± 0.02	0.34 ± 0.01	0.33 ± 0.02	
Glu	(mg/dL)	124.0 ± 8.1	110.7 ± 5.5	113.7 ± 11.0	123.9 ± 16.7	
T-Cho	(mg/dL)	65.0 ± 8.4	72.7 ± 14.5	60.5 ± 10.0	78.7 ± 15.5	
TG	(mg/dL)	15.2 ± 6.8	13.9 ± 3.1	14.8 ± 5.5	18.4 ± 9.4	
Na	(mEq/L)	146.1 ± 0.5	144.7 ± 0.5 *	146.2 ± 0.5	144.7 ± 1.1 *	
K	(mEq/L)	4.10 ± 0.25	4.22 ± 0.19	3.96 ± 0.29	3.94 ± 0.29	
Cl	(mEq/L)	108.7 ± 1.5	107.4 ± 2.0	108.8 ± 1.9	107.0 ± 1.9	
Ca	(mg/dL)	9.9 ± 0.2	9.9 ± 0.2	9.8 ± 0.4	10.2 ± 0.2	
IP	(mg/dL)	9.3 ± 0.3	9.2 ± 0.2	8.8 ± 0.6	9.1 ± 0.2	

Each value shows mean ± SD.

Significantly different from the control group (*: p<0.05 by Dunnett's test).

Table 27. Blood chemical findings in male rats (recovery period)

Group		Control		Ethyl propionate			
Dose (mg/kg)		0		300		1000	
Number of animals		5		5		5	
AST	(U/L)	95.5 ± 21.0		86.2 ± 10.3		93.0 ± 5.8	
ALT	(U/L)	30.6 ± 2.3		29.2 ± 3.5		31.6 ± 2.5	
ALP	(U/L)	161.3 ± 28.6		161.7 ± 20.1		182.5 ± 45.4	
TP	(g/dL)	5.50 ± 0.21		5.57 ± 0.11		5.65 ± 0.23	
Alb	(g/dL)	2.58 ± 0.15		2.52 ± 0.13		2.67 ± 0.18	
Protein fraction (%)							
alb		47.0 ± 4.4		45.2 ± 2.1		47.3 ± 2.6	
α ₁ -glb		22.1 ± 5.1		23.2 ± 3.8		22.1 ± 3.2	
α ₂ -glb		8.9 ± 0.7		8.7 ± 0.7		8.3 ± 0.6	
β-glb		17.1 ± 2.2		17.4 ± 2.0		17.6 ± 1.3	
γ-glb		4.8 ± 1.4		5.5 ± 0.6		4.8 ± 1.1	
A/G		0.90 ± 0.16		0.83 ± 0.07		0.90 ± 0.09	
T-Bil	(mg/dL)	0.11 ± 0.01		0.11 ± 0.01		0.13 ± 0.01	
UN	(mg/dL)	14.6 ± 1.3		13.0 ± 1.5		12.8 ± 1.3	
CRE	(mg/dL)	0.38 ± 0.03		0.38 ± 0.02		0.36 ± 0.02	
Glu	(mg/dL)	128.1 ± 10.9		129.2 ± 11.2		127.2 ± 14.3	
T-Cho	(mg/dL)	62.2 ± 13.8		71.3 ± 13.1		55.5 ± 10.8	
TG	(mg/dL)	54.9 ± 10.6		52.9 ± 15.8		63.9 ± 12.1	
Na	(mEq/L)	142.9 ± 0.9		142.7 ± 0.5		142.6 ± 1.4	
K	(mEq/L)	4.05 ± 0.21		3.99 ± 0.27		4.24 ± 0.18	
Cl	(mEq/L)	105.3 ± 0.9		105.8 ± 2.2		105.3 ± 1.4	
Ca	(mg/dL)	9.6 ± 0.2		9.7 ± 0.3		9.7 ± 0.2	
IP	(mg/dL)	7.6 ± 0.4		7.6 ± 0.5		7.7 ± 0.5	

Each value shows mean ± SD.

Table 28. Blood chemical findings in female rats (recovery period)

Group		Control		Ethyl propionate			
Dose (mg/kg)		0		300		1000	
Number of animals		5		5		5	
AST	(U/L)	78.1 ± 14.5		81.3 ± 10.1		73.6 ± 11.4	
ALT	(U/L)	23.3 ± 1.9		21.9 ± 1.5		21.9 ± 1.3	
ALP	(U/L)	83.5 ± 37.2		84.0 ± 19.6		75.4 ± 7.7	
TP	(g/dL)	5.96 ± 0.36		5.88 ± 0.23		6.04 ± 0.34	
Alb	(g/dL)	3.02 ± 0.29		3.06 ± 0.21		3.07 ± 0.18	
Protein fraction (%)							
alb		50.6 ± 3.3		52.0 ± 2.2		50.9 ± 2.6	
α ₁ -glb		18.8 ± 1.7		18.3 ± 2.2		19.7 ± 0.8	
α ₂ -glb		8.3 ± 1.1		8.3 ± 0.6		7.9 ± 0.8	
β-glb		15.4 ± 1.2		15.7 ± 1.6		15.6 ± 1.5	
γ-glb		6.9 ± 1.1		5.7 ± 2.0		5.9 ± 1.2	
A/G		1.03 ± 0.13		1.09 ± 0.10		1.04 ± 0.10	
T-Bil	(mg/dL)	0.12 ± 0.01		0.12 ± 0.03		0.13 ± 0.02	
UN	(mg/dL)	12.7 ± 2.3		12.0 ± 1.6		13.7 ± 2.5	
CRE	(mg/dL)	0.39 ± 0.02		0.38 ± 0.03		0.39 ± 0.02	
Glu	(mg/dL)	117.4 ± 6.4		122.1 ± 10.0		122.2 ± 15.3	
T-Cho	(mg/dL)	67.9 ± 13.8		59.2 ± 9.5		60.3 ± 13.6	
TG	(mg/dL)	24.5 ± 8.6		19.8 ± 5.4		20.5 ± 6.7	
Na	(mEq/L)	144.1 ± 0.8		143.2 ± 1.0		142.8 ± 0.7	
K	(mEq/L)	3.95 ± 0.11		4.06 ± 0.32		3.91 ± 0.19	
Cl	(mEq/L)	107.2 ± 1.0		107.8 ± 1.3		106.8 ± 1.0	
Ca	(mg/dL)	10.0 ± 0.3		9.9 ± 0.4		10.0 ± 0.3	
IP	(mg/dL)	6.2 ± 1.4		6.8 ± 0.7		7.0 ± 0.5	

Each value shows mean ± SD.

Table 29. Necropsy findings in male rats (administration period)

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Findings				
Normal	5	5	5	4
Testis				
Small in size, bilateral	0	0	0	1
Epididymis				
Small in size, bilateral	0	0	0	1

Table 30. Necropsy findings in female rats (administration period)

Group	Control	Ethyl propionate		
Dose (mg/kg)	0	100	300	1000
Number of animals	5	5	5	5
Findings				
Normal	5	5	5	5

Table 31. Necropsy findings in male rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
Findings			
Normal	5	4	5
Testis			
Small in size, bilateral	0	1	0
Epididymis			
Small in size, bilateral	0	1	0

Table 32. Necropsy findings in female rats (recovery period)

Group	Control	Ethyl propionate	
Dose (mg/kg)	0	300	1000
Number of animals	5	5	5
Findings			
Normal	5	5	5

Table 33. Organ weights of male rats (administration period)

Group	Control		Ethyl propionate					
Dose (mg/kg)	0		100		300		1000	
Number of animals	5		5		5		5	
Body weight (g)	338 ± 27		336 ± 31		324 ± 29		337 ± 36	
Brain (g)	1.99 ± 0.06		1.99 ± 0.08		1.96 ± 0.07		1.97 ± 0.11	
	(g%)	0.59 ± 0.04	(g%)	0.60 ± 0.06	(g%)	0.61 ± 0.05	(g%)	0.59 ± 0.05
Thyroids (mg)	19.1 ± 1.5		21.4 ± 5.0		21.2 ± 3.3		20.2 ± 1.7	
	(mg%)	5.6 ± 0.5	(mg%)	6.5 ± 1.8	(mg%)	6.5 ± 0.6	(mg%)	6.0 ± 0.5
Thymus (g)	0.58 ± 0.12		0.58 ± 0.21		0.54 ± 0.07		0.60 ± 0.13	
	(g%)	0.17 ± 0.04	(g%)	0.17 ± 0.05	(g%)	0.17 ± 0.02	(g%)	0.18 ± 0.05
Heart (g)	1.27 ± 0.14		1.18 ± 0.09		1.17 ± 0.10		1.23 ± 0.10	
	(g%)	0.38 ± 0.04	(g%)	0.36 ± 0.02	(g%)	0.36 ± 0.03	(g%)	0.36 ± 0.03
Liver (g)	10.04 ± 0.76		9.54 ± 1.25		9.34 ± 0.94		9.49 ± 1.08	
	(g%)	2.97 ± 0.09	(g%)	2.84 ± 0.18	(g%)	2.88 ± 0.12	(g%)	2.81 ± 0.12
Spleen (g)	0.59 ± 0.11		0.70 ± 0.11		0.56 ± 0.12		0.62 ± 0.05	
	(g%)	0.18 ± 0.03	(g%)	0.21 ± 0.02	(g%)	0.17 ± 0.03	(g%)	0.18 ± 0.02
Kidneys (g)	2.65 ± 0.25		2.66 ± 0.06		2.50 ± 0.17		2.58 ± 0.17	
	(g%)	0.79 ± 0.05	(g%)	0.79 ± 0.07	(g%)	0.77 ± 0.05	(g%)	0.77 ± 0.04
Adrenals (mg)	55.5 ± 4.5		46.5 ± 5.6 *		46.9 ± 3.9 *		52.7 ± 4.9	
	(mg%)	16.4 ± 0.5	(mg%)	13.9 ± 1.9	(mg%)	14.6 ± 2.1	(mg%)	15.7 ± 1.6
Testes (g)	3.07 ± 0.11		3.05 ± 0.07		3.08 ± 0.08		2.76 ± 1.27	
	(g%)	0.92 ± 0.08	(g%)	0.91 ± 0.08	(g%)	0.96 ± 0.08	(g%)	0.81 ± 0.35
Epididymides (g)	0.74 ± 0.01		0.79 ± 0.12		0.83 ± 0.15		0.70 ± 0.19	
	(g%)	0.22 ± 0.02	(g%)	0.23 ± 0.03	(g%)	0.26 ± 0.05	(g%)	0.21 ± 0.06
Seminal vesicles (g)	1.47 ± 0.16		1.44 ± 0.27		1.27 ± 0.30		1.47 ± 0.29	
	(g%)	0.43 ± 0.05	(g%)	0.43 ± 0.06	(g%)	0.39 ± 0.07	(g%)	0.44 ± 0.07
Prostate (g)	0.41 ± 0.13		0.43 ± 0.06		0.34 ± 0.04		0.42 ± 0.11	
	(g%)	0.12 ± 0.04	(g%)	0.13 ± 0.01	(g%)	0.10 ± 0.01	(g%)	0.12 ± 0.03

Each value shows mean ± SD.

Significantly different from the control group (*: p<0.05 by Dunnett's test).

Table 34. Organ weights of female rats (administration period)

Group		Control	Ethyl propionate			
mg/kg		0	100	300	1000	
Number of animals		5	5	5	5	5
Body weight	(g)	229 ± 20	225 ± 13	229 ± 24	231 ± 28	
Brain	(g)	1.86 ± 0.04	1.88 ± 0.06	1.89 ± 0.10	1.83 ± 0.07	
	(g%)	0.81 ± 0.07	0.84 ± 0.05	0.83 ± 0.06	0.80 ± 0.09	
Thyroids	(mg)	19.2 ± 1.2	19.5 ± 3.9	15.7 ± 4.2	17.1 ± 3.9	
	(mg%)	8.4 ± 0.6	8.7 ± 1.9	6.8 ± 1.6	7.5 ± 2.1	
Thymus	(g)	0.51 ± 0.13	0.48 ± 0.16	0.58 ± 0.13	0.53 ± 0.08	
	(g%)	0.22 ± 0.04	0.21 ± 0.06	0.25 ± 0.05	0.23 ± 0.04	
Heart	(g)	0.79 ± 0.10	0.83 ± 0.08	0.84 ± 0.11	0.85 ± 0.07	
	(g%)	0.34 ± 0.02	0.37 ± 0.02	0.37 ± 0.03	0.37 ± 0.03	
Liver	(g)	7.13 ± 1.55	6.65 ± 0.38	6.91 ± 0.79	7.08 ± 0.78	
	(g%)	3.10 ± 0.49	2.97 ± 0.16	3.02 ± 0.20	3.07 ± 0.08	
Spleen	(g)	0.53 ± 0.06	0.48 ± 0.07	0.51 ± 0.05	0.45 ± 0.07	
	(g%)	0.23 ± 0.02	0.21 ± 0.04	0.22 ± 0.02	0.20 ± 0.03	
Kidneys	(g)	1.78 ± 0.18	1.77 ± 0.18	1.82 ± 0.17	1.87 ± 0.09	
	(g%)	0.78 ± 0.04	0.79 ± 0.06	0.80 ± 0.08	0.81 ± 0.06	
Adrenals	(mg)	66.3 ± 6.2	64.9 ± 2.6	68.1 ± 10.6	61.3 ± 10.4	
	(mg%)	29.2 ± 4.2	29.0 ± 0.9	29.7 ± 2.7	26.8 ± 5.7	
Ovaries	(mg)	83.7 ± 17.7	83.7 ± 14.6	86.2 ± 12.7	79.5 ± 17.3	
	(mg%)	36.6 ± 7.9	37.2 ± 5.4	37.6 ± 3.4	35.0 ± 10.4	
Uterus	(g)	0.63 ± 0.20	0.46 ± 0.15	0.54 ± 0.13	0.48 ± 0.06	
	(g%)	0.28 ± 0.08	0.21 ± 0.06	0.24 ± 0.06	0.21 ± 0.04	

Each value shows mean ± SD.

Table 35. Organ weights of male rats (recovery period)

Group		Control	Ethyl propionate	
Dose (mg/kg)		0	300	1000
Number of animals		5	5	5
Body weight	(g)	429 ± 28	456 ± 27	424 ± 32
Brain	(g)	2.07 ± 0.06	2.08 ± 0.06	2.06 ± 0.15
	(g%)	0.48 ± 0.04	0.46 ± 0.02	0.49 ± 0.05
Thyroids	(mg)	19.5 ± 5.3	24.3 ± 5.8	20.2 ± 3.1
	(mg%)	4.5 ± 1.2	5.3 ± 1.1	4.7 ± 0.6
Thymus	(g)	0.55 ± 0.10	0.51 ± 0.14	0.46 ± 0.05
	(g%)	0.13 ± 0.02	0.11 ± 0.03	0.11 ± 0.02
Heart	(g)	1.46 ± 0.09	1.45 ± 0.06	1.34 ± 0.07 *
	(g%)	0.34 ± 0.03	0.32 ± 0.02	0.32 ± 0.03
Liver	(g)	12.16 ± 0.82	12.72 ± 1.21	11.73 ± 1.12
	(g%)	2.83 ± 0.08	2.79 ± 0.16	2.77 ± 0.21
Spleen	(g)	0.70 ± 0.07	0.79 ± 0.11	0.70 ± 0.08
	(g%)	0.16 ± 0.01	0.17 ± 0.02	0.17 ± 0.03
Kidneys	(g)	2.83 ± 0.20	2.93 ± 0.22	2.92 ± 0.11
	(g%)	0.66 ± 0.05	0.65 ± 0.04	0.69 ± 0.06
Adrenals	(mg)	58.5 ± 8.9	54.0 ± 10.1	63.0 ± 13.7
	(mg%)	13.7 ± 2.7	11.8 ± 1.5	14.9 ± 3.2
Testes	(g)	3.00 ± 0.22	2.99 ± 0.70	3.15 ± 0.12
	(g%)	0.70 ± 0.09	0.66 ± 0.18	0.74 ± 0.04
Epididymides	(g)	1.12 ± 0.10	1.03 ± 0.15	1.09 ± 0.08
	(g%)	0.26 ± 0.03	0.23 ± 0.04	0.26 ± 0.04
Seminal vesicles	(g)	1.93 ± 0.28	1.87 ± 0.30	2.03 ± 0.26
	(g%)	0.45 ± 0.05	0.41 ± 0.08	0.48 ± 0.07
Prostate	(g)	0.57 ± 0.08	0.55 ± 0.09	0.50 ± 0.11
	(g%)	0.13 ± 0.03	0.12 ± 0.01	0.12 ± 0.03

Each value shows mean ± SD.

Significantly different from the control group (*: p<0.05 by Dunnett's test).

Table 36. Organ weights of female rats (recovery period)

Group		Control	Ethyl propionate	
Dose (mg/kg)		0	300	1000
Number of animals		5	5	5
Body weight	(g)	256 ± 19	249 ± 22	261 ± 14
Brain	(g)	1.90 ± 0.11	1.88 ± 0.06	1.96 ± 0.06
	(g%)	0.74 ± 0.06	0.76 ± 0.06	0.75 ± 0.05
Thyroids	(mg)	18.5 ± 4.1	16.6 ± 2.6	18.6 ± 1.8
	(mg%)	7.2 ± 1.8	6.7 ± 1.3	7.2 ± 0.8
Thymus	(g)	0.38 ± 0.04	0.39 ± 0.06	0.46 ± 0.08
	(g%)	0.15 ± 0.01	0.16 ± 0.03	0.18 ± 0.02
Heart	(g)	0.89 ± 0.08	0.86 ± 0.09	0.90 ± 0.07
	(g%)	0.35 ± 0.02	0.35 ± 0.03	0.35 ± 0.03
Liver	(g)	6.80 ± 0.55	6.65 ± 0.56	7.08 ± 0.59
	(g%)	2.65 ± 0.09	2.67 ± 0.18	2.71 ± 0.12
Spleen	(g)	0.51 ± 0.09	0.51 ± 0.04	0.52 ± 0.03
	(g%)	0.20 ± 0.03	0.20 ± 0.02	0.20 ± 0.02
Kidneys	(g)	1.83 ± 0.19	1.79 ± 0.17	1.77 ± 0.11
	(g%)	0.72 ± 0.04	0.72 ± 0.04	0.68 ± 0.07
Adrenals	(mg)	69.3 ± 4.2	62.7 ± 9.7	70.0 ± 7.7
	(mg%)	27.2 ± 3.1	25.2 ± 3.2	26.9 ± 3.1
Ovaries	(mg)	93.2 ± 9.6	93.9 ± 24.3	95.6 ± 12.0
	(mg%)	36.7 ± 6.1	37.9 ± 9.7	36.6 ± 3.6
Uterus	(g)	0.55 ± 0.19	0.48 ± 0.05	0.48 ± 0.10
	(g%)	0.21 ± 0.06	0.19 ± 0.04	0.18 ± 0.04

Each value shows mean ± SD.

Table 37. Histopathological findings in male rats (administration period)

Group	Control						Ethyl propionate					
Dose (mg/kg)	0						1000					
Grade	N ^{a)}	A ^{b)}	±	+	2+	3+	N ^{a)}	A ^{b)}	±	+	2+	3+
Findings												
Heart	[5] ^{c)}						[5] ^{c)}					
Cellular infiltration, mononuclear cell, focal	5	0	0	0	0	0	4	1	1	0	0	0
Lung	[5]						[5]					
Trachea	[5]						[5]					
Liver	[5]						[5]					
Pancreas	[5]						[5]					
Submandibular gland	[5]						[5]					
Stomach	[5]						[5]					
Duodenum	[5]						[5]					
Jejunum	[5]						[5]					
Mineralization, Peyer's patch	4	1	1	0	0	0	3	2	2	0	0	0
Ileum	[5]						[5]					
Cecum	[5]						[5]					
Colon	[5]						[5]					
Rectum	[5]						[5]					
Thymus	[5]						[5]					
Spleen	[5]						[5]					
Mesenteric lymph node	[5]						[5]					
Axillary lymph node	[5]						[5]					
Kidney	[5]						[5]					
Cyst, lateral	3	2	2	0	0	0	5	0	0	0	0	0
Urinary bladder	[5]						[5]					
Testis	[5]						[5]					
Degeneration/atrophy, seminiferous tubule, bilateral	5	0	0	0	0	0	4	1	0	0	1	0

Grade of histopathological findings; ±: slight, +: mild, 2+: moderate, 3+: marked.

(Continued)

a): No abnormality detected.

b): Abnormality detected.

c): Number in brackets is number of animals examined.

Table 37. (Continued) Histopathological findings in male rats (administration period)

Group	Control						Ethyl propionate					
	0						1000					
Dose (mg/kg)												
Grade	N ^{a)}	A ^{b)}	±	+	2+	3+	N ^{a)}	A ^{b)}	±	+	2+	3+
Findings												
Epididymis	[5] ^{c)}						[5] ^{c)}					
Decrease, sperm, bilateral	5	0	0	0	0	0	4	1	0	0	0	1
Prostate	[5]						[5]					
Cellular infiltration, lymphoid cell	4	1	1	0	0	0	4	1	1	0	0	0
Seminal vesicle	[5]						[5]					
Coagulation gland	[5]						[5]					
Skin	[5]						[5]					
Mammary gland	[5]						[5]					
Pituitary	[5]						[5]					
Cyst	5	0	0	0	0	0	4	1	1	0	0	0
Adrenal	[5]						[5]					
Thyroid	[5]						[5]					
Ectopic, thymic tissue	5	0	0	0	0	0	4	1	1	0	0	0
Ultimobranchial remnant	5	0	0	0	0	0	4	1	1	0	0	0
Parathyroid	[4]						[5]					
Cerebrum	[5]						[5]					
Cerebellum	[5]						[5]					
Pons	[5]						[5]					
Spinal cord	[5]						[5]					
Sciatic nerve	[5]						[5]					
Eyeball	[5]						[5]					
Retinal dysplasia, lateral	4	1	1	0	0	0	5	0	0	0	0	0
Harderian gland	[5]						[5]					
Rectus femoris muscle	[5]						[5]					
Sternum	[5]						[5]					
Femur	[5]						[5]					

Grade of histopathological findings; ±: slight, +: mild, 2+: moderate, 3+: marked.

a): No abnormality detected. b): Abnormality detected. c): Number in brackets is number of animals examined.

Table 38. Histopathological findings in female rats (administration period)

Group	Control						Ethyl propionate					
	0						1000					
Dose (mg/kg)												
Grade	N ^{a)}	A ^{b)}	±	+	2+	3+	N ^{a)}	A ^{b)}	±	+	2+	3+
Findings												
Heart	[5] ^{c)}						[5] ^{c)}					
Lung	[5]						[5]					
Trachea	[5]						[5]					
Liver	[5]						[5]					
Pancreas	[5]						[5]					
Submandibular gland	[5]						[5]					
Stomach	[5]						[5]					
Duodenum	[5]						[5]					
Jejunum	[5]						[5]					
Mineralization, Peyer's patch	3	2	2	0	0	0	4	1	1	0	0	0
Ileum	[5]						[5]					
Cecum	[5]						[5]					
Colon	[5]						[5]					
Rectum	[5]						[5]					
Thymus	[5]						[5]					
Spleen	[5]						[5]					
Mesenteric lymph node	[5]						[5]					
Axillary lymph node	[5]						[5]					
Kidney	[5]						[5]					
Cyst, lateral	4	1	1	0	0	0	5	0	0	0	0	0
Infarct, lateral	4	1	1	0	0	0	5	0	0	0	0	0
Urinary bladder	[5]						[5]					
Ovary	[5]						[5]					
Uterus	[5]						[5]					
Vagina	[5]						[5]					

Grade of histopathological findings; ±: slight, +: mild, 2+: moderate, 3+: marked.

(Continued)

a): No abnormality detected. b): Abnormality detected. c): Number in brackets is number of animals examined.

Table 38. (Continued) Histopathological findings in female rats (administration period)

Group	Control						Ethyl propionate					
	0						1000					
Dose (mg/kg)												
Grade	N ^{a)}	A ^{b)}	±	+	2+	3+	N ^{a)}	A ^{b)}	±	+	2+	3+
Findings												
Skin	[5] ^{c)}						[5] ^{c)}					
Mammary gland	[5]						[5]					
Pituitary	[5]						[5]					
Cyst	4	1	1	0	0	0	5	0	0	0	0	0
Adrenal	[5]						[5]					
Thyroid	[5]						[5]					
Ultimobranchial remnant	5	0	0	0	0	0	4	1	1	0	0	0
Parathyroid	[5]						[5]					
Cerebrum	[5]						[5]					
Cerebellum	[5]						[5]					
Pons	[5]						[5]					
Spinal cord	[5]						[5]					
Sciatic nerve	[5]						[5]					
Eyeball	[5]						[5]					
Retinal dysplasia, lateral	5	0	0	0	0	0	4	1	1	0	0	0
Harderian gland	[5]						[5]					
Rectus femoris muscle	[5]						[5]					
Sternum	[5]						[5]					
Femur	[5]						[5]					

Grade of histopathological findings; ±: slight, +: mild, 2+: moderate, 3+: marked.

a): No abnormality detected.

b): Abnormality detected.

c): Number in brackets is number of animals examined.

Table 39. Histopathological findings in male rats (recovery period)

Group	Control						Ethyl propionate					
Dose (mg/kg)	0						300					
Grade	N ^{a)}	A ^{b)}	±	+	2+	3+	N ^{a)}	A ^{b)}	±	+	2+	3+
Findings												
Testis	[1] ^{c)}						[1] ^{c)}					
Degeneration/atrophy, seminiferous tubule, bilateral	1	0	0	0	0	0	0	1	0	1	0	0
Epididymis	[1]						[1]					
Decrease, sperm, bilateral	1	0	0	0	0	0	0	1	0	0	0	1

Grade of histopathological findings; ±: slight, +: mild, 2+: moderate, 3+: marked.

a): No abnormality detected.

b): Abnormality detected.

c): Number in brackets is number of animals examined.

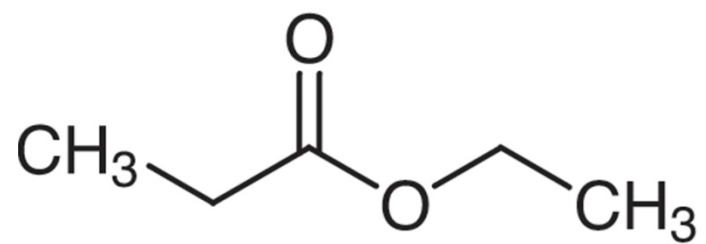


Fig 1. Chemical structure of Ethyl propionate.

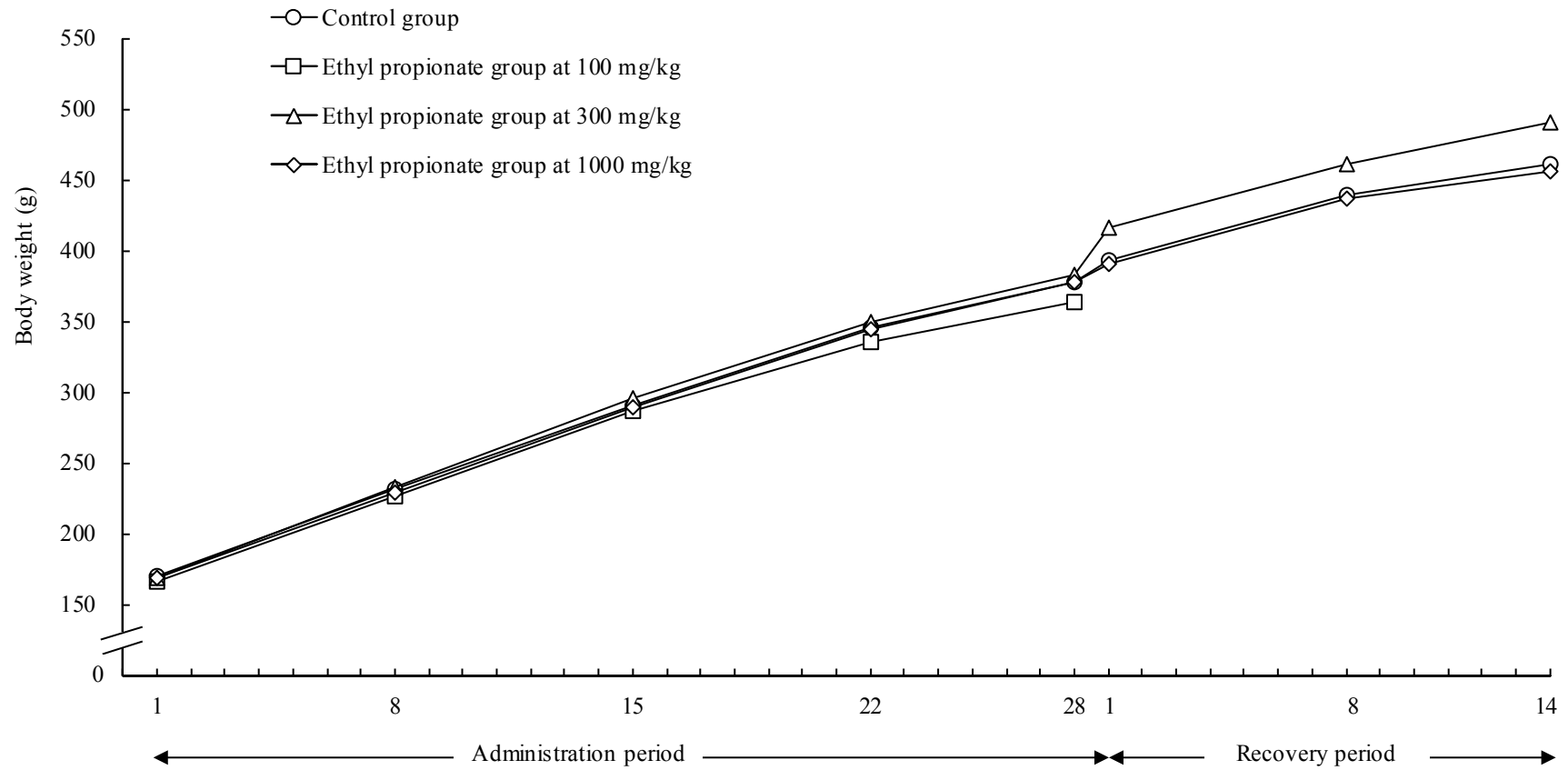


Fig 2. Body weights of male rats.

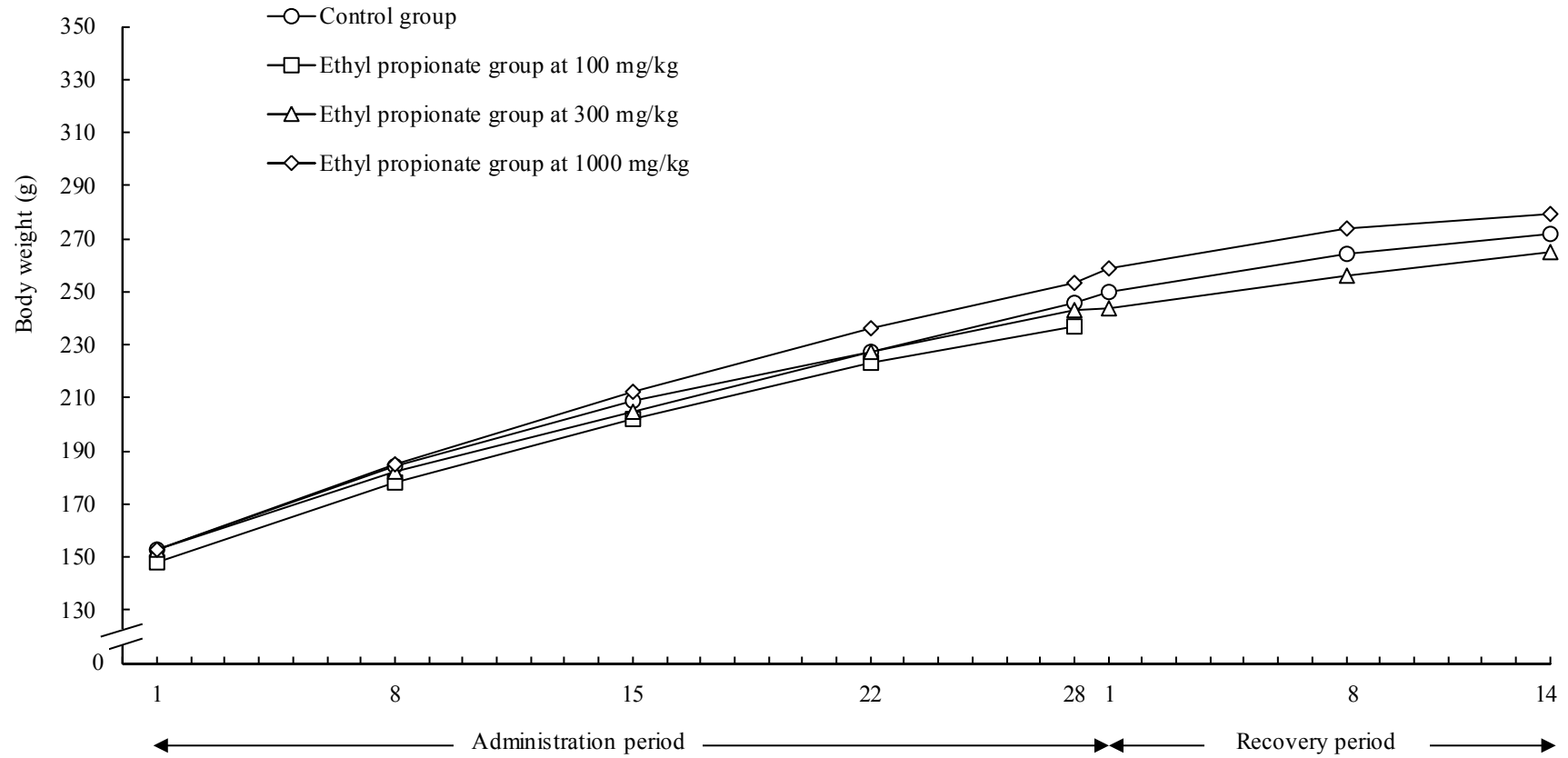


Fig 3. Body weights of female rats.

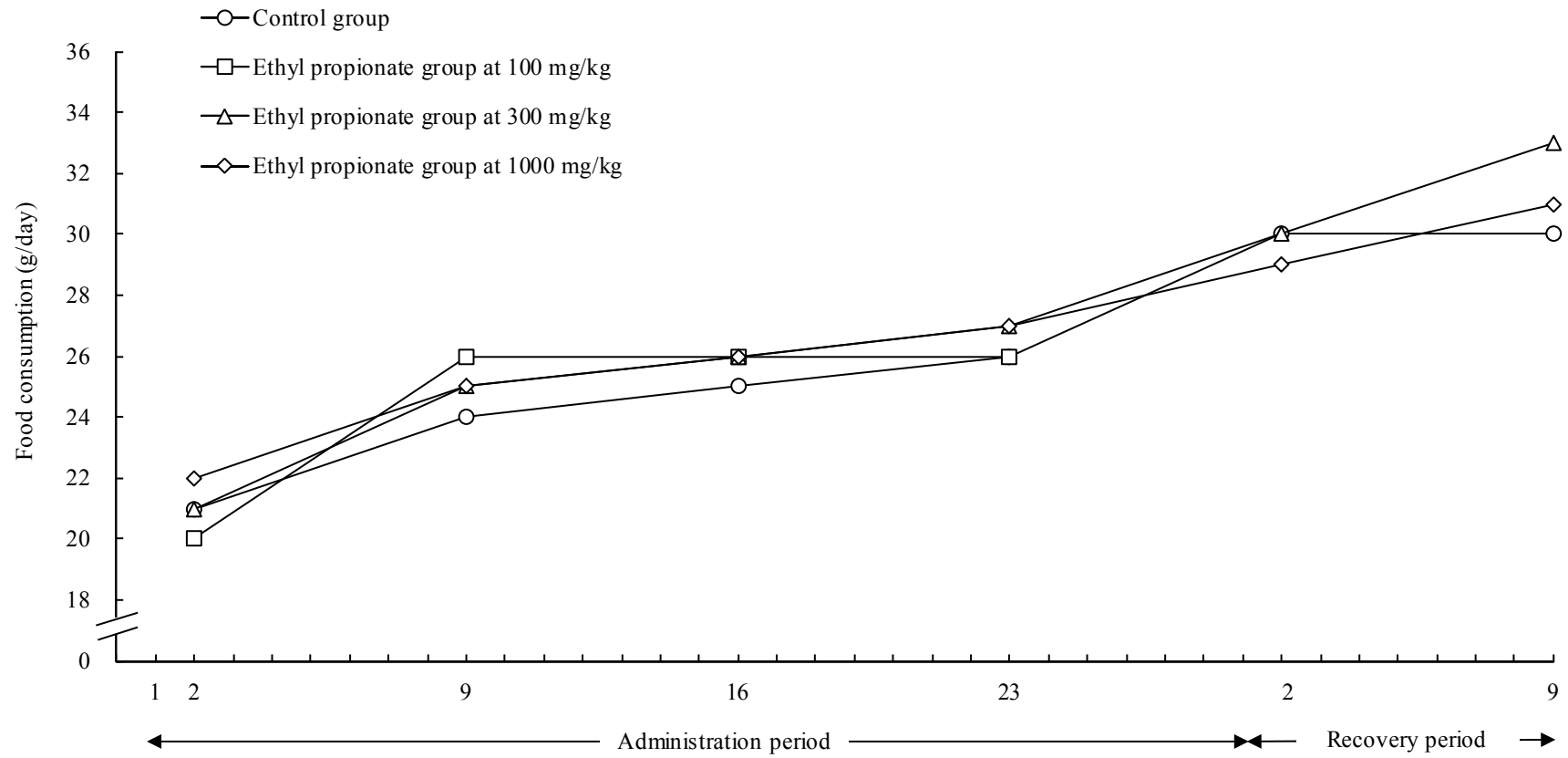


Fig 4. Food consumption in male rats.

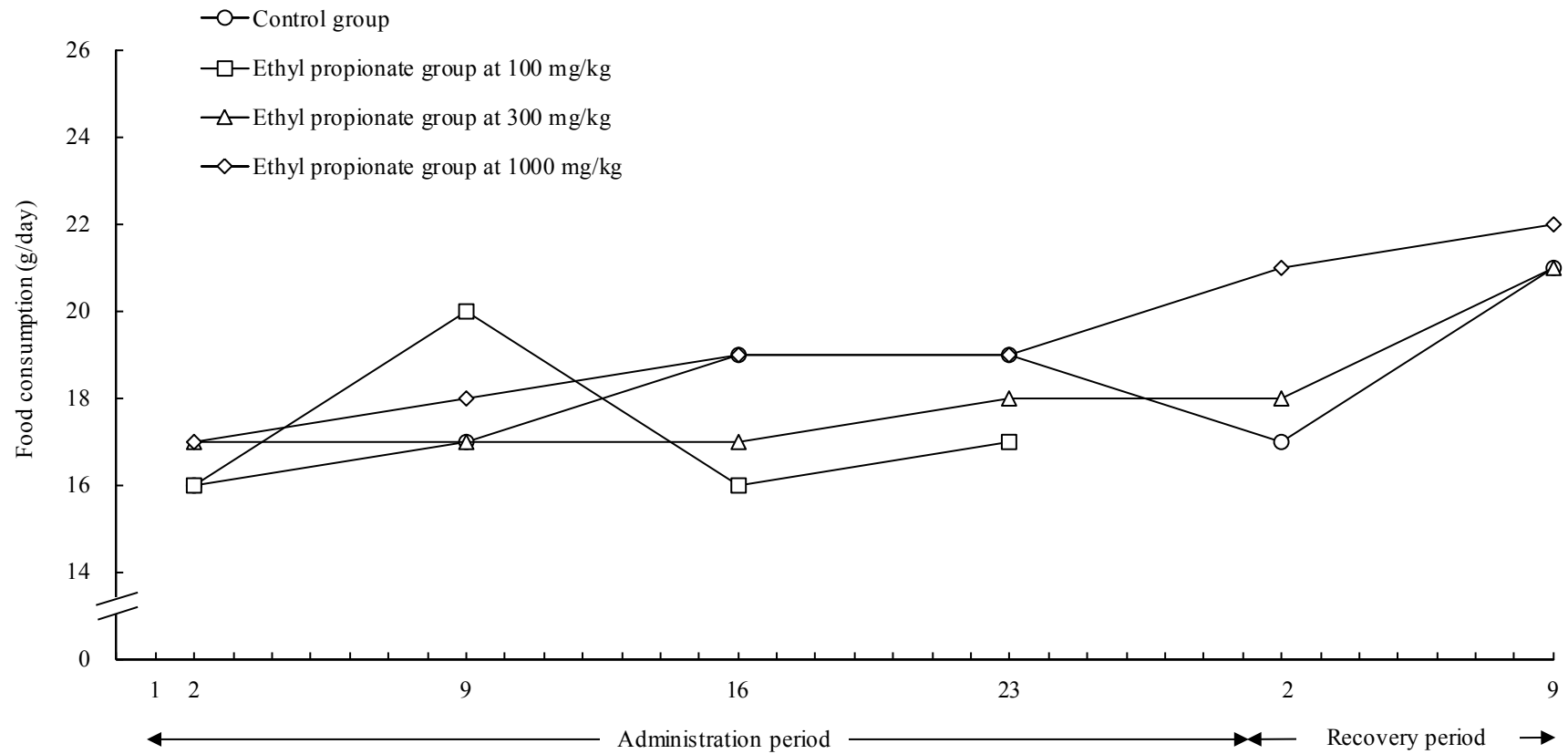


Fig 5. Food consumption in female rats.

Appendix 1-1. Individual clinical signs in male rats

Control group																														
Animal No.	Days of administration																													
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M01101	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01102	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01103	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01104	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01105	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01106	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01107	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01108	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01109	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01110	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 1-1. (Continued) Individual clinical signs in male rats

Control group																													
Animal No.	Days of administration																												
	16		17		18		19		20		21		22		23		24		25		26		27		28		29		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
M01101	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M01102	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M01103	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M01104	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M01105	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M01106	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M01107	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M01108	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M01109	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M01110	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

(Continued)

Appendix 1-1. (Continued) Individual clinical signs in male rats

Control group															
Animal No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
M01106	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01107	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01108	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01109	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M01110	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

N: Normal.

Appendix 1-2. Individual clinical signs in male rats

Ethyl propionate group at 100 mg/kg

Animal No.	Days of administration																															
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15			
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post		
M02201	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M02202	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M02203	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M02204	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M02205	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 1-2. (Continued) Individual clinical signs in male rats

Ethyl propionate group at 100 mg/kg																													
Animal No.	Days of administration																												
	16		17		18		19		20		21		22		23		24		25		26		27		28		29		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post			
M02201	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*	
M02202	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M02203	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M02204	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M02205	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

Appendix 1-3. Individual clinical signs in male rats

Ethyl propionate group at 300 mg/kg																														
Animal No.	Days of administration																													
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M03301	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03302	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03303	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03304	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03305	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03306	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03307	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03308	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03309	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03310	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 1-3. (Continued) Individual clinical signs in male rats

Ethyl propionate group at 300 mg/kg																												
Animal No.	Days of administration																											
	16		17		18		19		20		21		22		23		24		25		26		27		28		29	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M03301	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M03302	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M03303	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M03304	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M03305	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M03306	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M03307	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M03308	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M03309	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M03310	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

(Continued)

Appendix 1-3. (Continued) Individual clinical signs in male rats

Ethyl propionate group at 300 mg/kg															
Animal No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
M03306	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03307	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03308	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03309	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M03310	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

N: Normal.

Appendix 1-4. Individual clinical signs in male rats

Ethyl propionate group at 1000 mg/kg																														
Animal No.	Days of administration																													
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M04401	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04402	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04403	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04404	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04405	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04406	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04407	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04408	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04409	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04410	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 1-4. (Continued) Individual clinical signs in male rats

Ethyl propionate group at 1000 mg/kg																												
Animal No.	Days of administration																											
	16		17		18		19		20		21		22		23		24		25		26		27		28		29	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M04401	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M04402	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M04403	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M04404	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M04405	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
M04406	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M04407	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M04408	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M04409	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
M04410	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

(Continued)

Appendix 1-4. (Continued) Individual clinical signs in male rats

Ethyl propionate group at 1000 mg/kg															
Animal No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
M04406	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04407	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04408	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04409	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
M04410	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

N: Normal.

Appendix 2-1. Individual clinical signs in female rats

Control group																														
Animal No.	Days of administration																													
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F01151	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01152	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01153	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01154	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01155	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01156	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01157	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01158	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01159	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01160	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

N: Normal.

(Continued)

Appendix 2-1. (Continued) Individual clinical signs in female rats

Control group																													
Animal No.	Days of administration																												
	16		17		18		19		20		21		22		23		24		25		26		27		28		29		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
F01151	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F01152	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F01153	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F01154	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F01155	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F01156	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F01157	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F01158	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F01159	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F01160	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

(Continued)

Appendix 2-1. (Continued) Individual clinical signs in female rats

Control group															
Animal No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
F01156	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01157	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01158	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01159	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F01160	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

N: Normal.

Appendix 2-2. Individual clinical signs in female rats

Ethyl propionate group at 100 mg/kg

Animal No.	Days of administration																														
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
F02251	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F02252	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F02253	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F02254	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F02255	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 2-2. (Continued) Individual clinical signs in female rats

Ethyl propionate group at 100 mg/kg																													
Animal No.	Days of administration																												
	16		17		18		19		20		21		22		23		24		25		26		27		28		29		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post			
F02251	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*	
F02252	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F02253	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F02254	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F02255	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

Appendix 2-3. Individual clinical signs in female rats

Ethyl propionate group at 300 mg/kg																														
Animal No.	Days of administration																													
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03351	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03352	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03353	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03354	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03355	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03356	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03357	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03358	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03359	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03360	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 2-3. (Continued) Individual clinical signs in female rats

Ethyl propionate group at 300 mg/kg																												
Animal No.	Days of administration																											
	16		17		18		19		20		21		22		23		24		25		26		27		28		29	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F03351	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F03352	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F03353	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F03354	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F03355	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F03356	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F03357	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F03358	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F03359	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F03360	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

(Continued)

Appendix 2-3. (Continued) Individual clinical signs in female rats

Ethyl propionate group at 300 mg/kg															
Animal No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
F03356	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03357	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03358	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03359	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F03360	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

N: Normal.

Appendix 2-4. Individual clinical signs in female rats

Ethyl propionate group at 1000 mg/kg																														
Animal No.	Days of administration																													
	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04451	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04452	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04453	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04454	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04455	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04456	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04457	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04458	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04459	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04460	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

Appendix 2-4. (Continued) Individual clinical signs in female rats

Ethyl propionate group at 1000 mg/kg																												
Animal No.	Days of administration																											
	16		17		18		19		20		21		22		23		24		25		26		27		28		29	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
F04451	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F04452	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F04453	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F04454	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F04455	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*
F04456	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F04457	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F04458	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F04459	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
F04460	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Number of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	

Pre: Before administration, Post: after administration.

N: Normal.

*: Euthanized.

(Continued)

Appendix 2-4. (Continued) Individual clinical signs in female rats

Ethyl propionate group at 1000 mg/kg															
Animal No.	Days of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
F04456	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04457	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04458	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04459	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
F04460	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

N: Normal.

Appendix 3-1. Individual body weights of male rats

Control group									
Animal No.	Days of administration					Days of recovery			
	1	8	15	22	28	1	8	14	
M01101	169	229	288	343	373	-	-	-	
M01102	168	236	303	354	388	-	-	-	
M01103	153	209	257	300	325	-	-	-	
M01104	172	241	304	361	395	-	-	-	
M01105	164	219	274	329	354	-	-	-	
M01106	176	236	299	363	398	404	452	475	
M01107	180	245	300	355	389	398	446	463	
M01108	176	243	309	369	409	409	465	484	
M01109	164	226	278	325	353	353	390	415	
M01110	173	235	300	355	397	402	444	470	
Number of animals	10	10	10	10	10	5	5	5	
Mean	170	232	291	345	378	393	439	461	
SD	8	11	17	21	26	23	29	27	

Unit: g

Appendix 3-2. Individual body weights of male rats

Ethyl propionate group at 100 mg/kg

Animal No.	Days of administration				
	1	8	15	22	28
M02201	170	238	302	357	394
M02202	168	230	283	323	339
M02203	161	216	275	317	338
M02204	174	237	309	368	409
M02205	158	208	265	311	340
Number of animals	5	5	5	5	5
Mean	166	226	287	335	364
SD	7	13	18	26	35
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

Unit: g

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 3-3. Individual body weights of male rats

Ethyl propionate group at 300 mg/kg

Animal No.	Days of administration					Days of recovery		
	1	8	15	22	28	1	8	14
M03301	159	217	282	324	345	-	-	-
M03302	169	232	299	354	384	-	-	-
M03303	164	214	269	321	347	-	-	-
M03304	176	246	305	359	385	-	-	-
M03305	157	215	254	293	311	-	-	-
M03306	174	244	317	389	438	440	492	529
M03307	175	244	321	394	439	446	493	519
M03308	170	227	284	339	381	385	431	456
M03309	164	233	289	351	390	396	435	470
M03310	185	262	329	372	407	411	452	475
Number of animals	10	10	10	10	10	5	5	5
Mean	169	233	295	350	383	416	461	490
SD	9	16	24	31	40	27	30	32
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

Unit: g

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 3-4. Individual body weights of male rats

Ethyl propionate group at 1000 mg/kg									
Animal No.	Days of administration					Days of recovery			
	1	8	15	22	28	1	8	14	
M04401	162	222	271	328	360	-	-	-	
M04402	169	229	296	346	377	-	-	-	
M04403	161	215	261	304	322	-	-	-	
M04404	158	212	274	324	344	-	-	-	
M04405	175	251	320	376	422	-	-	-	
M04406	174	243	309	382	426	418	473	475	
M04407	185	254	319	380	420	416	456	477	
M04408	169	213	265	321	353	356	399	427	
M04409	165	220	276	321	356	358	399	417	
M04410	174	232	296	359	402	406	457	486	
Number of animals	10	10	10	10	10	5	5	5	
Mean	169	229	289	344	378	391	437	456	
SD	8	16	22	28	37	31	35	32	
Significance	NS	NS	NS	NS	NS	NS	NS	NS	
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	

Unit: g

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 4-1. Individual body weights of female rats

Control group									
Animal No.	Days of administration					Days of recovery			
	1	8	15	22	28	1	8	14	
F01151	157	192	215	225	255	-	-	-	
F01152	138	171	194	210	227	-	-	-	
F01153	144	184	216	243	260	-	-	-	
F01154	148	165	189	204	210	-	-	-	
F01155	153	191	222	244	268	-	-	-	
F01156	148	170	187	209	218	217	232	240	
F01157	162	197	226	242	269	273	283	293	
F01158	155	190	215	238	253	261	276	293	
F01159	166	197	227	244	265	263	275	272	
F01160	160	184	199	214	236	235	255	261	
Number of animals	10	10	10	10	10	5	5	5	
Mean	153	184	209	227	246	250	264	272	
SD	9	12	15	17	22	23	21	23	

Unit: g

Appendix 4-2. Individual body weights of female rats

Ethyl propionate group at 100 mg/kg					
Animal No.	Days of administration				
	1	8	15	22	28
F02251	152	177	202	227	237
F02252	156	193	221	241	250
F02253	150	178	195	221	240
F02254	143	176	203	221	243
F02255	138	164	191	205	214
Number of animals	5	5	5	5	5
Mean	148	178	202	223	237
SD	7	10	12	13	14
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

Unit: g

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 4-3. Individual body weights of female rats

Ethyl propionate group at 300 mg/kg									
Animal No.	Days of administration					Days of recovery			
	1	8	15	22	28	1	8	14	
F03351	145	178	204	224	241	-	-	-	
F03352	144	175	195	215	238	-	-	-	
F03353	140	175	186	213	220	-	-	-	
F03354	151	179	199	213	237	-	-	-	
F03355	159	202	238	263	288	-	-	-	
F03356	150	175	188	210	223	230	240	242	
F03357	169	195	233	260	267	275	282	294	
F03358	160	191	214	235	246	242	265	284	
F03359	154	175	193	215	230	234	245	246	
F03360	157	177	196	217	236	237	248	257	
Number of animals	10	10	10	10	10	5	5	5	
Mean	153	182	205	227	243	244	256	265	
SD	9	10	18	20	21	18	17	23	
Significance	NS	NS	NS	NS	NS	NS	NS	NS	
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	

Unit: g

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 4-4. Individual body weights of female rats

Ethyl propionate group at 1000 mg/kg									
Animal No.	Days of administration					Days of recovery			
	1	8	15	22	28	1	8	14	
F04451	150	172	186	206	216	-	-	-	
F04452	157	206	244	277	300	-	-	-	
F04453	141	177	202	224	242	-	-	-	
F04454	140	175	199	222	237	-	-	-	
F04455	153	184	212	232	250	-	-	-	
F04456	148	170	202	222	229	229	251	253	
F04457	156	185	212	241	260	265	282	290	
F04458	167	198	223	252	273	272	287	291	
F04459	158	191	219	238	251	258	263	276	
F04460	163	196	222	241	269	269	288	286	
Number of animals	10	10	10	10	10	5	5	5	
Mean	153	185	212	236	253	259	274	279	
SD	9	12	16	20	24	17	16	16	
Significance	NS	NS	NS	NS	NS	NS	NS	NS	
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	

Unit: g

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 5-1. Individual food consumption in male rats

Control group						
Animal No.	Days of administration				Days of recovery	
	2	9	16	23	2	9
M01101	23	25	25	26	-	-
M01102	21	26	23	26	-	-
M01103	19	22	22	24	-	-
M01104	19	24	26	22	-	-
M01105	19	20	24	29	-	-
M01106	24	25	26	28	32	34
M01107	22	25	25	27	30	29
M01108	23	27	29	30	34	30
M01109	19	22	22	24	27	29
M01110	22	22	24	28	29	30
Number of animals	10	10	10	10	5	5
Mean	21	24	25	26	30	30
SD	2	2	2	3	3	2

Unit: g/day.

Appendix 5-2. Individual food consumption in male rats

Ethyl propionate group at 100 mg/kg				
Animal No.	Days of administration			
	2	9	16	23
M02201	21	25	25	28
M02202	21	26	24	24
M02203	19	24	24	24
M02204	21	28	28	28
M02205	19	26	27	27
Number of animals	5	5	5	5
Mean	20	26	26	26
SD	1	1	2	2
Significance	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU

Unit: g/day.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 5-3. Individual food consumption in male rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Days of administration				Days of recovery	
	2	9	16	23	2	9
M03301	21	25	27	27	-	-
M03302	19	22	25	27	-	-
M03303	20	21	23	25	-	-
M03304	20	28	30	26	-	-
M03305	20	23	22	20	-	-
M03306	20	27	26	32	35	39
M03307	21	26	28	30	31	34
M03308	19	23	22	28	28	32
M03309	21	23	27	23	28	33
M03310	24	29	26	31	29	29
Number of animals	10	10	10	10	5	5
Mean	21	25	26	27	30	33
SD	1	3	3	4	3	4
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

Unit: g/day.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 5-4. Individual food consumption in male rats

Ethyl propionate group at 1000 mg/kg						
Animal No.	Days of administration				Days of recovery	
	2	9	16	23	2	9
M04401	20	22	23	27	-	-
M04402	22	27	28	27	-	-
M04403	20	24	22	23	-	-
M04404	21	23	24	24	-	-
M04405	23	29	28	30	-	-
M04406	23	27	28	31	34	29
M04407	24	28	28	28	26	31
M04408	21	22	24	24	28	35
M04409	20	21	20	25	28	30
M04410	23	27	30	30	30	32
Number of animals	10	10	10	10	5	5
Mean	22	25	26	27	29	31
SD	1	3	3	3	3	2
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

Unit: g/day.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 6-1. Individual food consumption in female rats

Control group						
Animal No.	Days of administration				Days of recovery	
	2	9	16	23	2	9
F01151	15	18	20	18	-	-
F01152	17	16	17	18	-	-
F01153	18	17	20	20	-	-
F01154	15	18	12	16	-	-
F01155	18	22	24	21	-	-
F01156	17	13	16	13	16	19
F01157	11	13	18	22	19	21
F01158	17	19	21	18	24	23
F01159	15	20	20	22	16	20
F01160	15	18	18	19	12	22
Number of animals	10	10	10	10	5	5
Mean	16	17	19	19	17	21
SD	2	3	3	3	4	2

Unit: g/day.

Appendix 6-2. Individual food consumption in female rats

Ethyl propionate group at 100 mg/kg				
Animal No.	Days of administration			
	2	9	16	23
F02251	17	20	12	19
F02252	17	19	19	18
F02253	17	20	18	16
F02254	14	21	18	18
F02255	16	18	13	16
Number of animals	5	5	5	5
Mean	16	20	16	17
SD	1	1	3	1
Significance	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU

Unit: g/day.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 6-3. Individual food consumption in female rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Days of administration				Days of recovery	
	2	9	16	23	2	9
F03351	17	18	14	21	-	-
F03352	16	19	19	21	-	-
F03353	16	19	18	18	-	-
F03354	17	13	17	18	-	-
F03355	20	20	16	21	-	-
F03356	11	16	17	16	17	21
F03357	19	17	15	19	21	17
F03358	18	17	17	17	16	23
F03359	18	17	18	15	18	21
F03360	17	17	17	15	18	22
Number of animals	10	10	10	10	5	5
Mean	17	17	17	18	18	21
SD	2	2	1	2	2	2
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

Unit: g/day.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 6-4. Individual food consumption in female rats

Ethyl propionate group at 1000 mg/kg						
Animal No.	Days of administration				Days of recovery	
	2	9	16	23	2	9
F04451	16	17	17	13	-	-
F04452	19	21	22	23	-	-
F04453	16	16	18	20	-	-
F04454	16	17	19	21	-	-
F04455	17	19	20	23	-	-
F04456	15	17	14	17	18	14
F04457	19	18	19	17	24	25
F04458	20	21	22	16	22	25
F04459	19	16	20	18	24	21
F04460	15	20	20	22	16	24
Number of animals	10	10	10	10	5	5
Mean	17	18	19	19	21	22
SD	2	2	2	3	4	5
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

Unit: g/day.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 7-1. Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals in cages									
Animal No.	Blind No.	Posture					Palpebral closure				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	2	2	2	2	2	1	1	1	1	1
M01102	M00005	2	2	2	2	2	1	1	1	1	1
M01103	M00001	2	2	2	2	2	1	1	1	1	1
M01104	M00011	2	2	2	2	2	1	1	1	1	1
M01105	M00014	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals in cages										
Animal No.	Blind No.	Excessive grooming					Repetitive circling					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
M01101	M00002	1	1	1	1	1	1	1	1	1	1	1
M01102	M00005	1	1	1	1	1	1	1	1	1	1	1
M01103	M00001	1	1	1	1	1	1	1	1	1	1	1
M01104	M00011	1	1	1	1	1	1	1	1	1	1	1
M01105	M00014	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	1	1	1	1	1	1	1	1	1	1
M01102	M00005	1	1	1	1	1	1	1	1	1	1
M01103	M00001	1	1	1	1	1	1	1	1	1	1
M01104	M00011	1	1	1	1	1	1	1	1	1	1
M01105	M00014	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals in cages				
Animal No.	Blind No.	Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
M01101	M00002	1	1	1	1	1
M01102	M00005	1	1	1	1	1
M01103	M00001	1	1	1	1	1
M01104	M00011	1	1	1	1	1
M01105	M00014	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M01101	M00002	2	2	2	2	2	2	2	2	2	2
M01102	M00005	2	2	2	2	2	2	2	2	2	2
M01103	M00001	2	2	2	2	2	2	2	2	2	2
M01104	M00011	2	2	2	2	2	2	2	2	2	2
M01105	M00014	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	2	2	2	2	2	1	1	1	1	1
M01102	M00005	2	2	2	2	2	1	1	1	1	1
M01103	M00001	2	2	2	2	2	1	1	1	1	1
M01104	M00011	2	2	2	2	2	1	1	1	1	1
M01105	M00014	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals on observer's palm										
Animal No.	Blind No.	Mucous membranes					Lacrimation					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
M01101	M00002	1	1	1	1	1	1	1	1	1	1	1
M01102	M00005	1	1	1	1	1	1	1	1	1	1	1
M01103	M00001	1	1	1	1	1	1	1	1	1	1	1
M01104	M00011	1	1	1	1	1	1	1	1	1	1	1
M01105	M00014	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals on observer's palm										
Animal No.	Blind No.	Salivation					Piloerection					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
M01101	M00002	1	1	1	1	1	1	1	1	1	1	1
M01102	M00005	1	1	1	1	1	1	1	1	1	1	1
M01103	M00001	1	1	1	1	1	1	1	1	1	1	1
M01104	M00011	1	1	1	1	1	1	1	1	1	1	1
M01105	M00014	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	2	2	2	2	2	1	1	1	1	1
M01102	M00005	2	2	2	2	2	1	1	1	1	1
M01103	M00001	2	2	2	2	2	1	1	1	1	1
M01104	M00011	2	2	2	2	2	1	1	1	1	1
M01105	M00014	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	1	0	1	1	1	2	1	2	3	1
M01102	M00005	0	1	1	0	0	1	1	1	0	0
M01103	M00001	2	1	1	1	1	2	5	2	2	0
M01104	M00011	2	1	1	1	0	1	2	2	2	3
M01105	M00014	0	0	0	0	0	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	0.6	0.8	0.6	0.4	1.2	1.8	1.4	1.4	0.8
SD		1.0	0.5	0.4	0.5	0.5	0.8	1.9	0.9	1.3	1.3

Pre: Before administration period.

(Continued)

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	3	3	0	0	6	0	3	0	0	0
M01102	M00005	15	7	4	4	10	0	0	0	0	0
M01103	M00001	3	4	1	1	20	0	0	0	0	0
M01104	M00011	7	3	0	2	0	0	0	0	0	0
M01105	M00014	12	4	0	1	10	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		8.0	4.2	1.0	1.6	9.2	0.0	0.6	0.0	0.0	0.0
SD		5.4	1.6	1.7	1.5	7.3	0.0	1.3	0.0	0.0	0.0

Pre: Before administration period.

(Continued)

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M01101	M00002	1	1	1	1	1	1	1	1	1	1
M01102	M00005	1	1	1	1	1	1	1	1	1	1
M01103	M00001	1	1	1	1	1	1	1	1	1	1
M01104	M00011	1	1	1	1	1	1	1	1	1	1
M01105	M00014	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Open-field test									
Animal No.	Blind No.	Consciousness					Behavioral abnormalities				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M01101	M00002	2	2	2	2	2	1	1	1	1	1
M01102	M00005	2	2	2	2	2	1	1	1	1	1
M01103	M00001	2	2	2	2	2	1	1	1	1	1
M01104	M00011	2	2	2	2	2	1	1	1	1	1
M01105	M00014	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

Appendix 7-1. (Continued) Individual detailed clinical signs by FOB in male rats

Control group		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
M01101	M00002	1	1	1	1	1
M01102	M00005	1	1	1	1	1
M01103	M00001	1	1	1	1	1
M01104	M00011	1	1	1	1	1
M01105	M00014	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 7-2. Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Posture					Palpebral closure				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	2	2	2	2	2	1	1	1	1	1
M02202	M00022	2	2	2	2	2	1	1	1	1	1
M02203	M00020	2	2	2	2	2	1	1	1	1	1
M02204	M00021	2	2	2	2	2	1	1	1	1	1
M02205	M00010	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Observation of animals in cages									
		Excessive grooming					Repetitive circling				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M02201	M00019	1	1	1	1	1	1	1	1	1	1
M02202	M00022	1	1	1	1	1	1	1	1	1	1
M02203	M00020	1	1	1	1	1	1	1	1	1	1
M02204	M00021	1	1	1	1	1	1	1	1	1	1
M02205	M00010	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	1	1	1	1	1	1	1	1	1	1
M02202	M00022	1	1	1	1	1	1	1	1	1	1
M02203	M00020	1	1	1	1	1	1	1	1	1	1
M02204	M00021	1	1	1	1	1	1	1	1	1	1
M02205	M00010	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg						
Animal No.	Blind No.	Observation of animals in cages				
		Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
M02201	M00019	1	1	1	1	1
M02202	M00022	1	1	1	1	1
M02203	M00020	1	1	1	1	1
M02204	M00021	1	1	1	1	1
M02205	M00010	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	2	2	2	2	2	2	2	2	2	2
M02202	M00022	2	2	2	2	2	2	2	2	2	2
M02203	M00020	2	2	2	2	2	2	2	2	2	2
M02204	M00021	2	2	2	2	2	2	2	2	2	2
M02205	M00010	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	2	2	2	2	2	1	1	1	1	1
M02202	M00022	2	2	2	2	2	1	1	1	1	1
M02203	M00020	2	2	2	2	2	1	1	1	1	1
M02204	M00021	2	2	2	2	2	1	1	1	1	1
M02205	M00010	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Mucous membranes					Lacrimation				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	1	1	1	1	1	1	1	1	1	1
M02202	M00022	1	1	1	1	1	1	1	1	1	1
M02203	M00020	1	1	1	1	1	1	1	1	1	1
M02204	M00021	1	1	1	1	1	1	1	1	1	1
M02205	M00010	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Salivation					Piloerection				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	1	1	1	1	1	1	1	1	1	1
M02202	M00022	1	1	1	1	1	1	1	1	1	1
M02203	M00020	1	1	1	1	1	1	1	1	1	1
M02204	M00021	1	1	1	1	1	1	1	1	1	1
M02205	M00010	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M02201	M00019	2	2	2	2	2	1	1	1	1	1
M02202	M00022	2	2	2	2	2	1	1	1	1	1
M02203	M00020	2	2	2	2	2	1	1	1	1	1
M02204	M00021	2	2	2	2	2	1	1	1	1	1
M02205	M00010	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M02201	M00019	0	1	1	1	2	1	2	2	3	3
M02202	M00022	1	1	0	0	0	0	1	1	5	3
M02203	M00020	1	1	1	0	0	0	1	3	0	0
M02204	M00021	0	0	0	0	0	2	2	2	0	0
M02205	M00010	1	1	1	0	1	2	4	3	2	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		0.6	0.8	0.6	0.2	0.6	1.0	2.0	2.2	2.0	1.2
SD		0.5	0.4	0.5	0.4	0.9	1.0	1.2	0.8	2.1	1.6
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M02201	M00019	8	1	6	3	2	0	0	0	0	0
M02202	M00022	1	2	0	0	2	0	0	0	0	0
M02203	M00020	9	3	1	6	9	1	0	0	0	0
M02204	M00021	7	6	5	8	7	0	0	0	0	0
M02205	M00010	1	2	1	0	7	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		5.2	2.8	2.6	3.4	5.4	0.2	0.0	0.0	0.0	0.0
SD		3.9	1.9	2.7	3.6	3.2	0.4	0.0	0.0	0.0	0.0
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	STL	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M02201	M00019	1	1	1	1	1	1	1	1	1	1
M02202	M00022	1	1	1	1	1	1	1	1	1	1
M02203	M00020	1	1	1	1	1	1	1	1	1	1
M02204	M00021	1	1	1	1	1	1	1	1	1	1
M02205	M00010	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Open-field test									
		Consciousness					Behavioral abnormalities				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M02201	M00019	2	2	2	2	2	1	1	1	1	1
M02202	M00022	2	2	2	2	2	1	1	1	1	1
M02203	M00020	2	2	2	2	2	1	1	1	1	1
M02204	M00021	2	2	2	2	2	1	1	1	1	1
M02205	M00010	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-2. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 100 mg/kg		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
M02201	M00019	1	1	1	1	1
M02202	M00022	1	1	1	1	1
M02203	M00020	1	1	1	1	1
M02204	M00021	1	1	1	1	1
M02205	M00010	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Posture					Palpebral closure				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	2	2	2	2	2	1	1	1	1	1
M03302	M00013	2	2	2	2	2	1	1	1	1	1
M03303	M00006	2	2	2	2	2	1	1	1	1	1
M03304	M00007	2	2	2	2	2	1	1	1	1	1
M03305	M00016	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg											
Animal No.	Blind No.	Observation of animals in cages									
		Excessive grooming					Repetitive circling				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M03301	M00015	1	1	1	1	1	1	1	1	1	1
M03302	M00013	1	1	1	1	1	1	1	1	1	1
M03303	M00006	1	1	1	1	1	1	1	1	1	1
M03304	M00007	1	1	1	1	1	1	1	1	1	1
M03305	M00016	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	1	1	1	1	1	1	1	1	1	1
M03302	M00013	1	1	1	1	1	1	1	1	1	1
M03303	M00006	1	1	1	1	1	1	1	1	1	1
M03304	M00007	1	1	1	1	1	1	1	1	1	1
M03305	M00016	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Blind No.	Observation of animals in cages				
		Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
M03301	M00015	1	1	1	1	1
M03302	M00013	1	1	1	1	1
M03303	M00006	1	1	1	1	1
M03304	M00007	1	1	1	1	1
M03305	M00016	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	2	2	2	2	2	2	2	2	2	2
M03302	M00013	2	2	2	2	2	2	2	2	2	2
M03303	M00006	2	2	2	2	2	2	2	2	2	2
M03304	M00007	2	2	2	2	2	2	2	2	2	2
M03305	M00016	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	2	2	2	2	2	1	1	1	1	1
M03302	M00013	2	2	2	2	2	1	1	1	1	1
M03303	M00006	2	2	2	2	2	1	1	1	1	1
M03304	M00007	2	2	2	2	2	1	1	1	1	1
M03305	M00016	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Mucous membranes					Lacrimation				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	1	1	1	1	1	1	1	1	1	1
M03302	M00013	1	1	1	1	1	1	1	1	1	1
M03303	M00006	1	1	1	1	1	1	1	1	1	1
M03304	M00007	1	1	1	1	1	1	1	1	1	1
M03305	M00016	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm										
Animal No.	Blind No.	Salivation					Piloerection					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
M03301	M00015	1	1	1	1	1	1	1	1	1	1	1
M03302	M00013	1	1	1	1	1	1	1	1	1	1	1
M03303	M00006	1	1	1	1	1	1	1	1	1	1	1
M03304	M00007	1	1	1	1	1	1	1	1	1	1	1
M03305	M00016	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	2	2	2	2	2	1	1	1	1	1
M03302	M00013	2	2	2	2	2	1	1	1	1	1
M03303	M00006	2	2	2	2	2	1	1	1	1	1
M03304	M00007	2	2	2	2	2	1	1	1	1	1
M03305	M00016	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M03301	M00015	1	1	1	1	1	3	6	2	6	3
M03302	M00013	0	0	0	0	0	0	0	2	2	1
M03303	M00006	0	0	0	0	0	4	4	1	0	0
M03304	M00007	0	1	0	0	0	1	0	3	0	0
M03305	M00016	1	0	0	0	0	2	4	5	1	7
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		0.4	0.4	0.2	0.2	0.2	2.0	2.8	2.6	1.8	2.2
SD		0.5	0.5	0.4	0.4	0.4	1.6	2.7	1.5	2.5	2.9
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M03301	M00015	13	2	2	1	10	0	0	0	0	0
M03302	M00013	6	2	1	1	4	0	0	0	0	0
M03303	M00006	7	8	4	13	10	0	0	0	0	0
M03304	M00007	8	4	0	5	8	0	0	0	0	0
M03305	M00016	3	0	0	0	1	1	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		7.4	3.2	1.4	4.0	6.6	0.2	0.0	0.0	0.0	0.0
SD		3.6	3.0	1.7	5.4	4.0	0.4	0.0	0.0	0.0	0.0
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	STL	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M03301	M00015	1	1	1	1	1	1	1	1	1	1
M03302	M00013	1	1	1	1	1	1	1	1	1	1
M03303	M00006	1	1	1	1	1	1	1	1	1	1
M03304	M00007	1	1	1	1	1	1	1	1	1	1
M03305	M00016	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg		Open-field test									
Animal No.	Blind No.	Consciousness					Behavioral abnormalities				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M03301	M00015	2	2	2	2	2	1	1	1	1	1
M03302	M00013	2	2	2	2	2	1	1	1	1	1
M03303	M00006	2	2	2	2	2	1	1	1	1	1
M03304	M00007	2	2	2	2	2	1	1	1	1	1
M03305	M00016	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-3. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Blind No.	Open-field test				
		Righting reflex				
		Days of administration				
		Pre	7	14	21	27
M03301	M00015	1	1	1	1	1
M03302	M00013	1	1	1	1	1
M03303	M00006	1	1	1	1	1
M03304	M00007	1	1	1	1	1
M03305	M00016	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Observation of animals in cages									
		Posture					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M04401	M00018	2	2	2	2	2	1	1	1	1	1
M04402	M00017	2	2	2	2	2	1	1	1	1	1
M04403	M00023	2	2	2	2	2	1	1	1	1	1
M04404	M00008	2	2	2	2	2	1	1	1	1	1
M04405	M00004	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Excessive grooming					Repetitive circling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	1	1	1	1	1	1	1	1	1	1
M04402	M00017	1	1	1	1	1	1	1	1	1	1
M04403	M00023	1	1	1	1	1	1	1	1	1	1
M04404	M00008	1	1	1	1	1	1	1	1	1	1
M04405	M00004	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	1	1	1	1	1	1	1	1	1	1
M04402	M00017	1	1	1	1	1	1	1	1	1	1
M04403	M00023	1	1	1	1	1	1	1	1	1	1
M04404	M00008	1	1	1	1	1	1	1	1	1	1
M04405	M00004	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg						
Animal No.	Blind No.	Observation of animals in cages				
		Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
M04401	M00018	1	1	1	1	1
M04402	M00017	1	1	1	1	1
M04403	M00023	1	1	1	1	1
M04404	M00008	1	1	1	1	1
M04405	M00004	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	2	2	2	2	2	2	2	2	2	2
M04402	M00017	2	2	2	2	2	2	2	2	2	2
M04403	M00023	2	2	2	2	2	2	2	2	2	2
M04404	M00008	2	2	2	2	2	2	2	2	2	2
M04405	M00004	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	2	2	2	2	2	1	1	1	1	1
M04402	M00017	2	2	2	2	2	1	1	1	1	1
M04403	M00023	2	2	2	2	2	1	1	1	1	1
M04404	M00008	2	2	2	2	2	1	1	1	1	1
M04405	M00004	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Mucous membranes					Lacrimation				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	1	1	1	1	1	1	1	1	1	1
M04402	M00017	1	1	1	1	1	1	1	1	1	1
M04403	M00023	1	1	1	1	1	1	1	1	1	1
M04404	M00008	1	1	1	1	1	1	1	1	1	1
M04405	M00004	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Salivation					Piloerection				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	1	1	1	1	1	1	1	1	1	1
M04402	M00017	1	1	1	1	1	1	1	1	1	1
M04403	M00023	1	1	1	1	1	1	1	1	1	1
M04404	M00008	1	1	1	1	1	1	1	1	1	1
M04405	M00004	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
M04401	M00018	2	2	2	2	2	1	1	1	1	1
M04402	M00017	2	2	2	2	2	1	1	1	1	1
M04403	M00023	2	2	2	2	2	1	1	1	1	1
M04404	M00008	2	2	2	2	2	1	1	1	1	1
M04405	M00004	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Open-field test									
		Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M04401	M00018	1	0	0	1	1	0	2	1	2	0
M04402	M00017	0	1	2	0	0	3	3	3	1	0
M04403	M00023	2	1	0	0	0	0	1	0	1	0
M04404	M00008	0	2	1	1	0	0	0	0	2	3
M04405	M00004	0	1	1	1	0	0	0	0	2	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		0.6	1.0	0.8	0.6	0.2	0.6	1.2	0.8	1.6	0.6
SD		0.9	0.7	0.8	0.5	0.4	1.3	1.3	1.3	0.5	1.3
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M04401	M00018	6	1	0	0	11	0	0	0	0	0
M04402	M00017	4	0	1	0	7	0	1	0	0	0
M04403	M00023	2	2	1	1	3	0	0	0	0	0
M04404	M00008	4	2	0	0	0	0	0	0	0	0
M04405	M00004	6	2	0	0	3	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		4.4	1.4	0.4	0.2	4.8	0.0	0.2	0.0	0.0	0.0
SD		1.7	0.9	0.5	0.4	4.3	0.0	0.4	0.0	0.0	0.0
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	STL	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M04401	M00018	1	1	1	1	1	1	1	1	1	1
M04402	M00017	1	1	1	1	1	1	1	1	1	1
M04403	M00023	1	1	1	1	1	1	1	1	1	1
M04404	M00008	1	1	1	1	1	1	1	1	1	1
M04405	M00004	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Open-field test									
		Consciousness					Behavioral abnormalities				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
M04401	M00018	2	2	2	2	2	1	1	1	1	1
M04402	M00017	2	2	2	2	2	1	1	1	1	1
M04403	M00023	2	2	2	2	2	1	1	1	1	1
M04404	M00008	2	2	2	2	2	1	1	1	1	1
M04405	M00004	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 7-4. (Continued) Individual detailed clinical signs by FOB in male rats

Ethyl propionate group at 1000 mg/kg		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
M04401	M00018	1	1	1	1	1
M04402	M00017	1	1	1	1	1
M04403	M00023	1	1	1	1	1
M04404	M00008	1	1	1	1	1
M04405	M00004	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-1. Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals in cages									
Animal No.	Blind No.	Posture					Palpebral closure				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	2	2	2	2	2	1	1	1	1	1
F01152	F00004	2	2	2	2	2	1	1	1	1	1
F01153	F00005	2	2	2	2	2	1	1	1	1	1
F01154	F00012	2	2	2	2	2	1	1	1	1	1
F01155	F00017	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals in cages									
Animal No.	Blind No.	Excessive grooming					Repetitive circling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	1	1	1	1	1	1	1	1	1	1
F01152	F00004	1	1	1	1	1	1	1	1	1	1
F01153	F00005	1	1	1	1	1	1	1	1	1	1
F01154	F00012	1	1	1	1	1	1	1	1	1	1
F01155	F00017	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	1	1	1	1	1	1	1	1	1	1
F01152	F00004	1	1	1	1	1	1	1	1	1	1
F01153	F00005	1	1	1	1	1	1	1	1	1	1
F01154	F00012	1	1	1	1	1	1	1	1	1	1
F01155	F00017	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals in cages				
Animal No.	Blind No.	Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
F01151	F00018	1	1	1	1	1
F01152	F00004	1	1	1	1	1
F01153	F00005	1	1	1	1	1
F01154	F00012	1	1	1	1	1
F01155	F00017	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals on observer's palm										
Animal No.	Blind No.	Ease of removal from cage					Ease of handling					
		Pre	Days of administration				Pre	Days of administration				
			7	14	21	27		7	14	21	27	
F01151	F00018	2	2	2	2	2	2	2	2	2	2	2
F01152	F00004	2	2	2	2	2	2	2	2	2	2	2
F01153	F00005	2	2	2	2	2	2	2	2	2	2	2
F01154	F00012	2	2	2	2	2	2	2	2	2	2	2
F01155	F00017	2	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2	2

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	2	2	2	2	2	1	1	1	1	1
F01152	F00004	2	2	2	2	2	1	1	1	1	1
F01153	F00005	2	2	2	2	2	1	1	1	1	1
F01154	F00012	2	2	2	2	2	1	1	1	1	1
F01155	F00017	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals on observer's palm										
Animal No.	Blind No.	Mucous membranes					Lacrimation					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
F01151	F00018	1	1	1	1	1	1	1	1	1	1	1
F01152	F00004	1	1	1	1	1	1	1	1	1	1	1
F01153	F00005	1	1	1	1	1	1	1	1	1	1	1
F01154	F00012	1	1	1	1	1	1	1	1	1	1	1
F01155	F00017	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals on observer's palm										
Animal No.	Blind No.	Salivation					Piloerection					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
F01151	F00018	1	1	1	1	1	1	1	1	1	1	1
F01152	F00004	1	1	1	1	1	1	1	1	1	1	1
F01153	F00005	1	1	1	1	1	1	1	1	1	1	1
F01154	F00012	1	1	1	1	1	1	1	1	1	1	1
F01155	F00017	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	2	2	2	2	2	1	1	1	1	1
F01152	F00004	2	2	2	2	2	1	1	1	1	1
F01153	F00005	2	2	2	2	2	1	1	1	1	1
F01154	F00012	2	2	2	2	2	1	1	1	1	1
F01155	F00017	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	0	0	0	0	0	0	0	0	0	0
F01152	F00004	1	1	0	0	0	0	0	0	0	0
F01153	F00005	0	0	0	0	0	1	0	0	0	0
F01154	F00012	1	0	0	0	0	0	0	0	0	0
F01155	F00017	3	0	0	1	1	2	4	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	0.2	0.0	0.2	0.2	0.6	0.8	0.0	0.0	0.0
SD		1.2	0.4	0.0	0.4	0.4	0.9	1.8	0.0	0.0	0.0

Pre: Before administration period.

(Continued)

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	9	10	23	23	15	0	0	0	0	0
F01152	F00004	5	3	4	8	7	0	0	0	0	0
F01153	F00005	8	1	2	10	8	0	0	0	0	0
F01154	F00012	9	0	0	5	12	0	0	0	0	0
F01155	F00017	4	0	1	1	9	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		7.0	2.8	6.0	9.4	10.2	0.0	0.0	0.0	0.0	0.0
SD		2.3	4.2	9.6	8.3	3.3	0.0	0.0	0.0	0.0	0.0

Pre: Before administration period.

(Continued)

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F01151	F00018	1	1	1	1	1	1	1	1	1	1
F01152	F00004	1	1	1	1	1	1	1	1	1	1
F01153	F00005	1	1	1	1	1	1	1	1	1	1
F01154	F00012	1	1	1	1	1	1	1	1	1	1
F01155	F00017	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Open-field test									
Animal No.	Blind No.	Consciousness					Behavioral abnormalities				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F01151	F00018	2	2	2	2	2	1	1	1	1	1
F01152	F00004	2	2	2	2	2	1	1	1	1	1
F01153	F00005	2	2	2	2	2	1	1	1	1	1
F01154	F00012	2	2	2	2	2	1	1	1	1	1
F01155	F00017	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

Appendix 8-1. (Continued) Individual detailed clinical signs by FOB in female rats

Control group		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
F01151	F00018	1	1	1	1	1
F01152	F00004	1	1	1	1	1
F01153	F00005	1	1	1	1	1
F01154	F00012	1	1	1	1	1
F01155	F00017	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 8-2. Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Observation of animals in cages									
		Posture					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F02251	F00014	2	2	2	2	2	1	1	1	1	1
F02252	F00022	2	2	2	2	2	1	1	1	1	1
F02253	F00023	2	2	2	2	2	1	1	1	1	1
F02254	F00003	2	2	2	2	2	1	1	1	1	1
F02255	F00006	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Excessive grooming					Repetitive circling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F02251	F00014	1	1	1	1	1	1	1	1	1	1
F02252	F00022	1	1	1	1	1	1	1	1	1	1
F02253	F00023	1	1	1	1	1	1	1	1	1	1
F02254	F00003	1	1	1	1	1	1	1	1	1	1
F02255	F00006	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Observation of animals in cages									
		Biting behavior					Clonic convulsions				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F02251	F00014	1	1	1	1	1	1	1	1	1	1
F02252	F00022	1	1	1	1	1	1	1	1	1	1
F02253	F00023	1	1	1	1	1	1	1	1	1	1
F02254	F00003	1	1	1	1	1	1	1	1	1	1
F02255	F00006	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg						
Animal No.	Blind No.	Observation of animals in cages				
		Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
F02251	F00014	1	1	1	1	1
F02252	F00022	1	1	1	1	1
F02253	F00023	1	1	1	1	1
F02254	F00003	1	1	1	1	1
F02255	F00006	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F02251	F00014	2	2	2	2	2	2	2	2	2	2
F02252	F00022	2	2	2	2	2	2	2	2	2	2
F02253	F00023	2	2	2	2	2	2	2	2	2	2
F02254	F00003	2	2	2	2	2	2	2	2	2	2
F02255	F00006	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F02251	F00014	2	2	2	2	2	1	1	1	1	1
F02252	F00022	2	2	2	2	2	1	1	1	1	1
F02253	F00023	2	2	2	2	2	1	1	1	1	1
F02254	F00003	2	2	2	2	2	1	1	1	1	1
F02255	F00006	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Mucous membranes					Lacrimation				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F02251	F00014	1	1	1	1	1	1	1	1	1	1
F02252	F00022	1	1	1	1	1	1	1	1	1	1
F02253	F00023	1	1	1	1	1	1	1	1	1	1
F02254	F00003	1	1	1	1	1	1	1	1	1	1
F02255	F00006	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Salivation					Piloerection				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F02251	F00014	1	1	1	1	1	1	1	1	1	1
F02252	F00022	1	1	1	1	1	1	1	1	1	1
F02253	F00023	1	1	1	1	1	1	1	1	1	1
F02254	F00003	1	1	1	1	1	1	1	1	1	1
F02255	F00006	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F02251	F00014	2	2	2	2	2	1	1	1	1	1
F02252	F00022	2	2	2	2	2	1	1	1	1	1
F02253	F00023	2	2	2	2	2	1	1	1	1	1
F02254	F00003	2	2	2	2	2	1	1	1	1	1
F02255	F00006	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F02251	F00014	1	0	1	0	0	0	0	0	0	0
F02252	F00022	2	0	1	0	1	1	4	5	3	5
F02253	F00023	0	1	0	0	1	0	0	0	0	0
F02254	F00003	0	0	0	0	0	0	0	0	0	0
F02255	F00006	1	0	0	0	0	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		0.8	0.2	0.4	0.0	0.4	0.2	0.8	1.0	0.6	1.0
SD		0.8	0.4	0.5	0.0	0.5	0.4	1.8	2.2	1.3	2.2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F02251	F00014	2	4	14	7	19	0	0	0	0	0
F02252	F00022	3	2	0	11	5	0	0	0	0	0
F02253	F00023	6	3	0	0	0	0	0	0	0	0
F02254	F00003	10	8	7	8	14	0	0	0	0	0
F02255	F00006	15	8	11	7	9	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		7.2	5.0	6.4	6.6	9.4	0.0	0.0	0.0	0.0	0.0
SD		5.4	2.8	6.3	4.0	7.4	0.0	0.0	0.0	0.0	0.0
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	STL	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
7	14		21	27	7	14		21	27		
F02251	F00014	1	1	1	1	1	1	1	1	1	1
F02252	F00022	1	1	1	1	1	1	1	1	1	1
F02253	F00023	1	1	1	1	1	1	1	1	1	1
F02254	F00003	1	1	1	1	1	1	1	1	1	1
F02255	F00006	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg											
Animal No.	Blind No.	Open-field test									
		Consciousness					Behavioral abnormalities				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F02251	F00014	2	2	2	2	2	1	1	1	1	1
F02252	F00022	2	2	2	2	2	1	1	1	1	1
F02253	F00023	2	2	2	2	2	1	1	1	1	1
F02254	F00003	2	2	2	2	2	1	1	1	1	1
F02255	F00006	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-2. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 100 mg/kg		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
F02251	F00014	1	1	1	1	1
F02252	F00022	1	1	1	1	1
F02253	F00023	1	1	1	1	1
F02254	F00003	1	1	1	1	1
F02255	F00006	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Posture					Palpebral closure				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F00008	2	2	2	2	2	1	1	1	1	1
F03352	F00011	2	2	2	2	2	1	1	1	1	1
F03353	F00020	2	2	2	2	2	1	1	1	1	1
F03354	F00019	2	2	2	2	2	1	1	1	1	1
F03355	F00021	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Excessive grooming					Repetitive circling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F00008	1	1	1	1	1	1	1	1	1	1
F03352	F00011	1	1	1	1	1	1	1	1	1	1
F03353	F00020	1	1	1	1	1	1	1	1	1	1
F03354	F00019	1	1	1	1	1	1	1	1	1	1
F03355	F00021	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F00008	1	1	1	1	1	1	1	1	1	1
F03352	F00011	1	1	1	1	1	1	1	1	1	1
F03353	F00020	1	1	1	1	1	1	1	1	1	1
F03354	F00019	1	1	1	1	1	1	1	1	1	1
F03355	F00021	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Blind No.	Observation of animals in cages				
		Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
F03351	F00008	1	1	1	1	1
F03352	F00011	1	1	1	1	1
F03353	F00020	1	1	1	1	1
F03354	F00019	1	1	1	1	1
F03355	F00021	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F00008	2	2	2	2	2	2	2	2	2	2
F03352	F00011	2	2	2	2	2	2	2	2	2	2
F03353	F00020	2	2	2	2	2	2	2	2	2	2
F03354	F00019	2	2	2	2	2	2	2	2	2	2
F03355	F00021	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F00008	2	2	2	2	2	1	1	1	1	1
F03352	F00011	2	2	2	2	2	1	1	1	1	1
F03353	F00020	2	2	2	2	2	1	1	1	1	1
F03354	F00019	2	2	2	2	2	1	1	1	1	1
F03355	F00021	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Mucous membranes					Lacrimation				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F0008	1	1	1	1	1	1	1	1	1	1
F03352	F0011	1	1	1	1	1	1	1	1	1	1
F03353	F0020	1	1	1	1	1	1	1	1	1	1
F03354	F0019	1	1	1	1	1	1	1	1	1	1
F03355	F0021	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm										
Animal No.	Blind No.	Salivation					Piloerection					
		Days of administration					Days of administration					
		Pre	7	14	21	27	Pre	7	14	21	27	
F03351	F00008	1	1	1	1	1	1	1	1	1	1	1
F03352	F00011	1	1	1	1	1	1	1	1	1	1	1
F03353	F00020	1	1	1	1	1	1	1	1	1	1	1
F03354	F00019	1	1	1	1	1	1	1	1	1	1	1
F03355	F00021	1	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F03351	F00008	2	2	2	2	2	1	1	1	1	1
F03352	F00011	2	2	2	2	2	1	1	1	1	1
F03353	F00020	2	2	2	2	2	1	1	1	1	1
F03354	F00019	2	2	2	2	2	1	1	1	1	1
F03355	F00021	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F03351	F00008	1	0	0	0	0	0	0	0	0	0
F03352	F00011	0	0	0	0	0	0	0	0	0	0
F03353	F00020	0	0	1	0	0	0	0	0	0	0
F03354	F00019	1	0	0	0	0	0	3	0	0	0
F03355	F00021	2	0	0	1	0	2	0	0	0	5
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		0.8	0.0	0.2	0.2	0.0	0.4	0.6	0.0	0.0	1.0
SD		0.8	0.0	0.4	0.4	0.0	0.9	1.3	0.0	0.0	2.2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F03351	F00008	5	7	5	16	14	0	0	0	0	0
F03352	F00011	1	1	8	12	6	0	0	0	0	0
F03353	F00020	6	5	1	0	6	0	0	0	0	0
F03354	F00019	3	1	3	4	6	0	0	0	0	0
F03355	F00021	4	3	3	7	8	0	0	1	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		3.8	3.4	4.0	7.8	8.0	0.0	0.0	0.2	0.0	0.0
SD		1.9	2.6	2.6	6.3	3.5	0.0	0.0	0.4	0.0	0.0
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	STL	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
7	14		21	27	7	14		21	27		
F03351	F00008	1	1	1	1	1	1	1	1	1	1
F03352	F00011	1	1	1	1	1	1	1	1	1	1
F03353	F00020	1	1	1	1	1	1	1	1	1	1
F03354	F00019	1	1	1	1	1	1	1	1	1	1
F03355	F00021	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg											
Animal No.	Blind No.	Open-field test									
		Consciousness					Behavioral abnormalities				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F03351	F00008	2	2	2	2	2	1	1	1	1	1
F03352	F00011	2	2	2	2	2	1	1	1	1	1
F03353	F00020	2	2	2	2	2	1	1	1	1	1
F03354	F00019	2	2	2	2	2	1	1	1	1	1
F03355	F00021	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-3. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 300 mg/kg		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
F03351	F00008	1	1	1	1	1
F03352	F00011	1	1	1	1	1
F03353	F00020	1	1	1	1	1
F03354	F00019	1	1	1	1	1
F03355	F00021	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Observation of animals in cages									
		Posture					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F04451	F00013	2	2	2	2	2	1	1	1	1	1
F04452	F00001	2	2	2	2	2	1	1	1	1	1
F04453	F00015	2	2	2	2	2	1	1	1	1	1
F04454	F00016	2	2	2	2	2	1	1	1	1	1
F04455	F00007	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Excessive grooming					Repetitive circling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	1	1	1	1	1	1	1	1	1	1
F04452	F00001	1	1	1	1	1	1	1	1	1	1
F04453	F00015	1	1	1	1	1	1	1	1	1	1
F04454	F00016	1	1	1	1	1	1	1	1	1	1
F04455	F00007	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals in cages									
Animal No.	Blind No.	Biting behavior					Clonic convulsions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	1	1	1	1	1	1	1	1	1	1
F04452	F00001	1	1	1	1	1	1	1	1	1	1
F04453	F00015	1	1	1	1	1	1	1	1	1	1
F04454	F00016	1	1	1	1	1	1	1	1	1	1
F04455	F00007	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg						
Animal No.	Blind No.	Observation of animals in cages				
		Tonic convulsions				
		Days of administration				
		Pre	7	14	21	27
F04451	F00013	1	1	1	1	1
F04452	F00001	1	1	1	1	1
F04453	F00015	1	1	1	1	1
F04454	F00016	1	1	1	1	1
F04455	F00007	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Ease of removal from cage					Ease of handling				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	2	2	2	2	2	2	2	2	2	2
F04452	F00001	2	2	2	2	2	2	2	2	2	2
F04453	F00015	2	2	2	2	2	2	2	2	2	2
F04454	F00016	2	2	2	2	2	2	2	2	2	2
F04455	F00007	2	2	2	2	2	2	2	2	2	2
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Range		2	2	2	2	2	2	2	2	2	2
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Muscle tone					Fur conditions				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	2	2	2	2	2	1	1	1	1	1
F04452	F00001	2	2	2	2	2	1	1	1	1	1
F04453	F00015	2	2	2	2	2	1	1	1	1	1
F04454	F00016	2	2	2	2	2	1	1	1	1	1
F04455	F00007	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Mucous membranes					Lacrimation				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	1	1	1	1	1	1	1	1	1	1
F04452	F00001	1	1	1	1	1	1	1	1	1	1
F04453	F00015	1	1	1	1	1	1	1	1	1	1
F04454	F00016	1	1	1	1	1	1	1	1	1	1
F04455	F00007	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Salivation					Piloerection				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	1	1	1	1	1	1	1	1	1	1
F04452	F00001	1	1	1	1	1	1	1	1	1	1
F04453	F00015	1	1	1	1	1	1	1	1	1	1
F04454	F00016	1	1	1	1	1	1	1	1	1	1
F04455	F00007	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Observation of animals on observer's palm									
Animal No.	Blind No.	Pupil size					Respiration				
		Days of administration					Days of administration				
		Pre	7	14	21	27	Pre	7	14	21	27
F04451	F00013	2	2	2	2	2	1	1	1	1	1
F04452	F00001	2	2	2	2	2	1	1	1	1	1
F04453	F00015	2	2	2	2	2	1	1	1	1	1
F04454	F00016	2	2	2	2	2	1	1	1	1	1
F04455	F00007	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of urination (during a 2-minute period)					Frequency of defecation (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F04451	F00013	0	0	0	0	0	0	0	0	0	0
F04452	F00001	0	0	0	0	0	0	0	0	0	0
F04453	F00015	1	1	0	0	0	0	0	0	0	0
F04454	F00016	1	0	0	0	0	0	1	0	0	1
F04455	F00007	0	0	0	0	0	0	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		0.4	0.2	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.2
SD		0.5	0.4	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.4
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Open-field test									
Animal No.	Blind No.	Frequency of rearing (during a 2-minute period)					Frequency of grooming (during a 2-minute period)				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F04451	F00013	4	3	6	8	9	0	0	0	0	0
F04452	F00001	10	3	7	11	10	0	0	0	0	0
F04453	F00015	5	3	1	7	6	0	0	0	0	0
F04454	F00016	6	0	2	4	1	0	0	0	0	0
F04455	F00007	6	4	1	5	0	1	0	0	0	0
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		6.2	2.6	3.4	7.0	5.2	0.2	0.0	0.0	0.0	0.0
SD		2.3	1.5	2.9	2.7	4.5	0.4	0.0	0.0	0.0	0.0
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		DU	DU	STL	DU	DU	DU	DU	DU	DU	DU

Pre: Before administration period.

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Open-field test									
		Gait					Palpebral closure				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F04451	F00013	1	1	1	1	1	1	1	1	1	1
F04452	F00001	1	1	1	1	1	1	1	1	1	1
F04453	F00015	1	1	1	1	1	1	1	1	1	1
F04454	F00016	1	1	1	1	1	1	1	1	1	1
F04455	F00007	1	1	1	1	1	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg											
Animal No.	Blind No.	Open-field test									
		Consciousness					Behavioral abnormalities				
		Pre	Days of administration				Pre	Days of administration			
			7	14	21	27		7	14	21	27
F04451	F00013	2	2	2	2	2	1	1	1	1	1
F04452	F00001	2	2	2	2	2	1	1	1	1	1
F04453	F00015	2	2	2	2	2	1	1	1	1	1
F04454	F00016	2	2	2	2	2	1	1	1	1	1
F04455	F00007	2	2	2	2	2	1	1	1	1	1
Number of animals		5	5	5	5	5	5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0	1.0	1.0
Range		2	2	2	2	2	1	1	1	1	1
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Pre: Before administration period.

(Continued)

Findings were graded as follows;

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 8-4. (Continued) Individual detailed clinical signs by FOB in female rats

Ethyl propionate group at 1000 mg/kg		Open-field test				
Animal No.	Blind No.	Righting reflex				
		Days of administration				
		Pre	7	14	21	27
F04451	F00013	1	1	1	1	1
F04452	F00001	1	1	1	1	1
F04453	F00015	1	1	1	1	1
F04454	F00016	1	1	1	1	1
F04455	F00007	1	1	1	1	1
Number of animals		5	5	5	5	5
Mean		1.0	1.0	1.0	1.0	1.0
Range		1	1	1	1	1
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

Pre: Before administration period.

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 9-1. Individual sensory response in male rats

Control group						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
M01101	M00002	2	2	2	2	3
M01102	M00005	2	2	2	2	3
M01103	M00001	2	2	2	2	3
M01104	M00011	2	2	2	2	3
M01105	M00014	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 9-2. Individual sensory response in male rats

Ethyl propionate group at 100 mg/kg						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
M02201	M00019	2	2	2	2	3
M02202	M00022	2	2	2	2	3
M02203	M00020	2	2	2	2	3
M02204	M00021	2	2	2	2	3
M02205	M00010	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 9-3. Individual sensory response in male rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
M03301	M00015	2	2	2	2	3
M03302	M00013	2	2	2	2	3
M03303	M00006	2	2	2	2	3
M03304	M00007	2	2	2	2	3
M03305	M00016	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 9-4. Individual sensory response in male rats

Ethyl propionate group at 1000 mg/kg						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
M04401	M00018	2	2	2	2	3
M04402	M00017	2	2	2	2	3
M04403	M00023	2	2	2	2	3
M04404	M00008	2	2	2	2	3
M04405	M00004	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 10-1. Individual sensory response in female rats

Control group						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
F01151	F00018	2	2	2	2	3
F01152	F00004	2	2	2	2	3
F01153	F00005	2	2	2	2	3
F01154	F00012	2	2	2	2	3
F01155	F00017	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 10-2. Individual sensory response in female rats

Ethyl propionate group at 100 mg/kg						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
F02251	F00014	2	2	2	2	3
F02252	F00022	2	2	2	2	3
F02253	F00023	2	2	2	2	3
F02254	F00003	2	2	2	2	3
F02255	F00006	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 10-3. Individual sensory response in female rats

Ethyl propionate group at 300 mg/kg						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
F03351	F00008	2	2	2	2	3
F03352	F00011	2	2	2	2	3
F03353	F00020	2	2	2	2	3
F03354	F00019	2	2	2	2	3
F03355	F00021	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 10-4. Individual sensory response in female rats

Ethyl propionate group at 1000 mg/kg						
Animal No.	Blind No.	Pupillary reflex	Approaching behavior	Response to touch	Auditory reflex	Pain reflex
F04451	F00013	2	2	2	2	3
F04452	F00001	2	2	2	2	3
F04453	F00015	2	2	2	2	3
F04454	F00016	2	2	2	2	3
F04455	F00007	2	2	2	2	3
Number of animals		5	5	5	5	5
Mean		2.0	2.0	2.0	2.0	3.0
Range		2	2	2	2	3
Significance		NS	NS	NS	NS	NS
Statistical method		STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows;

- Pupillary reflex 1: Pupils completely dilated, 2: normal pupillary contraction observed (normal score), 3: pupils completely contracted.
- Approaching behavior 1: Not observed, 2: approaching and sniffing object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Response to touch 1: No response, 2: looking back and leaving object (normal score), 3: reacting to stimulus, including vocalizing, 4: jumping or biting object.
- Auditory reflex 1: Not observed, 2: hesitating or moving ears (normal score), 3: jumping and trying to bite the source of sound.
- Pain reflex 1: Not observed, 2: slowly looking back or slowly moving forward to escape from object, 3: quickly moving forward to escape from object or biting it immediately after looking back (normal score), 4: jumping forward to escape from object, 5: loudly vocalizing and biting object after suddenly looking back.

Appendix 11-1. Individual grip strength of male rats

Control group			
Animal No.	Blind No.	Forelimb	Hindlimb
M01101	M00002	0.557	0.167
M01102	M00005	0.721	0.183
M01103	M00001	0.500	0.143
M01104	M00011	0.527	0.147
M01105	M00014	0.604	0.185
Number of animals		5	5
Mean		0.582	0.165
SD		0.087	0.020

Unit: kg

Appendix 11-2. Individual grip strength of male rats

Ethyl propionate group at 100 mg/kg			
Animal No.	Blind No.	Forelimb	Hindlimb
M02201	M00019	0.627	0.188
M02202	M00022	0.530	0.103
M02203	M00020	0.613	0.144
M02204	M00021	0.602	0.162
M02205	M00010	0.625	0.235
Number of animals		5	5
Mean		0.599	0.166
SD		0.040	0.049
Significance		NS	NS
Statistical method		DU	DU

Unit: kg

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 11-3. Individual grip strength of male rats

Ethyl propionate group at 300 mg/kg			
Animal No.	Blind No.	Forelimb	Hindlimb
M03301	M00015	0.658	0.127
M03302	M00013	0.527	0.179
M03303	M00006	0.732	0.167
M03304	M00007	0.621	0.159
M03305	M00016	0.528	0.156
Number of animals		5	5
Mean		0.613	0.158
SD		0.088	0.019
Significance		NS	NS
Statistical method		DU	DU

Unit: kg

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 11-4. Individual grip strength of male rats

Ethyl propionate group at 1000 mg/kg			
Animal No.	Blind No.	Forelimb	Hindlimb
M04401	M00018	0.637	0.191
M04402	M00017	0.643	0.165
M04403	M00023	0.633	0.126
M04404	M00008	0.539	0.141
M04405	M00004	0.700	0.200
Number of animals		5	5
Mean		0.630	0.165
SD		0.058	0.032
Significance		NS	NS
Statistical method		DU	DU

Unit: kg

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 12-1. Individual grip strength of female rats

Control group			
Animal No.	Blind No.	Forelimb	Hindlimb
F01151	F00018	0.412	0.141
F01152	F00004	0.417	0.154
F01153	F00005	0.406	0.112
F01154	F00012	0.422	0.107
F01155	F00017	0.421	0.125
Number of animals		5	5
Mean		0.416	0.128
SD		0.007	0.020

Unit: kg

Appendix 12-2. Individual grip strength of female rats

Ethyl propionate group at 100 mg/kg			
Animal No.	Blind No.	Forelimb	Hindlimb
F02251	F00014	0.416	0.126
F02252	F00022	0.532	0.105
F02253	F00023	0.524	0.152
F02254	F00003	0.482	0.129
F02255	F00006	0.439	0.161
Number of animals		5	5
Mean		0.479	0.135
SD		0.051	0.022
Significance		NS	NS
Statistical method		STL	DU

Unit: kg

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 12-3. Individual grip strength of female rats

Ethyl propionate group at 300 mg/kg			
Animal No.	Blind No.	Forelimb	Hindlimb
F03351	F00008	0.424	0.118
F03352	F00011	0.424	0.129
F03353	F00020	0.431	0.118
F03354	F00019	0.430	0.107
F03355	F00021	0.480	0.144
Number of animals		5	5
Mean		0.438	0.123
SD		0.024	0.014
Significance		#	NS
Statistical method		STL	DU

Unit: kg

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 12-4. Individual grip strength of female rats

Ethyl propionate group at 1000 mg/kg			
Animal No.	Blind No.	Forelimb	Hindlimb
F04451	F00013	0.423	0.128
F04452	F00001	0.498	0.146
F04453	F00015	0.514	0.171
F04454	F00016	0.456	0.136
F04455	F00007	0.434	0.151
Number of animals		5	5
Mean		0.465	0.146
SD		0.040	0.016
Significance		#	NS
Statistical method		STL	DU

Unit: kg

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 13-1. Individual spontaneous motor activity of male rats (administration period)

Control group														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
M01101	11	54	10	4	134	522	735	0	2	0	0	0	11	13
M01102	332	119	26	7	0	325	809	3	0	0	0	0	4	7
M01103	4	0	83	72	4	90	253	0	0	1	0	0	1	2
M01104	5	48	11	0	0	105	169	0	1	0	0	0	1	2
M01105	257	4	117	9	12	64	463	1	0	0	0	0	1	2
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	122	45	49	18	30	221	486	1	1	0	0	0	4	5
SD	160	48	48	30	58	198	284	1	1	0	0	0	4	5

Appendix 13-2. Individual spontaneous motor activity of male rats (administration period)

Ethyl propionate group at 100 mg/kg

Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
M02201	608	692	831	1231	1062	409	4833	12	11	20	33	19	12	107
M02202	2	4	0	4	73	69	152	0	0	0	0	2	0	2
M02203	10	124	7	2	4	42	189	0	0	0	0	0	1	1
M02204	755	0	0	34	2	19	810	17	0	0	6	0	1	24
M02205	0	19	1	0	6	121	147	0	0	0	0	0	1	1
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	275	168	168	254	229	132	1226	6	2	4	8	4	3	27
SD	375	297	371	546	466	159	2036	8	5	9	14	8	5	46
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 13-3. Individual spontaneous motor activity of male rats (administration period)

Ethyl propionate group at 300 mg/kg														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
M03301	2	2	28	32	79	6	149	0	0	1	2	0	0	3
M03302	551	0	29	19	6	21	626	6	0	3	1	0	0	10
M03303	29	24	43	12	52	23	183	0	0	0	0	0	0	0
M03304	0	26	0	0	0	0	26	0	0	0	0	0	0	0
M03305	246	13	251	0	2	12	524	0	2	0	0	0	0	2
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	166	13	70	13	28	12	302	1	0	1	1	0	0	3
SD	239	12	102	14	36	10	259	3	1	1	1	0	0	4
Significance	NS	NS	NS	NS	NS	#	NS	NS	NS	NS	NS	NS	#	NS
Statistical method	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 13-4. Individual spontaneous motor activity of male rats (administration period)

Ethyl propionate group at 1000 mg/kg														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
M04401	2	6	4	0	30	71	113	0	0	0	0	2	0	2
M04402	0	86	30	0	0	4	120	0	1	0	0	0	0	1
M04403	32	15	26	11	46	6	136	0	0	0	0	0	0	0
M04404	12	13	0	0	6	16	47	0	0	0	0	2	0	2
M04405	85	17	18	28	14	15	177	0	0	0	0	0	0	0
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	26	27	16	8	19	22	119	0	0	0	0	1	0	1
SD	35	33	13	12	19	28	47	0	0	0	0	1	0	1
Significance	NS	NS	NS	NS	NS	#	#	NS	NS	NS	NS	NS	#	NS
Statistical method	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 14-1. Individual spontaneous motor activity of female rats (administration period)

Control group														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
F01151	3	118	1773	61	22	12	1989	0	1	15	0	0	0	16
F01152	262	95	2140	544	102	587	3730	2	2	19	8	0	3	34
F01153	2149	229	14	33	0	2	2427	12	1	0	0	0	0	13
F01154	12	2628	173	16	63	7	2899	0	8	0	0	0	0	8
F01155	2	12	36	135	0	0	185	0	0	1	0	0	0	1
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	486	616	827	158	37	122	2246	3	2	7	2	0	1	14
SD	936	1127	1041	221	44	260	1321	5	3	9	4	0	1	12

Appendix 14-2. Individual spontaneous motor activity of female rats (administration period)

Ethyl propionate group at 100 mg/kg

Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
F02251	756	1269	17	2669	68	7	4786	4	5	0	11	0	0	20
F02252	1060	20	2	1057	42	2	2183	3	0	0	12	0	0	15
F02253	3	2567	137	38	622	12	3379	0	47	14	0	4	0	65
F02254	6	26	2	4	75	0	113	0	0	0	0	0	0	0
F02255	15	21	0	22	46	31	135	0	0	0	0	0	0	0
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	368	781	32	758	171	10	2119	1	10	3	5	1	0	20
SD	505	1135	59	1159	253	12	2041	2	21	6	6	2	0	27
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 14-3. Individual spontaneous motor activity of female rats (administration period)

Ethyl propionate group at 300 mg/kg

Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
F03351	4701	1870	2499	1138	971	2393	13572	51	25	34	9	10	24	153
F03352	3	0	4	31	25	0	63	0	0	0	1	1	0	2
F03353	423	2	6	83	3	14	531	2	0	0	0	0	0	2
F03354	3	50	3	6	6	12	80	0	0	0	0	0	0	0
F03355	2828	952	14	13	0	17	3824	24	5	0	1	0	0	30
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	1592	575	505	254	201	487	3614	15	6	7	2	2	5	37
SD	2098	830	1115	495	431	1065	5784	22	11	15	4	4	11	66
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 14-4. Individual spontaneous motor activity of female rats (administration period)

Ethyl propionate group at 1000 mg/kg														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes after administration							Minutes after administration						
	60-70	70-80	80-90	90-100	100-110	110-120	Total	60-70	70-80	80-90	90-100	100-110	110-120	Total
F04451	2	33	21	33	14	24	127	0	0	0	0	0	0	0
F04452	57	26	8	81	2543	52	2767	0	0	0	0	22	0	22
F04453	18	7	72	30	20	23	170	0	0	0	0	0	0	0
F04454	438	43	39	6	21	0	547	0	0	0	0	0	0	0
F04455	272	15	81	14	2	54	438	0	0	1	0	0	1	2
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	157	25	44	33	520	31	810	0	0	0	0	4	0	5
SD	191	14	32	29	1131	23	1108	0	0	0	0	10	0	10
Significance	NS	NS	NS	NS	NS	NS	NS	NS	#	NS	NS	NS	NS	NS
Statistical method	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL	STL

Significantly different from the control group (#: $p < 0.05$ by Steel's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Appendix 15-1. Individual spontaneous motor activity of male rats (recovery period)

Control group														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes							Minutes						
	0-10	10-20	20-30	30-40	40-50	50-60	Total	0-10	10-20	20-30	30-40	40-50	50-60	Total
M01106	2724	1744	338	119	58	1254	6237	72	52	9	1	0	30	164
M01107	525	44	38	15	586	1720	2928	31	0	0	0	26	82	139
M01108	1611	1716	1396	197	123	51	5094	45	62	18	0	0	4	129
M01109	6	10	453	1560	14	16	2059	0	0	13	37	0	0	50
M01110	37	17	0	538	0	14	606	0	0	0	3	0	0	3
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	981	706	445	486	156	611	3385	30	23	8	8	5	23	97
SD	1171	935	566	632	245	817	2277	31	31	8	16	12	35	68

Appendix 15-2. Individual spontaneous motor activity of male rats (recovery period)

Ethyl propionate group at 300 mg/kg														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes							Minutes						
	0-10	10-20	20-30	30-40	40-50	50-60	Total	0-10	10-20	20-30	30-40	40-50	50-60	Total
M03306	11	43	23	81	246	36	440	0	2	0	0	4	0	6
M03307	625	80	196	4	477	849	2231	20	1	1	0	7	19	48
M03308	849	112	5	0	244	16	1226	48	3	0	0	4	0	55
M03309	2	42	0	8	36	45	133	0	0	0	0	1	0	1
M03310	176	3	94	0	13	46	332	0	0	0	0	3	0	3
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	333	56	64	19	203	198	872	14	1	0	0	4	4	23
SD	384	41	83	35	189	364	866	21	1	0	0	2	8	27
Significance	NS	NS	NS	#	NS	NS	*	NS	NS	NS	NS	NS	NS	*
Statistical method	STL	STL	STL	STL	DU	STL	DU	DU	STL	STL	STL	STL	STL	DU

Significantly different from the control group (#; $p < 0.05$ by Steel's test).

Significantly different from the control group (*; $p < 0.05$ by Dunnett's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 15-3. Individual spontaneous motor activity of male rats (recovery period)

Ethyl propionate group at 1000 mg/kg														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes							Minutes						
	0-10	10-20	20-30	30-40	40-50	50-60	Total	0-10	10-20	20-30	30-40	40-50	50-60	Total
M04406	554	410	439	225	470	202	2300	20	25	12	6	21	8	92
M04407	16	1337	11	11	41	47	1463	0	35	0	0	1	0	36
M04408	710	370	65	47	141	0	1333	13	0	0	0	1	0	14
M04409	33	31	189	19	36	70	378	0	1	1	0	1	1	4
M04410	189	82	27	18	72	29	417	13	10	0	0	2	3	28
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	300	446	146	64	152	70	1178	9	14	3	1	5	2	35
SD	315	526	178	91	183	78	804	9	15	5	3	9	3	34
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	STL	STL	STL	DU	STL	DU	DU	STL	STL	STL	STL	STL	DU

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 16-1. Individual spontaneous motor activity of female rats (recovery period)

Control group														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes							Minutes						
	0-10	10-20	20-30	30-40	40-50	50-60	Total	0-10	10-20	20-30	30-40	40-50	50-60	Total
F01156	2562	1550	331	27	7	9	4486	18	9	0	0	0	0	27
F01157	256	58	21	13	2318	3642	6308	3	0	0	0	34	83	120
F01158	0	62	813	599	0	5	1479	0	1	7	4	0	0	12
F01159	134	6	15	33	3	2	193	2	0	0	0	0	0	2
F01160	3418	2644	568	16	82	19	6747	37	45	18	0	0	0	100
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	1274	864	350	138	482	735	3843	12	11	5	1	7	17	52
SD	1598	1190	347	258	1027	1625	2908	16	19	8	2	15	37	54

Appendix 16-2. Individual spontaneous motor activity of female rats (recovery period)

Ethyl propionate group at 300 mg/kg

Animal No.	Ambulatory counts							Rearing counts						
	Minutes							Minutes						
	0-10	10-20	20-30	30-40	40-50	50-60	Total	0-10	10-20	20-30	30-40	40-50	50-60	Total
F03356	2322	41	2	6	1173	1347	4891	26	0	0	0	7	9	42
F03357	260	2858	231	156	4	67	3576	6	38	3	1	0	1	49
F03358	15	11	27	0	0	77	130	1	0	1	0	0	2	4
F03359	4	0	997	56	40	41	1138	0	0	14	0	0	0	14
F03360	44	1678	2886	260	14	15	4897	0	20	47	1	0	0	68
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	529	918	829	96	246	309	2926	7	12	13	0	1	2	35
SD	1008	1302	1219	111	518	581	2190	11	17	20	1	3	4	26
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	STL	STL	STL	DU	DU	DU	STL	STL	STL	STL	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 16-3. Individual spontaneous motor activity of female rats (recovery period)

Ethyl propionate group at 1000 mg/kg														
Animal No.	Ambulatory counts							Rearing counts						
	Minutes							Minutes						
	0-10	10-20	20-30	30-40	40-50	50-60	Total	0-10	10-20	20-30	30-40	40-50	50-60	Total
F04456	2	1484	2	0	0	0	1488	0	12	0	0	0	0	12
F04457	1909	905	827	1683	29	60	5413	15	13	6	16	0	0	50
F04458	0	0	0	0	62	14	76	0	0	0	0	2	0	2
F04459	1539	1699	19	34	11	14	3316	12	36	0	0	0	0	48
F04460	62	20	28	7	79	0	196	0	0	0	0	0	0	0
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	702	822	175	345	36	18	2098	5	12	1	3	0	0	22
SD	942	796	365	748	34	25	2267	7	15	3	7	1	0	25
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	STL	STL	STL	DU	DU	DU	STL	STL	STL	STL	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 17-1. Individual urinalysis in male rats (administration period)

Control group								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M01101	18.3	1.042	100.8	216.2	144.5	1.84	3.96	2.64
M01102	6.8	1.075	175.0	411.6 a)	285.4	1.19	2.80	1.94
M01103	9.8	1.054	132.8	286.6	220.8	1.30	2.81	2.16
M01104	23.1	1.025	71.0	135.4	97.5	1.64	3.13	2.25
M01105	11.9	1.036	66.9	176.8	94.5	0.80	2.10	1.12
Number of animals	5	5	5	5	5	5	5	5
Mean	14.0	1.046	109.3	245.3	168.5	1.35	2.96	2.02
SD	6.6	0.019	45.3	108.4	82.9	0.40	0.67	0.56

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

(Continued)

Appendix 17-1. (Continued) Individual urinalysis in male rats (administration period)

Control group													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M01101	Light yellow	8.5	+	-	±	-	-	0.1	±	±	±	-	-
M01102	Light yellow	8.5	++	-	+	-	-	1.0	±	±	±	-	-
M01103	Light yellow	8.5	+	-	±	-	-	0.1	±	±	±	-	-
M01104	Light yellow	8.5	+	-	+	-	±	0.1	+	±	±	-	-
M01105	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -; not observed.

Crystals: -; not observed, Mp; magnesium ammonium phosphate.

Appendix 17-2. Individual urinalysis in male rats (administration period)

Ethyl propionate group at 100 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M02201	11.7	1.055	135.2	299.2	199.4	1.58	3.50	2.33
M02202	27.7	1.020	49.1	106.4	67.6	1.36	2.95	1.87
M02203	23.8	1.017	29.2	86.7	39.0	0.69	2.06	0.93
M02204	11.9	1.055	147.0	282.3	192.8	1.75	3.36	2.29
M02205	7.9	1.069	178.8	369.6 a)	264.2	1.41	2.92	2.09
Number of animals	5	5	5	5	5	5	5	5
Mean	16.6	1.043	107.9	228.8	152.6	1.36	2.96	1.90
SD	8.6	0.023	65.1	125.3	95.4	0.40	0.56	0.57
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

Appendix 17-2. (Continued) Individual urinalysis in male rats (administration period)

Ethyl propionate group at 100 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M02201	Light yellow	8.5	+	-	±	-	-	0.1	±	±	±	-	-
M02202	Light yellow	8.5	±	-	±	-	-	0.1	±	±	±	-	-
M02203	Light yellow	8.5	±	-	+	-	-	0.1	±	±	±	-	Mp
M02204	Light yellow	8.5	+	-	+	-	-	1.0	±	±	±	-	-
M02205	Light yellow	8.5	++	-	+	-	-	1.0	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 17-3. Individual urinalysis in male rats (administration period)

Ethyl propionate group at 300 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M03301	10.8	1.062	166.3	323.0 a)	213.6	1.80	3.49	2.31
M03302	8.4	1.050	51.2	238.1	106.6	0.43	2.00	0.90
M03303	12.1	1.028	30.6	141.1	62.4	0.37	1.71	0.76
M03304	16.0	1.022	25.9	94.9	42.9	0.41	1.52	0.69
M03305	13.9	1.021	14.4	72.6	37.9	0.20	1.01	0.53
Number of animals	5	5	5	5	5	5	5	5
Mean	12.2	1.037	57.7	173.9	92.7	0.64	1.95	1.04
SD	2.9	0.018	62.2	104.8	72.8	0.65	0.94	0.72
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

Appendix 17-3. (Continued) Individual urinalysis in male rats (administration period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M03301	Light yellow	8.5	+	-	±	-	-	0.1	±	±	±	-	-
M03302	Light yellow	8.5	++	-	+	-	-	1.0	+	±	±	-	Mp
M03303	Light yellow	8.5	+	-	±	-	-	0.1	±	±	±	-	-
M03304	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
M03305	Light yellow	8.5	+	-	+	-	-	0.1	+	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 17-4. Individual urinalysis in male rats (administration period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M04401	11.4	1.064	168.1	331.0 a)	238.2	1.92	3.77	2.72
M04402	12.7	1.058	154.5	294.3	227.8	1.96	3.74	2.89
M04403	17.1	1.018	19.5	80.5	45.1	0.33	1.38	0.77
M04404	10.0	1.038	59.5	177.8	87.3	0.60	1.78	0.87
M04405	15.0	1.040	117.3	209.4	150.5	1.76	3.14	2.26
Number of animals	5	5	5	5	5	5	5	5
Mean	13.2	1.044	103.8	218.6	149.8	1.31	2.76	1.90
SD	2.8	0.018	63.2	99.0	84.8	0.78	1.12	1.01
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

Appendix 17-4. (Continued) Individual urinalysis in male rats (administration period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M04401	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
M04402	Light yellow	8.5	±	-	±	-	-	0.1	±	±	±	-	-
M04403	Light yellow	8.0	++	-	+	-	-	1.0	±	±	±	-	-
M04404	Light yellow	8.5	±	-	±	-	-	0.1	±	±	±	-	-
M04405	Light yellow	8.5	+	-	±	-	-	0.1	+	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 18-1. Individual urinalysis in female rats (administration period)

Control group								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F01151	7.8	1.058	121.0	310.6 a)	200.8	0.94	2.42	1.57
F01152	6.7	1.065	140.7	295.2	206.9	0.94	1.98	1.39
F01153	10.9	1.047	95.1	224.2	135.3	1.04	2.44	1.47
F01154	5.1	1.047	118.9	215.8	158.7	0.61	1.10	0.81
F01155	9.8	1.048	82.3	214.7	142.1	0.81	2.10	1.39
Number of animals	5	5	5	5	5	5	5	5
Mean	8.1	1.053	111.6	252.1	168.8	0.87	2.01	1.33
SD	2.3	0.008	23.0	46.8	33.2	0.17	0.55	0.30

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

(Continued)

Appendix 18-1. (Continued) Individual urinalysis in female rats (administration period)

Control group Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobili- nogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F01151	Light yellow	≥ 9.0	+	-	-	-	-	1.0	±	±	±	-	-
F01152	Light yellow	8.5	+	-	±	-	-	1.0	±	±	±	-	Mp
F01153	Light yellow	8.0	-	-	-	-	-	0.1	+	±	±	-	-
F01154	Light yellow	≥ 9.0	+	-	±	-	-	1.0	±	±	±	-	-
F01155	Light yellow	8.5	±	-	-	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 18-2. Individual urinalysis in female rats (administration period)

Ethyl propionate group at 100 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F02251	9.0	1.038	104.8	173.9	127.3	0.94	1.57	1.15
F02252	5.4	1.052	125.1	185.2	125.4	0.68	1.00	0.68
F02253	13.3	1.019	17.8	52.4	27.0	0.24	0.70	0.36
F02254	4.8	1.078	169.9	388.4 a)	236.7	0.82	1.86	1.14
F02255	4.7	1.064	153.1	246.0	176.3	0.72	1.16	0.83
Number of animals	5	5	5	5	5	5	5	5
Mean	7.4	1.050	114.1	209.2	138.5	0.68	1.26	0.83
SD	3.7	0.023	59.4	122.3	77.1	0.27	0.46	0.33
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

Appendix 18-2. (Continued) Individual urinalysis in female rats (administration period)

Ethyl propionate group at 100 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F02251	Light yellow	8.5	±	-	-	-	-	0.1	±	±	±	-	-
F02252	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F02253	Light yellow	7.5	-	-	-	-	-	0.1	+	±	±	-	-
F02254	Light yellow	8.5	++	-	+	-	-	1.0	±	±	±	-	-
F02255	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 18-3. Individual urinalysis in female rats (administration period)

Ethyl propionate group at 300 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F03351	10.7	1.054	130.6	258.7	192.3	1.40	2.77	2.06
F03352	11.6	1.028	23.1	100.4	47.5	0.27	1.16	0.55
F03353	7.2	1.045	90.1	220.9	159.0	0.65	1.59	1.14
F03354	11.4	1.045	106.6	221.9	153.9	1.22	2.53	1.75
F03355	11.3	1.054	122.9	278.6	190.4	1.39	3.15	2.15
Number of animals	5	5	5	5	5	5	5	5
Mean	10.4	1.045	94.7	216.1	148.6	0.99	2.24	1.53
SD	1.8	0.011	42.9	69.2	59.2	0.50	0.83	0.68
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 18-3. (Continued) Individual urinalysis in female rats (administration period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F03351	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F03352	Light yellow	8.0	+	-	±	-	-	1.0	±	±	±	-	-
F03353	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F03354	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	Mp
F03355	Light yellow	8.0	-	-	-	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 18-4. Individual urinalysis in female rats (administration period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F04451	4.6	1.074	146.6	335.4 a)	224.0	0.67	1.54	1.03
F04452	13.7	1.037	71.0	194.1	106.6	0.97	2.66	1.46
F04453	17.7	1.031	71.0	161.0	99.5	1.26	2.85	1.76
F04454	13.5	1.039	91.1	193.5	120.8	1.23	2.61	1.63
F04455	5.4	1.052	12.3	137.1	72.5	0.07	0.74	0.39
Number of animals	5	5	5	5	5	5	5	5
Mean	11.0	1.047	78.4	204.2	124.7	0.84	2.08	1.25
SD	5.7	0.017	48.2	77.1	58.2	0.49	0.91	0.56
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

Appendix 18-4. (Continued) Individual urinalysis in female rats (administration period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F04451	Light yellow	8.5	+	-	±	-	-	1.0	±	±	±	-	-
F04452	Light yellow	8.5	±	-	-	-	-	0.1	±	±	±	-	-
F04453	Light yellow	8.5	-	-	-	-	-	0.1	+	±	±	-	-
F04454	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F04455	Light yellow	8.5	+	-	±	-	-	1.0	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed, Mp; magnesium ammonium phosphate.

Appendix 19-1. Individual urinalysis in male rats (recovery period)

Control group								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M01106	18.7	1.031	43.8	136.6	40.5	0.82	2.55	0.76
M01107	17.9	1.046	104.3	222.6	136.2	1.87	3.98	2.44
M01108	24.2	1.036	60.4	167.6	90.6	1.46	4.06	2.19
M01109	13.5	1.043	68.0	198.6	98.5	0.92	2.68	1.33
M01110	13.1	1.065	149.2	329.2 a)	207.6	1.95	4.31	2.72
Number of animals	5	5	5	5	5	5	5	5
Mean	17.5	1.044	85.1	210.9	114.7	1.40	3.52	1.89
SD	4.5	0.013	42.1	73.6	62.1	0.52	0.83	0.82

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

(Continued)

Appendix 19-1. (Continued) Individual urinalysis in male rats (recovery period)

Control group Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobili- nogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M01106	Light yellow	8.0	±	-	±	-	-	0.1	±	±	±	-	-
M01107	Light yellow	8.0	±	-	±	-	-	0.1	±	±	±	-	-
M01108	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
M01109	Light yellow	8.5	±	-	±	-	-	0.1	±	±	±	-	-
M01110	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed.

Appendix 19-2. Individual urinalysis in male rats (recovery period)

Ethyl propionate group at 300 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M03306	17.5	1.038	61.0	186.7	88.3	1.07	3.27	1.55
M03307	13.3	1.058	97.8	280.6	157.5	1.30	3.73	2.09
M03308	16.3	1.051	118.6	241.5	145.8	1.93	3.94	2.38
M03309	13.6	1.060	147.7	280.5	182.2	2.01	3.81	2.48
M03310	17.0	1.057	123.2	274.9	168.8	2.09	4.67	2.87
Number of animals	5	5	5	5	5	5	5	5
Mean	15.5	1.053	109.7	252.8	148.5	1.68	3.88	2.27
SD	2.0	0.009	32.5	40.4	36.3	0.46	0.51	0.49
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 19-2. (Continued) Individual urinalysis in male rats (recovery period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M03306	Light yellow	8.0	±	-	+	-	-	0.1	±	±	±	-	-
M03307	Light yellow	8.5	±	-	±	-	-	0.1	±	±	±	-	-
M03308	Light yellow	8.0	±	-	±	-	-	0.1	±	±	±	-	-
M03309	Light yellow	8.0	+	-	±	-	±	0.1	±	±	±	-	-
M03310	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -; not observed.

Crystals: -; not observed.

Appendix 19-3. Individual urinalysis in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
M04406	14.9	1.037	31.5	146.4	47.4	0.47	2.18	0.71
M04407	14.0	1.054	119.4	267.3	163.2	1.67	3.74	2.28
M04408	31.3	1.022	44.8	93.9	50.9	1.40	2.94	1.59
M04409	9.8	1.056	86.3	246.5	119.8	0.85	2.42	1.17
M04410	11.2	1.060	127.9	294.3	182.8	1.43	3.30	2.05
Number of animals	5	5	5	5	5	5	5	5
Mean	16.2	1.046	82.0	209.7	112.8	1.16	2.92	1.56
SD	8.7	0.016	43.2	85.5	62.4	0.49	0.64	0.64
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 19-3. (Continued) Individual urinalysis in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
M04406 b)	Light yellow	6.0	++	-	+	-	-	0.1	±	±	±	-	-
M04407	Light yellow	8.5	±	-	±	-	-	0.1	±	±	±	-	-
M04408	Light yellow	8.5	+	-	+	-	-	0.1	±	±	±	-	-
M04409	Light yellow	8.5	+	-	±	-	-	0.1	±	±	±	-	-
M04410	Light yellow	8.5	±	-	+	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -; not observed.

Crystals: -; not observed.

b): Obtained from the recollected urine; urine was collected twice, since external injury was noted at the first collection.

Appendix 20-1. Individual urinalysis in female rats (recovery period)

Control group								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F01156	9.2	1.028	26.2	66.6	25.7	0.24	0.61	0.24
F01157	8.9	1.049	80.5	203.7	96.0	0.72	1.81	0.85
F01158	8.4	1.058	126.9	265.8	161.5	1.07	2.23	1.36
F01159	8.5	1.044	38.3	164.0	75.3	0.33	1.39	0.64
F01160	5.1	1.062	112.1	297.6	173.4	0.57	1.52	0.88
Number of animals	5	5	5	5	5	5	5	5
Mean	8.0	1.048	76.8	199.5	106.4	0.59	1.51	0.79
SD	1.7	0.013	44.2	90.8	61.5	0.33	0.60	0.41

(Continued)

Appendix 20-1. (Continued) Individual urinalysis in female rats (recovery period)

Control group													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F01156	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F01157	Light yellow	8.5	+	-	±	-	-	1.0	±	±	±	-	-
F01158	Light yellow	8.5	+	-	±	-	-	1.0	±	±	±	-	-
F01159	Light yellow	8.5	+	-	-	-	-	1.0	±	±	±	-	-
F01160	Light yellow	8.0	-	-	-	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -; not observed.

Crystals: -; not observed.

Appendix 20-2. Individual urinalysis in female rats (recovery period)

Ethyl propionate group at 300 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F03356	14.8	1.019	11.7	54.7	11.3	0.17	0.81	0.17
F03357	5.0	1.065	150.5	295.6	181.4	0.75	1.48	0.91
F03358	9.7	1.065	133.5	335.6 a)	192.7	1.29	3.26	1.87
F03359	6.9	1.057	66.8	197.8	110.2	0.46	1.36	0.76
F03360	8.3	1.069	107.3	327.0 a)	194.3	0.89	2.71	1.61
Number of animals	5	5	5	5	5	5	5	5
Mean	8.9	1.055	94.0	242.1	138.0	0.71	1.92	1.06
SD	3.7	0.021	55.8	118.2	78.9	0.43	1.02	0.68
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; since the value obtained in the 1st measurement was outside the measurement range, the urine was diluted and subjected to the 2nd measurement.

Appendix 20-2. (Continued) Individual urinalysis in female rats (recovery period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F03356	Light yellow	7.0	±	-	-	-	-	0.1	±	±	±	-	-
F03357	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F03358	Light yellow	≥ 9.0	+	-	-	-	-	0.1	±	±	±	-	-
F03359	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F03360	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -, not observed.

Crystals: -, not observed.

Appendix 20-3. Individual urinalysis in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	UV mL	S.G.	Na mEq/L	K mEq/L	Cl mEq/L	Na mEq/day	K mEq/day	Cl mEq/day
F04456	10.7	1.032	16.3	87.7	38.5	0.17	0.94	0.41
F04457	13.4	1.049	107.1	223.6	150.8	1.44	3.00	2.02
F04458	11.9	1.025	22.7	60.3	25.9	0.27	0.72	0.31
F04459	16.1	1.043	78.0	205.1	117.0	1.26	3.30	1.88
F04460	11.4	1.033	41.8	106.8	70.9	0.48	1.22	0.81
Number of animals	5	5	5	5	5	5	5	5
Mean	12.7	1.036	53.2	136.7	80.6	0.72	1.84	1.09
SD	2.1	0.010	38.5	73.1	52.7	0.59	1.22	0.81
Significance	*	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

(Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 20-3. (Continued) Individual urinalysis in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Color	pH	Protein	Glucose	Ketone	Bilirubin	Occult blood	Urobilinogen E.U./dL	Urinary sediments				
									Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
F04456	Light yellow	8.0	-	-	-	-	-	0.1	±	±	±	-	-
F04457	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F04458	Light yellow	8.5	±	-	-	-	±	0.1	±	±	±	-	-
F04459	Light yellow	8.5	-	-	-	-	-	0.1	±	±	±	-	-
F04460	Light yellow	8.5	-	-	-	-	±	0.1	±	±	±	-	-
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5

Protein: -, negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≥300 mg/dL.

Glucose: -, negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≥1000 mg/dL.

Ketone: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Bilirubin: -, negative, +; slight, ++; moderate, +++; marked.

Occult blood: -, negative, ±; trace, +; slight, ++; moderate, +++; marked.

Epithelial cells: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Erythrocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Leukocytes: ±; <1 cell/HPF, +; 1 - 4 cells/HPF, ++; 5 - 9 cells/HPF, +++; 10 - 19 cells/HPF, ++++; ≥20 cells/HPF.

Casts: -; not observed.

Crystals: -; not observed.

Appendix 21-1. Individual hematological findings in male rats (administration period)

Control group												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
M01101	840	15.8	45.6	54.3	18.8	34.6	113.8	25.03	2.98	19.7	23.2	239.1
M01102	752	14.9	42.9	57.0	19.8	34.7	118.2	26.32	3.50	15.4	22.9	248.5
M01103	749	14.5	42.1	56.2	19.4	34.4	129.0	22.47	3.00	18.9	25.2	230.3
M01104	755	14.9	42.8	56.7	19.7	34.8	102.8	28.54	3.78	15.2	21.2	239.1
M01105	755	14.7	42.8	56.7	19.5	34.3	105.9	24.99	3.31	15.3	20.7	277.1
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	770	15.0	43.2	56.2	19.4	34.6	113.9	25.47	3.31	16.9	22.6	246.8
SD	39	0.5	1.4	1.1	0.4	0.2	10.4	2.21	0.34	2.2	1.8	18.1

(Continued)

Appendix 21-1. (Continued) Individual hematological findings in male rats (administration period)

Control group											
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%
M01101	128.0	115.0	8.3	1.1	0.2	3.4	89.8	6.4	0.9	0.2	2.7
M01102	78.5	59.9	15.1	0.8	0.1	2.6	76.3	19.3	1.0	0.1	3.3
M01103	55.2	43.7	9.3	0.6	0.1	1.5	79.1	16.9	1.1	0.2	2.7
M01104	68.1	51.1	13.9	0.4	0.1	2.6	75.0	20.5	0.6	0.1	3.8
M01105	75.6	58.2	15.5	0.3	0.1	1.5	77.0	20.5	0.4	0.1	2.0
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	81.1	65.6	12.4	0.6	0.1	2.3	79.4	16.7	0.8	0.1	2.9
SD	27.7	28.4	3.4	0.3	0.0	0.8	6.0	6.0	0.3	0.1	0.7

Appendix 21-2. Individual hematological findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg

Animal No.	RBC 10 ⁴ /μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT 10 ⁴ /μL	RET 10 ⁴ /μL	RET %	PT sec.	APTT sec.	Fbg mg/dL
M02201	776	15.7	44.7	57.6	20.2	35.1	111.2	25.22	3.25	11.3	17.7	274.0
M02202	783	15.1	43.4	55.4	19.3	34.8	117.0	16.68	2.13	13.6	20.4	262.0
M02203	748	14.6	42.5	56.8	19.5	34.4	135.6	23.19	3.10	15.7	22.3	219.5
M02204	742	14.9	42.7	57.5	20.1	34.9	124.5	24.86	3.35	13.9	20.0	258.5
M02205	778	15.8	44.7	57.5	20.3	35.3	112.9	17.89	2.30	20.6	22.3	222.1
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	765	15.2	43.6	57.0	19.9	34.9	120.2	21.57	2.83	15.0	20.5	247.2
SD	19	0.5	1.1	0.9	0.4	0.3	10.0	4.01	0.57	3.5	1.9	24.8
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 21-2. (Continued) Individual hematological findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg											
Animal No.	WBC 10 ² /μL	LYMPH 10 ² /μL	NEUT 10 ² /μL	EO 10 ² /μL	BASO 10 ² /μL	MONO 10 ² /μL	LYMPH %	NEUT %	EO %	BASO %	MONO %
M02201	54.2	43.2	9.4	0.2	0.0	1.4	79.7	17.3	0.4	0.0	2.6
M02202	60.9	49.0	9.0	1.0	0.1	1.8	80.4	14.8	1.6	0.2	3.0
M02203	57.3	47.1	8.3	0.8	0.0	1.1	82.2	14.5	1.4	0.0	1.9
M02204	71.7	56.0	12.8	0.6	0.1	2.2	78.1	17.9	0.8	0.1	3.1
M02205	71.5	55.4	12.2	1.6	0.1	2.2	77.4	17.2	2.2	0.1	3.1
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	63.1	50.1	10.3	0.8	0.1	1.7	79.6	16.3	1.3	0.1	2.7
SD	8.1	5.5	2.0	0.5	0.1	0.5	1.9	1.6	0.7	0.1	0.5
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	STL	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 21-3. Individual hematological findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg

Animal No.	RBC 10 ⁴ /μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT 10 ⁴ /μL	RET 10 ⁴ /μL	RET %	PT sec.	APTT sec.	Fbg mg/dL
M03301	803	16.2	46.2	57.5	20.2	35.1	117.5	22.56	2.81	16.0	23.5	255.1
M03302	799	16.0	46.5	58.2	20.0	34.4	103.2	26.53	3.32	14.5	21.6	251.7
M03303	766	14.8	43.0	56.1	19.3	34.4	120.1	24.36	3.18	11.5	20.4	239.1
M03304	746	14.5	41.3	55.4	19.4	35.1	112.5	23.05	3.09	13.8	21.1	236.1
M03305	774	15.3	43.8	56.6	19.8	34.9	115.7	20.28	2.62	17.0	23.3	227.5
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	778	15.4	44.2	56.8	19.7	34.8	113.8	23.36	3.00	14.6	22.0	241.9
SD	24	0.7	2.2	1.1	0.4	0.4	6.5	2.31	0.28	2.1	1.4	11.4
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 21-3. (Continued) Individual hematological findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg												
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO	
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%	
M03301	74.1	62.9	6.7	1.3	0.1	3.1	84.9	9.0	1.8	0.1	4.2	
M03302	56.2	48.1	5.9	0.9	0.0	1.3	85.6	10.5	1.6	0.0	2.3	
M03303	65.1	50.0	13.1	0.6	0.1	1.3	76.8	20.1	0.9	0.2	2.0	
M03304	66.0	52.1	11.4	0.8	0.1	1.6	78.9	17.3	1.2	0.2	2.4	
M03305	71.9	60.5	8.6	1.0	0.1	1.7	84.1	12.0	1.4	0.1	2.4	
Number of animals	5	5	5	5	5	5	5	5	5	5	5	
Mean	66.7	54.7	9.1	0.9	0.1	1.8	82.1	13.8	1.4	0.1	2.7	
SD	7.0	6.6	3.1	0.3	0.0	0.7	4.0	4.7	0.3	0.1	0.9	
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	
Statistical method	STL	STL	DU	DU	DU	DU	DU	DU	DU	DU	DU	

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 21-4. Individual hematological findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg

Animal No.	RBC 10 ⁴ /μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT 10 ⁴ /μL	RET 10 ⁴ /μL	RET %	PT sec.	APTT sec.	Fbg mg/dL
M04401	785	15.3	43.8	55.8	19.5	34.9	116.0	23.31	2.97	14.2	19.7	248.5
M04402	771	15.3	44.1	57.2	19.8	34.7	126.6	22.59	2.93	18.1	23.9	280.3
M04403	834	16.4	46.6	55.9	19.7	35.2	111.7	23.52	2.82	17.3	19.8	270.9
M04404	771	15.5	42.8	55.5	20.1	36.2	124.7	25.37	3.29	10.6	18.7	236.1
M04405	741	14.9	42.7	57.6	20.1	34.9	105.1	28.60	3.86	12.7	21.0	258.5
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	780	15.5	44.0	56.4	19.8	35.2	116.8	24.68	3.17	14.6	20.6	258.9
SD	34	0.6	1.6	0.9	0.3	0.6	9.0	2.42	0.42	3.1	2.0	17.5
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 21-4. (Continued) Individual hematological findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg											
Animal No.	WBC 10 ² /μL	LYMPH 10 ² /μL	NEUT 10 ² /μL	EO 10 ² /μL	BASO 10 ² /μL	MONO 10 ² /μL	LYMPH %	NEUT %	EO %	BASO %	MONO %
M04401	81.3	69.2	9.1	0.9	0.1	2.0	85.1	11.2	1.1	0.1	2.5
M04402	66.3	50.7	12.9	0.5	0.1	2.1	76.5	19.3	0.8	0.2	3.2
M04403	44.9	37.9	5.5	0.6	0.0	0.9	84.4	12.3	1.3	0.0	2.0
M04404	62.3	49.5	9.7	1.0	0.1	2.0	79.5	15.5	1.6	0.2	3.2
M04405	50.6	34.3	12.7	1.0	0.2	2.4	67.8	25.1	2.0	0.4	4.7
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	61.1	48.3	10.0	0.8	0.1	1.9	78.7	16.7	1.4	0.2	3.1
SD	14.2	13.7	3.0	0.2	0.1	0.6	7.0	5.7	0.5	0.1	1.0
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	STL	STL	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 22-1. Individual hematological findings in female rats (administration period)

Control group												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
F01151	778	15.4	43.8	56.3	19.8	35.2	110.6	20.93	2.69	9.5	16.8	202.5
F01152	787	15.5	43.5	55.3	19.7	35.6	122.4	21.33	2.71	9.7	16.9	200.3
F01153	738	15.4	43.0	58.3	20.9	35.8	103.9	22.21	3.01	9.4	18.2	202.5
F01154	775	15.3	42.8	55.2	19.7	35.7	106.3	13.49	1.74	10.3	17.8	193.8
F01155	746	14.5	41.9	56.2	19.4	34.6	116.9	19.02	2.55	9.3	17.4	187.7
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	765	15.2	43.0	56.3	19.9	35.4	112.0	19.40	2.54	9.6	17.4	197.4
SD	21	0.4	0.7	1.2	0.6	0.5	7.6	3.50	0.48	0.4	0.6	6.5

(Continued)

Appendix 22-1. (Continued) Individual hematological findings in female rats (administration period)

Control group											
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%
F01151	51.8	46.1	4.3	0.4	0.1	0.9	89.1	8.2	0.8	0.2	1.7
F01152	41.2	36.2	4.0	0.3	0.0	0.7	87.9	9.7	0.7	0.0	1.7
F01153	66.0	59.8	4.5	0.5	0.1	1.1	90.5	6.8	0.8	0.2	1.7
F01154	50.0	42.4	5.1	0.8	0.1	1.6	84.8	10.2	1.6	0.2	3.2
F01155	73.3	65.4	5.4	0.4	0.1	2.0	89.2	7.5	0.5	0.1	2.7
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	56.5	50.0	4.7	0.5	0.1	1.3	88.3	8.5	0.9	0.1	2.2
SD	13.0	12.2	0.6	0.2	0.0	0.5	2.2	1.4	0.4	0.1	0.7

Appendix 22-2. Individual hematological findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
F02251	752	14.7	41.9	55.7	19.5	35.1	118.5	17.67	2.35	9.5	16.9	174.6
F02252	777	14.8	41.8	53.8	19.0	35.4	146.2	12.35	1.59	9.7	16.9	161.6
F02253	734	14.4	41.6	56.7	19.6	34.6	117.9	19.52	2.66	10.1	17.6	148.8
F02254	678	14.0	38.8	57.2	20.6	36.1	116.6	18.51	2.73	9.6	18.3	193.8
F02255	730	14.5	40.2	55.1	19.9	36.1	107.9	13.65	1.87	9.2	17.9	172.9
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	734	14.5	40.9	55.7	19.7	35.5	121.4	16.34	2.24	9.6	17.5	170.3
SD	36	0.3	1.3	1.3	0.6	0.7	14.5	3.15	0.50	0.3	0.6	16.7
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 22-2. (Continued) Individual hematological findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg											
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%
F02251	67.6	59.5	5.0	1.1	0.1	1.9	88.0	7.5	1.6	0.1	2.8
F02252	45.9	42.0	2.4	0.6	0.0	0.9	91.5	5.2	1.3	0.0	2.0
F02253	46.2	39.1	5.0	0.4	0.0	1.7	84.6	10.8	0.9	0.0	3.7
F02254	43.7	35.6	6.7	0.4	0.1	0.9	81.4	15.4	0.9	0.2	2.1
F02255	64.9	50.5	11.7	0.8	0.1	1.8	77.7	18.1	1.2	0.2	2.8
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	53.7	45.3	6.2	0.7	0.1	1.4	84.6	11.4	1.2	0.1	2.7
SD	11.6	9.6	3.5	0.3	0.1	0.5	5.4	5.4	0.3	0.1	0.7
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 22-3. Individual hematological findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
F03351	730	14.5	40.6	55.6	19.9	35.7	143.5	20.00	2.74	9.7	16.9	209.5
F03352	679	13.8	39.1	57.6	20.3	35.3	101.4	20.78	3.06	9.8	17.4	169.5
F03353	816	15.8	44.5	54.5	19.4	35.5	143.4	16.24	1.99	9.3	17.4	193.8
F03354	732	14.9	41.7	57.0	20.4	35.7	127.3	25.84	3.53	9.4	18.2	193.8
F03355	706	14.5	40.8	57.8	20.5	35.5	119.7	19.63	2.78	9.6	17.7	222.1
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	733	14.7	41.3	56.5	20.1	35.5	127.1	20.50	2.82	9.6	17.5	197.7
SD	51	0.7	2.0	1.4	0.5	0.2	17.7	3.46	0.56	0.2	0.5	19.8
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 22-3. (Continued) Individual hematological findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg											
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%
F03351	58.7	52.2	4.6	0.3	0.0	1.6	89.0	7.8	0.5	0.0	2.7
F03352	18.7	14.9	3.2	0.2	0.0	0.4	79.7	17.1	1.1	0.0	2.1
F03353	68.7	63.2	2.9	0.9	0.2	1.5	92.0	4.2	1.3	0.3	2.2
F03354	38.1	33.0	3.3	0.5	0.0	1.3	86.6	8.7	1.3	0.0	3.4
F03355	56.3	47.5	7.0	0.3	0.1	1.4	84.4	12.4	0.5	0.2	2.5
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	48.1	42.2	4.2	0.4	0.1	1.2	86.3	10.0	0.9	0.1	2.6
SD	19.8	18.7	1.7	0.3	0.1	0.5	4.7	4.9	0.4	0.1	0.5
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 22-4. Individual hematological findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
F04451	704	14.3	39.7	56.4	20.3	36.0	104.9	15.00	2.13	9.7	16.0	160.0
F04452	783	15.3	43.7	55.8	19.5	35.0	120.8	21.30	2.72	9.3	17.8	227.5
F04453	770	15.5	44.2	57.4	20.1	35.1	121.5	24.87	3.23	9.3	18.1	204.8
F04454	752	15.4	43.4	57.7	20.5	35.5	104.5	21.13	2.81	9.3	17.4	230.3
F04455	736	14.4	40.6	55.2	19.6	35.5	117.0	16.41	2.23	9.3	18.5	181.9
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	749	15.0	42.3	56.5	20.0	35.4	113.7	19.74	2.62	9.4	17.6	200.9
SD	31	0.6	2.0	1.1	0.4	0.4	8.4	4.01	0.45	0.2	1.0	30.1
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 22-4. (Continued) Individual hematological findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg											
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%
F04451	55.6	44.8	8.1	0.7	0.1	1.9	80.6	14.5	1.3	0.2	3.4
F04452	50.8	44.3	4.7	0.6	0.1	1.1	87.1	9.3	1.2	0.2	2.2
F04453	49.4	41.6	6.5	0.4	0.1	0.8	84.2	13.2	0.8	0.2	1.6
F04454	40.7	35.4	4.2	0.4	0.1	0.6	86.9	10.4	1.0	0.2	1.5
F04455	46.2	37.4	6.9	0.6	0.0	1.3	80.9	15.0	1.3	0.0	2.8
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	48.5	40.7	6.1	0.5	0.1	1.1	83.9	12.5	1.1	0.2	2.3
SD	5.5	4.2	1.6	0.1	0.0	0.5	3.1	2.5	0.2	0.1	0.8
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 23-1. Individual hematological findings in male rats (recovery period)

Control group												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
M01106	838	15.2	44.5	53.1	18.1	34.2	99.0	22.54	2.69	16.4	22.8	231.5
M01107	869	15.5	45.3	52.1	17.8	34.2	113.1	18.25	2.10	15.7	21.1	207.1
M01108	815	15.7	44.0	54.0	19.3	35.7	112.6	23.06	2.83	13.2	22.2	244.4
M01109	800	15.7	44.2	55.3	19.6	35.5	100.9	23.20	2.90	14.9	23.6	222.0
M01110	755	14.7	42.9	56.8	19.5	34.3	93.5	22.35	2.96	11.4	19.5	239.1
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	815	15.4	44.2	54.3	18.9	34.8	103.8	21.88	2.70	14.3	21.8	228.8
SD	43	0.4	0.9	1.8	0.8	0.8	8.7	2.06	0.35	2.0	1.6	14.8

(Continued)

Appendix 23-1. (Continued) Individual hematological findings in male rats (recovery period)

Control group												
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO	
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%	
M01106	108.9	95.4	10.1	1.2	0.2	2.0	87.7	9.2	1.1	0.2	1.8	
M01107	80.1	70.2	7.4	1.0	0.1	1.4	87.7	9.3	1.2	0.1	1.7	
M01108	55.3	45.8	7.1	0.9	0.1	1.4	82.9	12.8	1.6	0.2	2.5	
M01109	59.6	45.9	11.4	0.7	0.2	1.4	77.1	19.1	1.2	0.3	2.3	
M01110	48.2	40.6	6.0	0.3	0.2	1.1	84.2	12.5	0.6	0.4	2.3	
Number of animals	5	5	5	5	5	5	5	5	5	5	5	
Mean	70.4	59.6	8.4	0.8	0.2	1.5	83.9	12.6	1.1	0.2	2.1	
SD	24.6	23.1	2.3	0.3	0.1	0.3	4.4	4.0	0.4	0.1	0.3	

Appendix 23-2. Individual hematological findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg

Animal No.	RBC 10 ⁴ /μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT 10 ⁴ /μL	RET 10 ⁴ /μL	RET %	PT sec.	APTT sec.	Fbg mg/dL
M03306	833	15.5	44.9	53.9	18.6	34.5	109.4	23.49	2.82	14.4	23.9	224.3
M03307	817 a)	15.7 a)	44.5 a)	54.5 a)	19.2 a)	35.3 a)	117.1 a)	20.75 a)	2.54 a)	18.4	25.1	205.1
M03308	826	14.8	42.7	51.7	17.9	34.7	117.0	24.86	3.01	12.4	20.6	215.3
M03309	815	15.8	45.1	55.3	19.4	35.0	110.6	21.03	2.58	17.2	23.5	244.4
M03310	850	15.7	45.3	53.3	18.5	34.7	103.1	22.61	2.66	14.5	20.2	252.9
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	828	15.5	44.5	53.7	18.7	34.8	111.4	22.55	2.72	15.4	22.7	228.4
SD	14	0.4	1.0	1.4	0.6	0.3	5.9	1.72	0.19	2.4	2.2	19.9
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; the 2nd measurement was performed because an error occurred during the 1st measurement.

Appendix 23-2. (Continued) Individual hematological findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg											
Animal No.	WBC 10 ² /μL	LYMPH 10 ² /μL	NEUT 10 ² /μL	EO 10 ² /μL	BASO 10 ² /μL	MONO 10 ² /μL	LYMPH %	NEUT %	EO %	BASO %	MONO %
M03306	69.3	57.9	9.2	0.6	0.1	1.5	83.5	13.3	0.9	0.1	2.2
M03307	95.6 a)	82.6 a)	8.8 a)	1.7 a)	0.2 a)	2.3 a)	86.4 a)	9.2 a)	1.8 a)	0.2 a)	2.4 a)
M03308	104.3	89.1	12.3	1.0	0.2	1.7	85.5	11.7	1.0	0.2	1.6
M03309	55.1	37.7	14.5	0.9	0.2	1.8	68.4	26.3	1.6	0.4	3.3
M03310	69.7	52.4	14.7	1.0	0.1	1.5	75.1	21.2	1.4	0.1	2.2
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	78.8	63.9	11.9	1.0	0.2	1.8	79.8	16.3	1.3	0.2	2.3
SD	20.4	21.4	2.8	0.4	0.1	0.3	7.8	7.2	0.4	0.1	0.6
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; the 2nd measurement was performed because an error occurred during the 1st measurement.

Appendix 23-3. Individual hematological findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg												
Animal No.	RBC 10 ⁴ /μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT 10 ⁴ /μL	RET 10 ⁴ /μL	RET %	PT sec.	APTT sec.	Fbg mg/dL
M04406	884	16.8	48.9	55.3	19.0	34.4	93.9	26.96	3.05	11.1	19.7	233.9
M04407	795	15.4	44.2	55.6	19.4	34.8	105.8	23.21	2.92	12.1	21.7	224.3
M04408	818	15.4	43.5	53.2	18.8	35.4	139.5	29.12	3.56	14.8	22.3	250.0
M04409	840 a)	15.6 a)	44.7 a)	53.2 a)	18.6 a)	34.9 a)	99.8 a)	22.85 a)	2.72 a)	15.3	20.6	231.5
M04410	865	15.3	44.8	51.8	17.7	34.2	109.2	21.88	2.53	20.1	21.6	229.0
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	840	15.7	45.2	53.8	18.7	34.7	109.6	24.80	2.96	14.7	21.2	233.7
SD	36	0.6	2.1	1.6	0.6	0.5	17.7	3.09	0.39	3.5	1.0	9.8
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; the 2nd measurement was performed because an error occurred during the 1st measurement.

Appendix 23-3. (Continued) Individual hematological findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg												
Animal No.	WBC 10 ² /μL	LYMPH 10 ² /μL	NEUT 10 ² /μL	EO 10 ² /μL	BASO 10 ² /μL	MONO 10 ² /μL	LYMPH %	NEUT %	EO %	BASO %	MONO %	
M04406	82.4	69.2	10.7	0.7	0.2	1.6	84.0	13.1	0.8	0.2	1.9	
M04407	64.8	54.6	7.8	1.0	0.1	1.3	84.3	12.0	1.5	0.2	2.0	
M04408	97.6	82.8	12.5	0.6	0.2	1.5	84.9	12.8	0.6	0.2	1.5	
M04409	43.8 a)	32.0 a)	9.6 a)	0.8 a)	0.1 a)	1.3 a)	73.1 a)	21.9 a)	1.8 a)	0.2 a)	3.0 a)	
M04410	54.2	34.6	16.6	0.7	0.1	2.2	63.8	30.6	1.3	0.2	4.1	
Number of animals	5	5	5	5	5	5	5	5	5	5	5	
Mean	68.6	54.6	11.4	0.8	0.1	1.6	78.0	18.1	1.2	0.2	2.5	
SD	21.6	21.9	3.4	0.2	0.1	0.4	9.3	8.1	0.5	0.0	1.1	
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; the 2nd measurement was performed because an error occurred during the 1st measurement.

Appendix 24-1. Individual hematological findings in female rats (recovery period)

Control group												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
F01156	786	14.8	41.2	52.4	18.8	35.9	109.3	15.56	1.98	9.4	17.5	207.1
F01157	757	14.4	40.5	53.5	19.0	35.6	126.9	18.09	2.39	9.9	18.3	199.4
F01158	809	15.5	44.9	55.5	19.2	34.5	117.1	22.89	2.83	9.8	17.2	185.5
F01159	790	15.0	42.4	53.7	19.0	35.4	112.2	14.54	1.84	9.3	18.5	180.8
F01160	723	14.1	40.9	56.6	19.5	34.5	105.0	19.74	2.73	9.4	16.5	182.3
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	773	14.8	42.0	54.3	19.1	35.2	114.1	18.16	2.35	9.6	17.6	191.0
SD	34	0.5	1.8	1.7	0.3	0.6	8.4	3.34	0.44	0.3	0.8	11.6

(Continued)

Appendix 24-1. (Continued) Individual hematological findings in female rats (recovery period)

Control group												
Animal No.	WBC	LYMPH	NEUT	EO	BASO	MONO	LYMPH	NEUT	EO	BASO	MONO	
	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	10 ² /μL	%	%	%	%	%	
F01156	23.8	16.6	6.2	0.6	0.0	0.4	69.7	26.1	2.5	0.0	1.7	
F01157	33.2	25.0	7.2	0.4	0.1	0.5	75.3	21.7	1.2	0.3	1.5	
F01158	50.3	33.2	14.9	1.0	0.1	1.1	66.0	29.6	2.0	0.2	2.2	
F01159	29.4	22.2	5.8	0.6	0.1	0.7	75.5	19.8	2.0	0.3	2.4	
F01160	19.9	15.4	3.8	0.4	0.0	0.3	77.4	19.1	2.0	0.0	1.5	
Number of animals	5	5	5	5	5	5	5	5	5	5	5	
Mean	31.3	22.5	7.6	0.6	0.1	0.6	72.8	23.3	1.9	0.2	1.9	
SD	11.8	7.2	4.3	0.2	0.1	0.3	4.8	4.5	0.5	0.2	0.4	

Appendix 24-2. Individual hematological findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg

Animal No.	RBC 10 ⁴ /μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT 10 ⁴ /μL	RET 10 ⁴ /μL	RET %	PT sec.	APTT sec.	Fbg mg/dL
F03356	773	14.7	41.3	53.4	19.0	35.6	110.6	19.63	2.54	9.4	16.9	201.2
F03357	775	14.4	40.7	52.5	18.6	35.4	125.4	17.67	2.28	10.1	16.7	183.9
F03358	799	14.5	42.8	53.6	18.1	33.9	119.3	25.41	3.18	9.7	18.0	192.2
F03359	857	16.1	46.1	53.8	18.8	34.9	107.4	17.40	2.03	9.4	19.0	182.3
F03360	749	14.2	41.3	55.1	19.0	34.4	104.3	20.52	2.74	9.9	18.2	164.0
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	791	14.8	42.4	53.7	18.7	34.8	113.4	20.13	2.55	9.7	17.8	184.7
SD	41	0.8	2.2	0.9	0.4	0.7	8.7	3.23	0.44	0.3	1.0	13.8
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 24-2. (Continued) Individual hematological findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg											
Animal No.	WBC 10 ² /μL	LYMPH 10 ² /μL	NEUT 10 ² /μL	EO 10 ² /μL	BASO 10 ² /μL	MONO 10 ² /μL	LYMPH %	NEUT %	EO %	BASO %	MONO %
F03356	26.8	19.2	6.2	0.7	0.1	0.6	71.7	23.1	2.6	0.4	2.2
F03357	25.9	17.1	7.5	0.6	0.1	0.6	66.0	29.0	2.3	0.4	2.3
F03358	42.6	33.5	7.0	0.7	0.1	1.3	78.6	16.5	1.6	0.2	3.1
F03359	36.3	26.6	8.2	0.8	0.0	0.7	73.3	22.6	2.2	0.0	1.9
F03360	15.7	10.8	4.4	0.2	0.0	0.3	68.8	28.0	1.3	0.0	1.9
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	29.5	21.4	6.7	0.6	0.1	0.7	71.7	23.8	2.0	0.2	2.3
SD	10.4	8.8	1.5	0.2	0.1	0.4	4.8	5.0	0.5	0.2	0.5
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 24-3. Individual hematological findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg												
Animal No.	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	RET	RET	PT	APTT	Fbg
	10 ⁴ /μL	g/dL	%	fL	pg	g/dL	10 ⁴ /μL	10 ⁴ /μL	%	sec.	sec.	mg/dL
F04456	730	14.3	40.2	55.1	19.6	35.6	98.9	13.94	1.91	9.8	17.3	180.8
F04457	810	15.2	44.1	54.4	18.8	34.5	114.8	19.60	2.42	9.1	16.6	203.1
F04458	766	14.6	42.5	55.5	19.1	34.4	109.6	20.30	2.65	9.3	17.9	199.4
F04459	757	15.0	41.5	54.8	19.8	36.1	107.1	16.88	2.23	9.3	17.8	190.5
F04460	860	15.9	44.7	52.0	18.5	35.6	95.0	15.65	1.82	9.4	17.8	177.8
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	785	15.0	42.6	54.4	19.2	35.2	105.1	17.27	2.21	9.4	17.5	190.3
SD	51	0.6	1.8	1.4	0.5	0.8	8.0	2.67	0.35	0.3	0.5	11.1
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 24-3. (Continued) Individual hematological findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg											
Animal No.	WBC 10 ² /μL	LYMPH 10 ² /μL	NEUT 10 ² /μL	EO 10 ² /μL	BASO 10 ² /μL	MONO 10 ² /μL	LYMPH %	NEUT %	EO %	BASO %	MONO %
F04456	26.9	21.7	3.9	0.7	0.1	0.5	80.6	14.5	2.6	0.4	1.9
F04457	69.7	45.9	21.6	1.0	0.1	1.1	65.9	31.0	1.4	0.1	1.6
F04458	37.2	26.5	9.1	0.6	0.1	0.9	71.2	24.5	1.6	0.3	2.4
F04459	46.8	32.2	13.2	0.6	0.1	0.7	68.8	28.2	1.3	0.2	1.5
F04460	40.7	29.1	9.9	0.6	0.0	1.1	71.5	24.3	1.5	0.0	2.7
Number of animals	5	5	5	5	5	5	5	5	5	5	5
Mean	44.3	31.1	11.5	0.7	0.1	0.9	71.6	24.5	1.7	0.2	2.0
SD	15.9	9.1	6.5	0.2	0.0	0.3	5.5	6.2	0.5	0.2	0.5
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-1. Individual blood chemical findings in male rats (administration period)

Control group			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M01101	77.5	33.0	250.0
M01102	90.2	38.8	198.2
M01103	112.7	30.9	181.4
M01104	86.0	25.3	249.6
M01105	78.7	26.1	233.0
Number of animals	5	5	5
Mean	89.0	30.8	222.4
SD	14.2	5.5	31.1

(Continued)

Appendix 25-1. (Continued) Individual blood chemical findings in male rats (administration period)

Control group								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M01101	5.35	2.58	48.2	22.2	9.0	16.9	3.7	0.93
M01102	5.21	2.55	49.0	22.7	8.0	16.8	3.5	0.96
M01103	5.62	2.46	43.7	24.7	7.7	17.3	6.6	0.78
M01104	5.33	2.54	47.7	19.3	9.0	18.1	5.9	0.91
M01105	5.47	2.88	52.6	16.9	9.3	17.4	3.8	1.11
Number of animals	5	5	5	5	5	5	5	5
Mean	5.40	2.60	48.2	21.2	8.6	17.3	4.7	0.94
SD	0.16	0.16	3.2	3.1	0.7	0.5	1.4	0.12

(Continued)

Appendix 25-1. (Continued) Individual blood chemical findings in male rats (administration period)

Control group						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
M01101	0.12	13.7	0.33	135.9	44.2	37.5
M01102	0.11	11.3	0.33	105.5	59.8	113.7 a)
M01103	0.11	11.9	0.30	117.7	43.2	25.0
M01104	0.12	10.5	0.30	127.8	53.0	30.0
M01105	0.11	13.7	0.32	153.5	73.0	58.5
Number of animals	5	5	5	5	5	5
Mean	0.11	12.2	0.32	128.1	54.6	52.9
SD	0.01	1.4	0.02	18.2	12.3	36.3

a): Obtained in the 1st measurement; the value, which is markedly higher than that in other animals, was confirmed to be correct in the 2nd measurement. (Continued)

Appendix 25-1. (Continued) Individual blood chemical findings in male rats (administration period)

Control group					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M01101	143.7	3.58	106.7	9.6	7.8
M01102	143.9	4.00	107.0	9.7	8.3
M01103	145.0	4.05	106.8	9.6	8.8
M01104	144.7	3.76	107.2	9.8	9.8
M01105	144.2	4.21	108.4	10.0	9.8
Number of animals	5	5	5	5	5
Mean	144.3	3.92	107.2	9.7	8.9
SD	0.5	0.25	0.7	0.2	0.9

Appendix 25-2. Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M02201	84.7	34.3	212.5
M02202	89.5	22.1	190.0
M02203	81.5	26.7	175.0
M02204	120.7	24.9	146.0
M02205	79.3	28.6	259.5
Number of animals	5	5	5
Mean	91.1	27.3	196.6
SD	17.0	4.6	42.7
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 25-2. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M02201	5.55	2.56	46.2	21.7	8.6	18.7	4.8	0.86
M02202	4.97	2.35	47.2	21.6	8.5	17.6	5.1	0.89
M02203	5.07	2.12	41.9	24.4	11.1	17.1	5.5	0.72
M02204	5.24	2.58	49.3	21.8	8.8	16.3	3.8	0.97
M02205	5.23	2.47	47.3	22.7	9.6	16.4	4.0	0.90
Number of animals	5	5	5	5	5	5	5	5
Mean	5.21	2.42	46.4	22.4	9.3	17.2	4.6	0.87
SD	0.22	0.19	2.7	1.2	1.1	1.0	0.7	0.09
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 25-2. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
M02201	0.11	12.0	0.31	132.0	53.2	34.9
M02202	0.10	12.9	0.30	118.4	49.0	43.8
M02203	0.11	13.5	0.30	131.1	48.8	28.9
M02204	0.11	8.9	0.28	112.5	53.0	50.2
M02205	0.11	12.0	0.28	122.8	46.1	24.4
Number of animals	5	5	5	5	5	5
Mean	0.11	11.9	0.29	123.4	50.0	36.4
SD	0.00	1.8	0.01	8.3	3.0	10.6
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	STL	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-2. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M02201	143.8	4.01	106.4	9.7	7.4
M02202	144.6	4.13	107.1	9.2	8.6
M02203	145.4	3.90	106.7	9.5	9.0
M02204	143.1	4.31	106.1	9.9	8.9
M02205	143.6	3.85	107.1	10.1	9.6
Number of animals	5	5	5	5	5
Mean	144.1	4.04	106.7	9.7	8.7
SD	0.9	0.19	0.4	0.3	0.8
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	STL	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-3. Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M03301	87.3	27.1	209.2
M03302	103.1	32.5	250.5
M03303	109.9	32.4	228.1
M03304	73.7	21.9	169.3
M03305	70.2	21.7	178.6
Number of animals	5	5	5
Mean	88.8	27.1	207.1
SD	17.5	5.3	33.8
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 25-3. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M03301	5.78	2.61	45.1	24.9	8.6	17.2	4.2	0.82
M03302	5.59	2.58	46.2	22.9	7.8	18.5	4.6	0.86
M03303	5.33	2.43	45.5	23.0	10.2	16.1	5.2	0.83
M03304	5.29	2.66	50.3	22.2	8.0	15.3	4.2	1.01
M03305	5.33	2.71	50.8	20.3	9.1	16.5	3.3	1.03
Number of animals	5	5	5	5	5	5	5	5
Mean	5.46	2.60	47.6	22.7	8.7	16.7	4.3	0.91
SD	0.21	0.11	2.7	1.7	1.0	1.2	0.7	0.10
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 25-3. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
M03301	0.12	12.9	0.35	122.6	39.2	61.7
M03302	0.11	19.5	0.37	136.4	53.1	24.1
M03303	0.11	11.4	0.31	112.2	65.1	32.4
M03304	0.12	10.4	0.30	112.7	56.6	31.1
M03305	0.12	13.5	0.28	126.3	48.1	28.0
Number of animals	5	5	5	5	5	5
Mean	0.12	13.5	0.32	122.0	52.4	35.5
SD	0.01	3.5	0.04	10.1	9.6	15.0
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	STL	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-3. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M03301	145.4	4.13	108.1	9.8	8.5
M03302	144.1	4.16	105.7	9.9	10.0
M03303	144.6	4.14	106.4	9.8	9.0
M03304	144.4	4.11	105.9	9.9	8.8
M03305	145.4	3.80	107.1	9.8	9.8
Number of animals	5	5	5	5	5
Mean	144.8	4.07	106.6	9.8	9.2
SD	0.6	0.15	1.0	0.1	0.6
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	STL	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-4. Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M04401	75.1	27.1	235.4
M04402	134.5	27.7	208.0
M04403	74.2	25.9	257.0
M04404	104.7	19.9	188.8
M04405	75.9	25.1	207.4
Number of animals	5	5	5
Mean	92.9	25.1	219.3
SD	26.6	3.1	26.8
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 25-4. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M04401	5.32	2.31	43.5	24.8	8.0	17.4	6.3	0.77
M04402	5.10	2.22	43.5	22.7	9.1	19.8	4.9	0.77
M04403	5.52	2.61	47.2	20.2	9.6	17.2	5.8	0.89
M04404	5.46	2.59	47.4	23.4	8.6	16.3	4.3	0.90
M04405	5.22	2.40	46.0	26.9	8.2	15.4	3.5	0.85
Number of animals	5	5	5	5	5	5	5	5
Mean	5.32	2.43	45.5	23.6	8.7	17.2	5.0	0.84
SD	0.17	0.17	1.9	2.5	0.7	1.6	1.1	0.06
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 25-4. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
M04401	0.11	13.1	0.30	126.5	55.3	55.6
M04402	0.12	11.4	0.33	114.6	48.6	53.7
M04403	0.11	12.8	0.29	109.7	65.1	40.2
M04404	0.11	12.6	0.30	116.1	55.7	79.3
M04405	0.13	11.8	0.29	112.7	72.0	41.4
Number of animals	5	5	5	5	5	5
Mean	0.12	12.3	0.30	115.9	59.3	54.0
SD	0.01	0.7	0.02	6.4	9.2	15.7
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	STL	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-4. (Continued) Individual blood chemical findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M04401	143.4	3.95	106.3	9.6	9.2
M04402	144.8	4.28	107.0	9.4	9.8
M04403	145.2	3.75	107.0	9.9	9.1
M04404	142.4	4.48	105.1	9.8	9.9
M04405	144.6	3.76	106.6	10.2	8.7
Number of animals	5	5	5	5	5
Mean	144.1	4.04	106.4	9.8	9.3
SD	1.2	0.32	0.8	0.3	0.5
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	STL	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-1. Individual blood chemical findings in female rats (administration period)

Control group			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F01151	82.8	17.4	155.9
F01152	74.2	13.8	159.1
F01153	89.1	20.5	153.5
F01154	112.8	20.9	101.6
F01155	97.0	14.6	83.5
Number of animals	5	5	5
Mean	91.2	17.4	130.7
SD	14.7	3.3	35.5

(Continued)

Appendix 26-1. (Continued) Individual blood chemical findings in female rats (administration period)

Control group								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F01151	5.62	2.88	51.2	20.4	8.2	16.0	4.2	1.05
F01152	5.40	2.81	52.0	20.6	7.3	16.3	3.8	1.08
F01153	5.80	2.91	50.1	21.2	8.7	16.0	4.0	1.00
F01154	5.25	2.66	50.7	18.3	8.5	17.2	5.3	1.03
F01155	5.77	2.99	51.8	16.0	8.3	17.0	6.9	1.07
Number of animals	5	5	5	5	5	5	5	5
Mean	5.57	2.85	51.2	19.3	8.2	16.5	4.8	1.05
SD	0.24	0.12	0.8	2.1	0.5	0.6	1.3	0.03

(Continued)

Appendix 26-1. (Continued) Individual blood chemical findings in female rats (administration period)

Control group						
Animal No.	T-Bil	UN	CRE	Glu	T-Cho	TG
	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
F01151	0.12	13.8	0.41	126.0	66.6	14.5
F01152	0.12	13.1	0.46	116.2	68.6	16.8
F01153	0.11	14.5	0.37	135.8	65.0	12.2
F01154	0.11	14.5	0.36	116.3	51.2	6.9
F01155	0.12	10.4	0.33	125.5	73.6	25.5
Number of animals	5	5	5	5	5	5
Mean	0.12	13.3	0.39	124.0	65.0	15.2
SD	0.01	1.7	0.05	8.1	8.4	6.8

(Continued)

Appendix 26-1. (Continued) Individual blood chemical findings in female rats (administration period)

Control group					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F01151	145.8	4.00	109.2	9.9	9.4
F01152	146.7	4.26	109.6	9.7	9.3
F01153	145.9	3.72	109.6	10.0	9.4
F01154	145.7	4.21	106.1	9.7	9.5
F01155	146.6	4.33	109.0	10.0	8.7
Number of animals	5	5	5	5	5
Mean	146.1	4.10	108.7	9.9	9.3
SD	0.5	0.25	1.5	0.2	0.3

Appendix 26-2. Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F02251	90.5	22.5	97.0
F02252	89.3	18.3	135.3
F02253	70.3	15.6	90.1
F02254	72.9	15.6	63.6
F02255	86.9	20.6	86.5
Number of animals	5	5	5
Mean	82.0	18.5	94.5
SD	9.6	3.1	26.0
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 26-2. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F02251	5.97	3.04	50.9	21.8	7.8	14.4	5.1	1.04
F02252	5.39	2.72	50.5	21.7	8.7	15.1	4.0	1.02
F02253	5.34	2.69	50.4	17.0	9.2	17.6	5.8	1.02
F02254	5.57	2.95	53.0	19.2	8.2	15.0	4.6	1.13
F02255	6.19	3.14	50.8	17.1	8.5	16.1	7.5	1.03
Number of animals	5	5	5	5	5	5	5	5
Mean	5.69	2.91	51.1	19.4	8.5	15.6	5.4	1.05
SD	0.37	0.20	1.1	2.4	0.5	1.3	1.3	0.05
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 26-2. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
F02251	0.13	13.2	0.35	115.0	81.9	17.9
F02252	0.12	10.2	0.31	109.3	62.6	16.1
F02253	0.12	9.8	0.31	108.3	72.2	10.7
F02254	0.13	12.6	0.34	117.3	55.5	13.5
F02255	0.13	13.1	0.36	103.4	91.5	11.4
Number of animals	5	5	5	5	5	5
Mean	0.13	11.8	0.33	110.7	72.7	13.9
SD	0.01	1.6	0.02	5.5	14.5	3.1
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-2. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F02251	144.3	4.36	105.9	10.2	9.5
F02252	145.1	4.31	107.0	9.8	9.1
F02253	144.9	3.98	110.6	9.7	9.3
F02254	145.3	4.05	107.7	9.8	9.0
F02255	144.0	4.41	105.8	9.9	8.9
Number of animals	5	5	5	5	5
Mean	144.7	4.22	107.4	9.9	9.2
SD	0.5	0.19	2.0	0.2	0.2
Significance	*	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 26-3. Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F03351	119.7	19.4	138.1
F03352	71.3	12.4	119.4
F03353	80.2	19.3	120.1
F03354	95.2	17.1	111.4
F03355	98.8	17.7	165.2
Number of animals	5	5	5
Mean	93.0	17.2	130.8
SD	18.6	2.9	21.5
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 26-3. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F03351	5.71	3.08	53.9	19.4	7.5	15.2	4.0	1.17
F03352	4.87	2.59	53.2	21.2	8.2	13.4	4.0	1.14
F03353	5.93	2.99	50.5	20.3	8.8	15.7	4.7	1.02
F03354	5.84	2.81	48.1	20.1	8.8	17.9	5.1	0.93
F03355	5.44	2.65	48.7	21.5	8.8	16.3	4.7	0.95
Number of animals	5	5	5	5	5	5	5	5
Mean	5.56	2.82	50.9	20.5	8.4	15.7	4.5	1.04
SD	0.43	0.21	2.6	0.9	0.6	1.6	0.5	0.11
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 26-3. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
F03351	0.11	12.6	0.35	96.2	66.5	10.6
F03352	0.11	11.8	0.34	123.3	57.2	9.3
F03353	0.11	13.7	0.33	117.1	74.9	12.9
F03354	0.12	12.7	0.33	121.5	52.7	21.3
F03355	0.12	10.6	0.34	110.5	51.2	20.1
Number of animals	5	5	5	5	5	5
Mean	0.11	12.3	0.34	113.7	60.5	14.8
SD	0.01	1.2	0.01	11.0	10.0	5.5
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-3. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F03351	146.6	3.86	110.5	9.5	8.8
F03352	145.4	3.79	110.4	9.4	7.9
F03353	146.3	3.67	107.7	10.4	8.5
F03354	146.3	4.05	106.2	10.0	9.4
F03355	146.5	4.42	109.4	9.9	9.3
Number of animals	5	5	5	5	5
Mean	146.2	3.96	108.8	9.8	8.8
SD	0.5	0.29	1.9	0.4	0.6
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 26-4. Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F04451	80.3	17.2	135.3
F04452	72.3	17.6	146.1
F04453	64.7	11.9	157.3
F04454	101.0	19.7	154.6
F04455	75.3	15.2	73.3
Number of animals	5	5	5
Mean	78.7	16.3	133.3
SD	13.7	2.9	34.6
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 26-4. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F04451	5.55	2.87	51.7	19.8	7.5	16.1	4.9	1.07
F04452	5.82	3.05	52.4	22.2	6.9	15.7	2.8	1.10
F04453	6.11	2.88	47.2	21.0	10.0	17.5	4.3	0.89
F04454	5.71	2.83	49.6	20.7	8.3	18.4	3.0	0.98
F04455	5.72	3.14	54.9	19.0	7.2	16.0	2.9	1.22
Number of animals	5	5	5	5	5	5	5	5
Mean	5.78	2.95	51.2	20.5	8.0	16.7	3.6	1.05
SD	0.21	0.13	2.9	1.2	1.2	1.2	1.0	0.12
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 26-4. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
F04451	0.12	15.2	0.33	103.4	68.3	10.0
F04452	0.13	9.2	0.33	135.0	95.3	29.8
F04453	0.12	12.2	0.30	127.3	65.5	20.9
F04454	0.11	16.0	0.34	143.5	68.4	7.7
F04455	0.14	11.9	0.34	110.5	96.0	23.8
Number of animals	5	5	5	5	5	5
Mean	0.12	12.9	0.33	123.9	78.7	18.4
SD	0.01	2.7	0.02	16.7	15.5	9.4
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	STL	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-4. (Continued) Individual blood chemical findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F04451	144.0	3.76	107.0	9.9	9.3
F04452	143.7	3.73	103.8	10.4	8.8
F04453	145.6	3.79	107.5	10.4	8.9
F04454	146.1	3.97	108.6	10.1	9.3
F04455	144.0	4.43	108.1	10.0	9.2
Number of animals	5	5	5	5	5
Mean	144.7	3.94	107.0	10.2	9.1
SD	1.1	0.29	1.9	0.2	0.2
Significance	*	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 27-1. Individual blood chemical findings in male rats (recovery period)

Control group			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M01106	75.5	28.8	150.6
M01107	99.0	31.5	178.4
M01108	89.6	31.1	190.8
M01109	83.6	33.7	169.5
M01110	129.8	27.9	117.3
Number of animals	5	5	5
Mean	95.5	30.6	161.3
SD	21.0	2.3	28.6

(Continued)

Appendix 27-1. (Continued) Individual blood chemical findings in male rats (recovery period)

Control group								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M01106	5.79	2.33	40.2	29.1	8.0	17.2	5.5	0.67
M01107	5.22	2.73	52.3	18.7	9.3	16.5	3.2	1.10
M01108	5.43	2.63	48.5	20.2	9.1	17.2	5.0	0.94
M01109	5.54	2.65	47.8	25.6	8.5	14.3	3.8	0.92
M01110	5.50	2.55	46.3	17.0	9.7	20.4	6.6	0.86
Number of animals	5	5	5	5	5	5	5	5
Mean	5.50	2.58	47.0	22.1	8.9	17.1	4.8	0.90
SD	0.21	0.15	4.4	5.1	0.7	2.2	1.4	0.16

(Continued)

Appendix 27-1. (Continued) Individual blood chemical findings in male rats (recovery period)

Control group						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
M01106	0.12	16.2	0.42	134.8	47.6	43.6
M01107	0.11	13.4	0.39	136.2	67.2	62.3
M01108	0.12	15.0	0.36	137.1	76.0	61.9
M01109	0.11	15.2	0.36	115.1	47.3	63.6
M01110	0.10	13.1	0.39	117.4	72.7	43.1
Number of animals	5	5	5	5	5	5
Mean	0.11	14.6	0.38	128.1	62.2	54.9
SD	0.01	1.3	0.03	10.9	13.8	10.6

(Continued)

Appendix 27-1. (Continued) Individual blood chemical findings in male rats (recovery period)

Control group					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M01106	142.0	3.74	104.3	10.0	7.1
M01107	142.1	4.25	105.8	9.5	7.7
M01108	143.2	4.22	104.6	9.5	7.9
M01109	144.2	3.93	105.3	9.7	8.0
M01110	143.1	4.11	106.6	9.5	7.1
Number of animals	5	5	5	5	5
Mean	142.9	4.05	105.3	9.6	7.6
SD	0.9	0.21	0.9	0.2	0.4

Appendix 27-2. Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M03306	84.2	26.3	158.6
M03307	73.4	25.9	158.5
M03308	96.0	29.3	139.7
M03309	80.0	29.7	194.7
M03310	97.3	34.7	157.2
Number of animals	5	5	5
Mean	86.2	29.2	161.7
SD	10.3	3.5	20.1
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 27-2. (Continued) Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M03306	5.67	2.45	43.2	23.6	9.1	17.6	6.5	0.76
M03307	5.55	2.49	44.8	27.9	7.5	14.5	5.3	0.81
M03308	5.45	2.37	43.4	25.6	8.8	17.4	4.8	0.77
M03309	5.70	2.71	47.6	20.7	9.0	17.5	5.2	0.91
M03310	5.50	2.60	47.2	18.3	8.9	20.1	5.5	0.89
Number of animals	5	5	5	5	5	5	5	5
Mean	5.57	2.52	45.2	23.2	8.7	17.4	5.5	0.83
SD	0.11	0.13	2.1	3.8	0.7	2.0	0.6	0.07
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 27-2. (Continued) Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg						
Animal No.	T-Bil	UN	CRE	Glu	T-Cho	TG
	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
M03306	0.12	11.5	0.40	143.6	72.6	54.7
M03307	0.10	13.0	0.38	134.3	48.9	36.4
M03308	0.10	15.3	0.39	131.0	76.1	51.1
M03309	0.12	11.8	0.38	122.9	83.0	78.3
M03310	0.11	13.3	0.35	114.1	75.8	44.2
Number of animals	5	5	5	5	5	5
Mean	0.11	13.0	0.38	129.2	71.3	52.9
SD	0.01	1.5	0.02	11.2	13.1	15.8
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 27-2. (Continued) Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M03306	142.1	3.68	104.2	9.9	7.9
M03307	142.6	3.80	104.4	9.3	8.1
M03308	142.2	4.31	104.1	9.6	8.0
M03309	143.0	3.93	108.9	10.1	7.0
M03310	143.4	4.23	107.2	9.8	7.2
Number of animals	5	5	5	5	5
Mean	142.7	3.99	105.8	9.7	7.6
SD	0.5	0.27	2.2	0.3	0.5
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 27-3. Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
M04406	93.6	32.5	191.6
M04407	99.5	35.4	125.4
M04408	83.7	29.1	204.8
M04409	92.7	31.4	150.0
M04410	95.4	29.8	240.5
Number of animals	5	5	5
Mean	93.0	31.6	182.5
SD	5.8	2.5	45.4
Significance	NS	NS	NS
Statistical method	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 27-3. (Continued) Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
M04406	5.58	2.80	50.1	20.4	7.8	17.3	4.4	1.00
M04407	5.38	2.40	44.7	27.8	8.0	16.0	3.5	0.81
M04408	5.79	2.57	44.4	20.8	9.0	19.5	6.3	0.80
M04409	5.53	2.74	49.5	20.4	9.0	16.9	4.2	0.98
M04410	5.97	2.84	47.6	20.9	7.8	18.2	5.5	0.91
Number of animals	5	5	5	5	5	5	5	5
Mean	5.65	2.67	47.3	22.1	8.3	17.6	4.8	0.90
SD	0.23	0.18	2.6	3.2	0.6	1.3	1.1	0.09
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 27-3. (Continued) Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg						
Animal No.	T-Bil	UN	CRE	Glu	T-Cho	TG
	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
M04406	0.13	11.5	0.35	144.6	63.1	53.8
M04407	0.12	12.6 a)	0.37	112.0	50.2	79.3
M04408	0.11	14.6	0.38	140.1	70.6	70.2
M04409	0.14	13.5	0.34	118.3	45.8	49.7
M04410	0.14	11.9	0.37	121.2	47.7	66.5
Number of animals	5	5	5	5	5	5
Mean	0.13	12.8	0.36	127.2	55.5	63.9
SD	0.01	1.3	0.02	14.3	10.8	12.1
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

a): Obtained in the 2nd measurement; the value obtained in the 1st measurement was below the lower limit of quantification.

The value obtained in the 2nd measurement was confirmed to be correct in the 3rd measurement.

Appendix 27-3. (Continued) Individual blood chemical findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
M04406	140.7	4.19	103.3	9.5	7.7
M04407	143.8	4.42	106.1	9.8	7.9
M04408	141.5	4.35	104.3	9.6	8.5
M04409	143.4	3.96	106.1	9.9	7.2
M04410	143.6	4.30	106.7	9.9	7.4
Number of animals	5	5	5	5	5
Mean	142.6	4.24	105.3	9.7	7.7
SD	1.4	0.18	1.4	0.2	0.5
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 28-1. Individual blood chemical findings in female rats (recovery period)

Control group			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F01156	72.1	22.6	96.2
F01157	71.6	20.3	56.5
F01158	86.7	24.8	71.4
F01159	61.7	25.0	51.1
F01160	98.6	24.0	142.3
Number of animals	5	5	5
Mean	78.1	23.3	83.5
SD	14.5	1.9	37.2

(Continued)

Appendix 28-1. (Continued) Individual blood chemical findings in female rats (recovery period)

Control group								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F01156	5.52	2.89	52.4	17.2	8.8	14.4	7.2	1.10
F01157	5.72	2.61	45.7	19.5	9.9	16.6	8.3	0.84
F01158	6.28	3.06	48.7	19.9	7.6	16.6	7.2	0.95
F01159	6.35	3.37	53.0	20.6	7.0	14.2	5.2	1.13
F01160	5.92	3.16	53.3	16.9	8.1	15.2	6.5	1.14
Number of animals	5	5	5	5	5	5	5	5
Mean	5.96	3.02	50.6	18.8	8.3	15.4	6.9	1.03
SD	0.36	0.29	3.3	1.7	1.1	1.2	1.1	0.13

(Continued)

Appendix 28-1. (Continued) Individual blood chemical findings in female rats (recovery period)

Control group						
Animal No.	T-Bil mg/dL	UN mg/dL	CRE mg/dL	Glu mg/dL	T-Cho mg/dL	TG mg/dL
F01156	0.12	9.3	0.39	124.6	81.3	34.4
F01157	0.12	14.3	0.42	114.8	54.6	31.7
F01158	0.14	11.4	0.36	112.9	57.7	22.6
F01159	0.12	14.9	0.39	110.8	84.2	20.5
F01160	0.12	13.5	0.38	124.0	61.8	13.3
Number of animals	5	5	5	5	5	5
Mean	0.12	12.7	0.39	117.4	67.9	24.5
SD	0.01	2.3	0.02	6.4	13.8	8.6

(Continued)

Appendix 28-1. (Continued) Individual blood chemical findings in female rats (recovery period)

Control group					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F01156	143.9	3.85	107.0	9.7	4.8
F01157	144.9	3.90	108.4	9.5	6.1
F01158	143.0	4.04	106.6	10.2	5.8
F01159	143.6	3.86	106.0	10.2	6.0
F01160	144.9	4.09	108.2	10.2	8.5
Number of animals	5	5	5	5	5
Mean	144.1	3.95	107.2	10.0	6.2
SD	0.8	0.11	1.0	0.3	1.4

Appendix 28-2. Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F03356	81.8	20.2	84.4
F03357	87.7	22.9	98.5
F03358	89.2	22.8	55.7
F03359	64.0	20.4	105.4
F03360	83.7	23.2	76.0
Number of animals	5	5	5
Mean	81.3	21.9	84.0
SD	10.1	1.5	19.6
Significance	NS	NS	NS
Statistical method	DU	DU	STL

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 28-2. (Continued) Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F03356	5.88	2.95	50.2	16.1	8.9	16.4	8.4	1.01
F03357	5.60	2.76	49.3	17.9	8.0	17.7	7.1	0.97
F03358	5.75	3.06	53.3	18.1	7.4	16.0	5.2	1.14
F03359	6.22	3.25	52.3	21.9	8.6	13.5	3.7	1.10
F03360	5.96	3.26	54.7	17.3	8.8	14.9	4.3	1.21
Number of animals	5	5	5	5	5	5	5	5
Mean	5.88	3.06	52.0	18.3	8.3	15.7	5.7	1.09
SD	0.23	0.21	2.2	2.2	0.6	1.6	2.0	0.10
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 28-2. (Continued) Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg						
Animal No.	T-Bil	UN	CRE	Glu	T-Cho	TG
	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
F03356	0.10	12.0	0.41	112.2	63.1	16.0
F03357	0.10	13.4	0.40	112.0	44.1	12.2
F03358	0.17	13.6	0.41	134.4	64.3	21.9
F03359	0.13	10.1	0.34	128.7	68.3	24.8
F03360	0.12	10.7	0.36	123.2	56.2	23.9
Number of animals	5	5	5	5	5	5
Mean	0.12	12.0	0.38	122.1	59.2	19.8
SD	0.03	1.6	0.03	10.0	9.5	5.4
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 28-2. (Continued) Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F03356	143.1	3.98	108.2	9.6	5.8
F03357	143.2	4.19	108.4	9.6	6.9
F03358	141.6	3.95	106.4	10.2	7.0
F03359	144.0	3.67	106.5	10.4	6.5
F03360	144.2	4.52	109.3	9.9	7.8
Number of animals	5	5	5	5	5
Mean	143.2	4.06	107.8	9.9	6.8
SD	1.0	0.32	1.3	0.4	0.7
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 28-3. Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg			
Animal No.	AST	ALT	ALP
	U/L	U/L	U/L
F04456	64.9	21.5	77.0
F04457	77.9	22.1	62.0
F04458	65.6	20.7	77.4
F04459	91.7	24.1	80.9
F04460	67.7	21.0	79.8
Number of animals	5	5	5
Mean	73.6	21.9	75.4
SD	11.4	1.3	7.7
Significance	NS	NS	NS
Statistical method	DU	DU	STL

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 28-3. (Continued) Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	TP	Alb	alb	α_1 -glb	α_2 -glb	β -glb	γ -glb	A/G
	g/dL	g/dL	%	%	%	%	%	
F04456	5.69	2.87	50.5	19.7	8.5	14.0	7.3	1.02
F04457	6.31	2.96	46.9	20.6	7.7	18.1	6.7	0.88
F04458	5.94	3.20	53.8	19.1	7.7	14.8	4.6	1.16
F04459	6.46	3.30	51.1	20.5	6.7	15.5	6.2	1.05
F04460	5.78	3.02	52.2	18.7	8.9	15.4	4.8	1.09
Number of animals	5	5	5	5	5	5	5	5
Mean	6.04	3.07	50.9	19.7	7.9	15.6	5.9	1.04
SD	0.34	0.18	2.6	0.8	0.8	1.5	1.2	0.10
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 28-3. (Continued) Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg						
Animal No.	T-Bil	UN	CRE	Glu	T-Cho	TG
	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
F04456	0.12	16.6	0.40	116.5	62.5	16.0
F04457	0.11	14.0	0.39	128.8	78.5	11.0
F04458	0.15	9.7	0.40	141.9	40.3	24.3
F04459	0.14	14.6	0.37	100.5	60.3	25.4
F04460	0.13	13.4	0.37	123.5	59.7	25.9
Number of animals	5	5	5	5	5	5
Mean	0.13	13.7	0.39	122.2	60.3	20.5
SD	0.02	2.5	0.02	15.3	13.6	6.7
Significance	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

(Continued)

DU: Analysis by Dunnett's test.

Appendix 28-3. (Continued) Individual blood chemical findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg					
Animal No.	Na	K	Cl	Ca	IP
	mEq/L	mEq/L	mEq/L	mg/dL	mg/dL
F04456	142.5	3.77	106.1	9.7	6.3
F04457	141.9	4.20	108.3	9.8	6.9
F04458	143.2	3.90	107.2	10.3	7.6
F04459	143.7	3.97	106.7	10.2	7.4
F04460	142.5	3.73	105.6	10.0	6.9
Number of animals	5	5	5	5	5
Mean	142.8	3.91	106.8	10.0	7.0
SD	0.7	0.19	1.0	0.3	0.5
Significance	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 29-1. Individual necropsy findings in male rats (administration period)

Control group		
Animal No.		Finding
M01101	All organs and tissues	Normal
M01102	All organs and tissues	Normal
M01103	All organs and tissues	Normal
M01104	All organs and tissues	Normal
M01105	All organs and tissues	Normal

Appendix 29-2. Individual necropsy findings in male rats (administration period)

Ethyl propionate group at 100 mg/kg		
Animal No.		Finding
M02201	All organs and tissues	Normal
M02202	All organs and tissues	Normal
M02203	All organs and tissues	Normal
M02204	All organs and tissues	Normal
M02205	All organs and tissues	Normal

Appendix 29-3. Individual necropsy findings in male rats (administration period)

Ethyl propionate group at 300 mg/kg

Animal No.	Finding	
M03301	All organs and tissues	Normal
M03302	All organs and tissues	Normal
M03303	All organs and tissues	Normal
M03304	All organs and tissues	Normal
M03305	All organs and tissues	Normal

Appendix 29-4. Individual necropsy findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg

Animal No.	Finding	
M04401	All organs and tissues	Normal
M04402	All organs and tissues	Normal
M04403	All organs and tissues	Normal
M04404	Testis	Small in size, bilateral
	Epididymis	Small in size, bilateral
	Other organs and tissues	Normal
M04405	All organs and tissues	Normal

Appendix 30-1. Individual necropsy findings in female rats (administration period)

Control group			
Animal No.		Finding	Estrous cycle
F01151	All organs and tissues	Normal	P
F01152	All organs and tissues	Normal	P
F01153	All organs and tissues	Normal	E
F01154	All organs and tissues	Normal	M
F01155	All organs and tissues	Normal	P

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 30-2. Individual necropsy findings in female rats (administration period)

Ethyl propionate group at 100 mg/kg			
Animal No.		Finding	Estrous cycle
F02251	All organs and tissues	Normal	M
F02252	All organs and tissues	Normal	D
F02253	All organs and tissues	Normal	D
F02254	All organs and tissues	Normal	E
F02255	All organs and tissues	Normal	M

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 30-3. Individual necropsy findings in female rats (administration period)

Ethyl propionate group at 300 mg/kg

Animal No.		Finding	Estrous cycle
F03351	All organs and tissues	Normal	P
F03352	All organs and tissues	Normal	P
F03353	All organs and tissues	Normal	M
F03354	All organs and tissues	Normal	E
F03355	All organs and tissues	Normal	E

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 30-4. Individual necropsy findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg

Animal No.		Finding	Estrous cycle
F04451	All organs and tissues	Normal	D
F04452	All organs and tissues	Normal	E
F04453	All organs and tissues	Normal	E
F04454	All organs and tissues	Normal	E
F04455	All organs and tissues	Normal	E

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 31-1. Individual necropsy findings in male rats (recovery period)

Control group		
Animal No.		Finding
M01106	All organs and tissues	Normal
M01107	All organs and tissues	Normal
M01108	All organs and tissues	Normal
M01109	All organs and tissues	Normal
M01110	All organs and tissues	Normal

Appendix 31-2. Individual necropsy findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg		
Animal No.		Finding
M03306	Testis	Small in size, bilateral
	Epididymis	Small in size, bilateral
	Other organs and tissues	Normal
M03307	All organs and tissues	Normal
M03308	All organs and tissues	Normal
M03309	All organs and tissues	Normal
M03310	All organs and tissues	Normal

Appendix 31-3. Individual necropsy findings in male rats (recovery period)

Ethyl propionate group at 1000 mg/kg		
Animal No.		Finding
M04406	All organs and tissues	Normal
M04407	All organs and tissues	Normal
M04408	All organs and tissues	Normal
M04409	All organs and tissues	Normal
M04410	All organs and tissues	Normal

Appendix 32-1. Individual necropsy findings in female rats (recovery period)

Control group			
Animal No.		Finding	Estrous cycle
F01156	All organs and tissues	Normal	E
F01157	All organs and tissues	Normal	P
F01158	All organs and tissues	Normal	P
F01159	All organs and tissues	Normal	D
F01160	All organs and tissues	Normal	D

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 32-2. Individual necropsy findings in female rats (recovery period)

Ethyl propionate group at 300 mg/kg			
Animal No.		Finding	Estrous cycle
F03356	All organs and tissues	Normal	E
F03357	All organs and tissues	Normal	D
F03358	All organs and tissues	Normal	E
F03359	All organs and tissues	Normal	E
F03360	All organs and tissues	Normal	E

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 32-3. Individual necropsy findings in female rats (recovery period)

Ethyl propionate group at 1000 mg/kg

Animal No.		Finding	Estrous cycle
F04456	All organs and tissues	Normal	D
F04457	All organs and tissues	Normal	P
F04458	All organs and tissues	Normal	E
F04459	All organs and tissues	Normal	D
F04460	All organs and tissues	Normal	D

Estrous cycle; P: proestrus, E: estrus, M: metaestrus, D: diestrus.

Appendix 33-1. Individual organ weights of male rats (administration period)

Control group													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M01101	337	1.96	0.58	19.2	5.7	0.76	0.23	1.29	0.38	10.04	2.98	0.54	0.16
M01102	363	1.97	0.54	21.2	5.8	0.47	0.13	1.11	0.31	11.08	3.05	0.64	0.18
M01103	299	1.93	0.65	17.7	5.9	0.53	0.18	1.19	0.40	8.94	2.99	0.66	0.22
M01104	363	2.09	0.58	17.5	4.8	0.49	0.13	1.49	0.41	10.22	2.82	0.69	0.19
M01105	329	2.00	0.61	19.8	6.0	0.64	0.19	1.26	0.38	9.93	3.02	0.43	0.13
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	338	1.99	0.59	19.1	5.6	0.58	0.17	1.27	0.38	10.04	2.97	0.59	0.18
SD	27	0.06	0.04	1.5	0.5	0.12	0.04	0.14	0.04	0.76	0.09	0.11	0.03

(Continued)

Appendix 33-1. (Continued) Individual organ weights of male rats (administration period)

Control group												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M01101	2.68	0.80	57.1	16.9	3.24	0.96	0.75	0.22	1.37	0.41	0.29	0.09
M01102	2.67	0.74	59.9	16.5	2.97	0.82	0.72	0.20	1.53	0.42	0.40	0.11
M01103	2.47	0.83	49.9	16.7	2.98	1.00	0.74	0.25	1.50	0.50	0.52	0.17
M01104	3.04	0.84	58.9	16.2	3.07	0.85	0.76	0.21	1.68	0.46	0.55	0.15
M01105	2.41	0.73	51.5	15.7	3.11	0.95	0.74	0.22	1.25	0.38	0.27	0.08
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.65	0.79	55.5	16.4	3.07	0.92	0.74	0.22	1.47	0.43	0.41	0.12
SD	0.25	0.05	4.5	0.5	0.11	0.08	0.01	0.02	0.16	0.05	0.13	0.04

Appendix 33-2. Individual organ weights of male rats (administration period)

Ethyl propionate group at 100 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M02201	360	1.94	0.54	20.8	5.8	0.52	0.14	1.18	0.33	11.37	3.16	0.67	0.19
M02202	317	2.12	0.67	20.9	6.6	0.50	0.16	1.19	0.38	8.70	2.74	0.58	0.18
M02203	311	1.98	0.64	16.4	5.3	0.54	0.17	1.14	0.37	8.53	2.74	0.73	0.23
M02204	378	1.98	0.52	19.3	5.1	0.94	0.25	1.32	0.35	10.33	2.73	0.88	0.23
M02205	313	1.91	0.61	29.8	9.5	0.40	0.13	1.09	0.35	8.78	2.81	0.65	0.21
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	336	1.99	0.60	21.4	6.5	0.58	0.17	1.18	0.36	9.54	2.84	0.70	0.21
SD	31	0.08	0.06	5.0	1.8	0.21	0.05	0.09	0.02	1.25	0.18	0.11	0.02
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 33-2. (Continued) Individual organ weights of male rats (administration period)

Ethyl propionate group at 100 mg/kg												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M02201	2.64	0.73	55.5	15.4	3.07	0.85	0.98	0.27	1.70	0.47	0.51	0.14
M02202	2.67	0.84	47.3	14.9	2.93	0.92	0.80	0.25	1.38	0.44	0.44	0.14
M02203	2.72	0.87	45.1	14.5	3.10	1.00	0.69	0.22	1.42	0.46	0.40	0.13
M02204	2.69	0.71	40.3	10.7	3.06	0.81	0.74	0.20	1.66	0.44	0.44	0.12
M02205	2.56	0.82	44.3	14.2	3.09	0.99	0.72	0.23	1.03	0.33	0.36	0.12
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.66	0.79	46.5	13.9	3.05	0.91	0.79	0.23	1.44	0.43	0.43	0.13
SD	0.06	0.07	5.6	1.9	0.07	0.08	0.12	0.03	0.27	0.06	0.06	0.01
Significance	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	STL	STL	DU	DU	DU	DU	STL

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 33-3. Individual organ weights of male rats (administration period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M03301	318	1.86	0.58	18.3	5.8	0.53	0.17	1.11	0.35	9.76	3.07	0.48	0.15
M03302	344	2.02	0.59	25.2	7.3	0.63	0.18	1.33	0.39	10.12	2.94	0.58	0.17
M03303	317	1.93	0.61	21.5	6.8	0.56	0.18	1.08	0.34	9.03	2.85	0.68	0.21
M03304	357	2.01	0.56	23.6	6.6	0.55	0.15	1.17	0.33	9.95	2.79	0.64	0.18
M03305	283	1.98	0.70	17.6	6.2	0.43	0.15	1.15	0.41	7.84	2.77	0.40	0.14
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	324	1.96	0.61	21.2	6.5	0.54	0.17	1.17	0.36	9.34	2.88	0.56	0.17
SD	29	0.07	0.05	3.3	0.6	0.07	0.02	0.10	0.03	0.94	0.12	0.12	0.03
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 33-3. (Continued) Individual organ weights of male rats (administration period)

Ethyl propionate group at 300 mg/kg												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M03301	2.28	0.72	48.8	15.3	2.94	0.92	0.71	0.22	1.03	0.32	0.39	0.12
M03302	2.59	0.75	40.1	11.7	3.15	0.92	0.85	0.25	1.42	0.41	0.35	0.10
M03303	2.46	0.78	46.9	14.8	3.11	0.98	1.08	0.34	1.09	0.34	0.28	0.09
M03304	2.73	0.76	49.1	13.8	3.11	0.87	0.81	0.23	1.74	0.49	0.36	0.10
M03305	2.42	0.86	49.5	17.5	3.09	1.09	0.71	0.25	1.08	0.38	0.31	0.11
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.50	0.77	46.9	14.6	3.08	0.96	0.83	0.26	1.27	0.39	0.34	0.10
SD	0.17	0.05	3.9	2.1	0.08	0.08	0.15	0.05	0.30	0.07	0.04	0.01
Significance	NS	NS	*	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	STL	STL	DU	DU	DU	DU	STL

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 33-4. Individual organ weights of male rats (administration period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M04401	330	1.80	0.55	21.1	6.4	0.66	0.20	1.23	0.37	9.83	2.98	0.66	0.20
M04402	348	2.02	0.58	20.3	5.8	0.53	0.15	1.33	0.38	9.20	2.64	0.57	0.16
M04403	300	1.93	0.64	17.2	5.7	0.50	0.17	1.21	0.40	8.35	2.78	0.57	0.19
M04404	315	1.99	0.63	21.1	6.7	0.80	0.25	1.08	0.34	8.89	2.82	0.63	0.20
M04405	392	2.10	0.54	21.4	5.5	0.51	0.13	1.29	0.33	11.16	2.85	0.66	0.17
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	337	1.97	0.59	20.2	6.0	0.60	0.18	1.23	0.36	9.49	2.81	0.62	0.18
SD	36	0.11	0.05	1.7	0.5	0.13	0.05	0.10	0.03	1.08	0.12	0.05	0.02
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 33-4. (Continued) Individual organ weights of male rats (administration period)

Ethyl propionate group at 1000 mg/kg												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M04401	2.68	0.81	59.5	18.0	3.29	1.00	0.75	0.23	1.64	0.50	0.41	0.12
M04402	2.63	0.76	52.6	15.1	2.71	0.78	0.71	0.20	1.26	0.36	0.61	0.18
M04403	2.41	0.80	45.8	15.3	3.08	1.03	0.80	0.27	1.46	0.49	0.34	0.11
M04404	2.40	0.76	51.9	16.5	0.66	0.21	0.37	0.12	1.13	0.36	0.39	0.12
M04405	2.78	0.71	53.9	13.8	4.04	1.03	0.87	0.22	1.86	0.47	0.34	0.09
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.58	0.77	52.7	15.7	2.76	0.81	0.70	0.21	1.47	0.44	0.42	0.12
SD	0.17	0.04	4.9	1.6	1.27	0.35	0.19	0.06	0.29	0.07	0.11	0.03
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	STL	STL	DU	DU	DU	DU	STL

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 34-1. Individual organ weights of female rats (administration period)

Control group													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F01151	239	1.83	0.77	19.4	8.1	0.62	0.26	0.80	0.33	9.36	3.92	0.60	0.25
F01152	218	1.84	0.84	18.2	8.3	0.43	0.20	0.76	0.35	6.14	2.82	0.53	0.24
F01153	241	1.84	0.76	18.8	7.8	0.67	0.28	0.85	0.35	7.52	3.12	0.46	0.19
F01154	199	1.85	0.93	18.5	9.3	0.37	0.19	0.63	0.32	5.28	2.65	0.49	0.25
F01155	248	1.92	0.77	21.2	8.5	0.48	0.19	0.90	0.36	7.36	2.97	0.58	0.23
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	229	1.86	0.81	19.2	8.4	0.51	0.22	0.79	0.34	7.13	3.10	0.53	0.23
SD	20	0.04	0.07	1.2	0.6	0.13	0.04	0.10	0.02	1.55	0.49	0.06	0.02

(Continued)

Appendix 34-1. (Continued) Individual organ weights of female rats (administration period)

Control group								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F01151	1.95	0.82	66.3	27.7	73.0	30.5	0.76	0.32
F01152	1.77	0.81	57.8	26.5	108.5	49.8	0.83	0.38
F01153	1.76	0.73	72.9	30.2	90.8	37.7	0.48	0.20
F01154	1.50	0.75	71.5	35.9	61.9	31.1	0.36	0.18
F01155	1.92	0.77	63.2	25.5	84.5	34.1	0.74	0.30
Number of animals	5	5	5	5	5	5	5	5
Mean	1.78	0.78	66.3	29.2	83.7	36.6	0.63	0.28
SD	0.18	0.04	6.2	4.2	17.7	7.9	0.20	0.08

Appendix 34-2. Individual organ weights of female rats (administration period)

Ethyl propionate group at 100 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F02251	226	1.82	0.81	18.8	8.3	0.43	0.19	0.88	0.39	6.87	3.04	0.43	0.19
F02252	238	1.85	0.78	24.2	10.2	0.76	0.32	0.94	0.39	7.15	3.00	0.38	0.16
F02253	225	1.91	0.85	16.0	7.1	0.36	0.16	0.82	0.36	6.16	2.74	0.55	0.24
F02254	230	1.97	0.86	15.6	6.8	0.48	0.21	0.79	0.34	6.62	2.88	0.51	0.22
F02255	204	1.87	0.92	22.9	11.2	0.38	0.19	0.74	0.36	6.47	3.17	0.51	0.25
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	225	1.88	0.84	19.5	8.7	0.48	0.21	0.83	0.37	6.65	2.97	0.48	0.21
SD	13	0.06	0.05	3.9	1.9	0.16	0.06	0.08	0.02	0.38	0.16	0.07	0.04
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	STL	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 34-2. (Continued) Individual organ weights of female rats (administration period)

Ethyl propionate group at 100 mg/kg								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F02251	1.60	0.71	64.4	28.5	100.8	44.6	0.33	0.15
F02252	1.85	0.78	68.7	28.9	98.0	41.2	0.42	0.18
F02253	2.01	0.89	63.0	28.0	75.5	33.6	0.67	0.30
F02254	1.82	0.79	66.4	28.9	75.0	32.6	0.56	0.24
F02255	1.58	0.77	62.2	30.5	69.0	33.8	0.32	0.16
Number of animals	5	5	5	5	5	5	5	5
Mean	1.77	0.79	64.9	29.0	83.7	37.2	0.46	0.21
SD	0.18	0.06	2.6	0.9	14.6	5.4	0.15	0.06
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	STL	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 34-3. Individual organ weights of female rats (administration period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F03351	231	1.96	0.85	11.4	4.9	0.77	0.33	0.84	0.36	6.81	2.95	0.48	0.21
F03352	222	1.74	0.78	17.6	7.9	0.42	0.19	0.82	0.37	6.26	2.82	0.46	0.21
F03353	207	1.86	0.90	11.2	5.4	0.54	0.26	0.69	0.33	6.14	2.97	0.47	0.23
F03354	216	1.89	0.88	18.0	8.3	0.54	0.25	0.86	0.40	7.25	3.36	0.57	0.26
F03355	268	2.01	0.75	20.4	7.6	0.65	0.24	0.99	0.37	8.08	3.01	0.55	0.21
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	229	1.89	0.83	15.7	6.8	0.58	0.25	0.84	0.37	6.91	3.02	0.51	0.22
SD	24	0.10	0.06	4.2	1.6	0.13	0.05	0.11	0.03	0.79	0.20	0.05	0.02
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	STL	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 34-3. (Continued) Individual organ weights of female rats (administration period)

Ethyl propionate group at 300 mg/kg								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F03351	1.70	0.74	63.3	27.4	95.0	41.1	0.60	0.26
F03352	2.04	0.92	63.5	28.6	81.3	36.6	0.70	0.32
F03353	1.65	0.80	57.0	27.5	82.3	39.8	0.35	0.17
F03354	1.75	0.81	72.2	33.4	69.8	32.3	0.49	0.23
F03355	1.96	0.73	84.5	31.5	102.4	38.2	0.57	0.21
Number of animals	5	5	5	5	5	5	5	5
Mean	1.82	0.80	68.1	29.7	86.2	37.6	0.54	0.24
SD	0.17	0.08	10.6	2.7	12.7	3.4	0.13	0.06
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	STL	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 34-4. Individual organ weights of female rats (administration period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F04451	204	1.86	0.91	22.5	11.0	0.44	0.22	0.76	0.37	6.26	3.07	0.51	0.25
F04452	277	1.85	0.67	18.6	6.7	0.54	0.19	0.95	0.34	8.33	3.01	0.49	0.18
F04453	225	1.79	0.80	14.6	6.5	0.63	0.28	0.87	0.39	7.19	3.20	0.38	0.17
F04454	218	1.75	0.80	12.3	5.6	0.58	0.27	0.88	0.40	6.72	3.08	0.37	0.17
F04455	232	1.92	0.83	17.3	7.5	0.45	0.19	0.81	0.35	6.91	2.98	0.48	0.21
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	231	1.83	0.80	17.1	7.5	0.53	0.23	0.85	0.37	7.08	3.07	0.45	0.20
SD	28	0.07	0.09	3.9	2.1	0.08	0.04	0.07	0.03	0.78	0.08	0.07	0.03
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	STL	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 34-4. (Continued) Individual organ weights of female rats (administration period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F04451	1.84	0.90	72.4	35.5	108.5	53.2	0.52	0.25
F04452	2.01	0.73	68.9	24.9	79.3	28.6	0.50	0.18
F04453	1.80	0.80	59.7	26.5	76.6	34.0	0.43	0.19
F04454	1.80	0.83	59.9	27.5	67.2	30.8	0.56	0.26
F04455	1.88	0.81	45.7	19.7	65.7	28.3	0.41	0.18
Number of animals	5	5	5	5	5	5	5	5
Mean	1.87	0.81	61.3	26.8	79.5	35.0	0.48	0.21
SD	0.09	0.06	10.4	5.7	17.3	10.4	0.06	0.04
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	STL	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 35-1. Individual organ weights of male rats (recovery period)

Control group													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M01106	435	2.07	0.48	18.7	4.3	0.53	0.12	1.41	0.32	12.76	2.93	0.66	0.15
M01107	428	2.16	0.50	28.3	6.6	0.69	0.16	1.57	0.37	12.11	2.83	0.69	0.16
M01108	456	2.00	0.44	18.3	4.0	0.58	0.13	1.54	0.34	13.01	2.85	0.76	0.17
M01109	383	2.08	0.54	13.9	3.6	0.40	0.10	1.41	0.37	10.91	2.85	0.62	0.16
M01110	444	2.06	0.46	18.5	4.2	0.54	0.12	1.36	0.31	11.99	2.70	0.78	0.18
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	429	2.07	0.48	19.5	4.5	0.55	0.13	1.46	0.34	12.16	2.83	0.70	0.16
SD	28	0.06	0.04	5.3	1.2	0.10	0.02	0.09	0.03	0.82	0.08	0.07	0.01

(Continued)

Appendix 35-1. (Continued) Individual organ weights of male rats (recovery period)

Control group												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M01106	2.59	0.60	64.2	14.8	2.68	0.62	1.01	0.23	1.61	0.37	0.53	0.12
M01107	3.08	0.72	57.6	13.5	3.23	0.75	1.21	0.28	2.06	0.48	0.57	0.13
M01108	2.94	0.64	43.4	9.5	3.05	0.67	1.05	0.23	2.31	0.51	0.58	0.13
M01109	2.68	0.70	65.3	17.0	3.16	0.83	1.12	0.29	1.70	0.44	0.70	0.18
M01110	2.88	0.65	61.9	13.9	2.88	0.65	1.23	0.28	1.99	0.45	0.48	0.11
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.83	0.66	58.5	13.7	3.00	0.70	1.12	0.26	1.93	0.45	0.57	0.13
SD	0.20	0.05	8.9	2.7	0.22	0.09	0.10	0.03	0.28	0.05	0.08	0.03

Appendix 35-2. Individual organ weights of male rats (recovery period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M03306	485	2.15	0.44	28.6	5.9	0.66	0.14	1.47	0.30	14.76	3.04	0.96	0.20
M03307	485	2.09	0.43	29.4	6.1	0.47	0.10	1.44	0.30	12.79	2.64	0.70	0.14
M03308	428	2.03	0.47	16.8	3.9	0.64	0.15	1.38	0.32	11.94	2.79	0.80	0.19
M03309	440	2.01	0.46	19.3	4.4	0.41	0.09	1.54	0.35	11.73	2.67	0.70	0.16
M03310	440	2.14	0.49	27.3	6.2	0.35	0.08	1.43	0.33	12.36	2.81	0.77	0.18
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	456	2.08	0.46	24.3	5.3	0.51	0.11	1.45	0.32	12.72	2.79	0.79	0.17
SD	27	0.06	0.02	5.8	1.1	0.14	0.03	0.06	0.02	1.21	0.16	0.11	0.02
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 35-2. (Continued) Individual organ weights of male rats (recovery period)

Ethyl propionate group at 300 mg/kg												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M03306	3.10	0.64	66.5	13.7	1.75	0.36	0.78	0.16	1.73	0.36	0.70	0.14
M03307	3.01	0.62	63.1	13.0	3.13	0.65	1.10	0.23	1.59	0.33	0.53	0.11
M03308	2.72	0.64	44.6	10.4	3.27	0.76	1.02	0.24	1.72	0.40	0.49	0.11
M03309	2.68	0.61	46.9	10.7	3.50	0.80	1.16	0.26	1.94	0.44	0.52	0.12
M03310	3.15	0.72	48.8	11.1	3.29	0.75	1.08	0.25	2.36	0.54	0.49	0.11
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.93	0.65	54.0	11.8	2.99	0.66	1.03	0.23	1.87	0.41	0.55	0.12
SD	0.22	0.04	10.1	1.5	0.70	0.18	0.15	0.04	0.30	0.08	0.09	0.01
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	STL	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 35-3. Individual organ weights of male rats (recovery period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M04406	444	2.20	0.50	17.9	4.0	0.45	0.10	1.40	0.32	12.91	2.91	0.65	0.15
M04407	449	2.19	0.49	21.5	4.8	0.49	0.11	1.38	0.31	12.55	2.80	0.58	0.13
M04408	394	2.07	0.53	19.5	4.9	0.51	0.13	1.37	0.35	11.86	3.01	0.73	0.19
M04409	385	1.97	0.51	17.2	4.5	0.49	0.13	1.28	0.33	10.10	2.62	0.80	0.21
M04410	449	1.85	0.41	24.9	5.5	0.38	0.08	1.25	0.28	11.23	2.50	0.72	0.16
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	424	2.06	0.49	20.2	4.7	0.46	0.11	1.34	0.32	11.73	2.77	0.70	0.17
SD	32	0.15	0.05	3.1	0.6	0.05	0.02	0.07	0.03	1.12	0.21	0.08	0.03
Significance	NS	NS	NS	NS	NS	NS	NS	*	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

Significantly different from the control group (*: $p < 0.05$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 35-3. (Continued) Individual organ weights of male rats (recovery period)

Ethyl propionate group at 1000 mg/kg												
Animal No.	Kidneys		Adrenals		Testes		Epididymides		Seminal vesicles		Prostate	
	(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
M04406	3.02	0.68	80.5	18.1	3.14	0.71	1.02	0.23	2.20	0.50	0.43	0.10
M04407	2.95	0.66	67.8	15.1	3.19	0.71	1.10	0.24	2.29	0.51	0.61	0.14
M04408	3.01	0.76	64.3	16.3	3.11	0.79	1.15	0.29	1.89	0.48	0.41	0.10
M04409	2.85	0.74	59.7	15.5	2.98	0.77	1.18	0.31	2.14	0.56	0.63	0.16
M04410	2.75	0.61	42.7	9.5	3.31	0.74	0.99	0.22	1.64	0.37	0.44	0.10
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5
Mean	2.92	0.69	63.0	14.9	3.15	0.74	1.09	0.26	2.03	0.48	0.50	0.12
SD	0.11	0.06	13.7	3.2	0.12	0.04	0.08	0.04	0.26	0.07	0.11	0.03
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	STL	STL	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 36-1. Individual organ weights of female rats (recovery period)

Control group													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F01156	227	1.78	0.78	20.3	8.9	0.36	0.16	0.75	0.33	5.89	2.59	0.42	0.19
F01157	275	1.93	0.70	17.3	6.3	0.38	0.14	0.87	0.32	6.97	2.53	0.62	0.23
F01158	271	1.89	0.70	16.8	6.2	0.45	0.17	0.96	0.35	7.35	2.71	0.57	0.21
F01159	259	1.85	0.71	24.4	9.4	0.36	0.14	0.92	0.36	7.00	2.70	0.41	0.16
F01160	249	2.07	0.83	13.5	5.4	0.36	0.14	0.93	0.37	6.79	2.73	0.51	0.20
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	256	1.90	0.74	18.5	7.2	0.38	0.15	0.89	0.35	6.80	2.65	0.51	0.20
SD	19	0.11	0.06	4.1	1.8	0.04	0.01	0.08	0.02	0.55	0.09	0.09	0.03

(Continued)

Appendix 36-1. (Continued) Individual organ weights of female rats (recovery period)

Control group								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F01156	1.50	0.66	73.5	32.4	101.6	44.8	0.46	0.20
F01157	1.90	0.69	74.1	26.9	93.7	34.1	0.72	0.26
F01158	1.97	0.73	65.4	24.1	76.8	28.3	0.79	0.29
F01159	1.96	0.76	67.4	26.0	95.9	37.0	0.45	0.17
F01160	1.84	0.74	66.1	26.5	98.0	39.4	0.35	0.14
Number of animals	5	5	5	5	5	5	5	5
Mean	1.83	0.72	69.3	27.2	93.2	36.7	0.55	0.21
SD	0.19	0.04	4.2	3.1	9.6	6.1	0.19	0.06

Appendix 36-2. Individual organ weights of female rats (recovery period)

Ethyl propionate group at 300 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F03356	230	1.94	0.84	14.7	6.4	0.44	0.19	0.78	0.34	6.05	2.63	0.50	0.22
F03357	278	1.94	0.70	18.2	6.5	0.34	0.12	0.88	0.32	6.87	2.47	0.54	0.19
F03358	266	1.86	0.70	14.7	5.5	0.47	0.18	1.01	0.38	7.47	2.81	0.55	0.21
F03359	228	1.84	0.81	20.4	8.9	0.33	0.14	0.84	0.37	6.63	2.91	0.50	0.22
F03360	244	1.81	0.74	14.9	6.1	0.37	0.15	0.79	0.32	6.21	2.55	0.44	0.18
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	249	1.88	0.76	16.6	6.7	0.39	0.16	0.86	0.35	6.65	2.67	0.51	0.20
SD	22	0.06	0.06	2.6	1.3	0.06	0.03	0.09	0.03	0.56	0.18	0.04	0.02
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 36-2. (Continued) Individual organ weights of female rats (recovery period)

Ethyl propionate group at 300 mg/kg								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F03356	1.61	0.70	64.0	27.8	100.5	43.7	0.53	0.23
F03357	2.05	0.74	65.2	23.5	81.4	29.3	0.39	0.14
F03358	1.84	0.69	76.6	28.8	129.2	48.6	0.48	0.18
F03359	1.77	0.78	56.7	24.9	94.8	41.6	0.51	0.22
F03360	1.70	0.70	50.9	20.9	63.7	26.1	0.48	0.20
Number of animals	5	5	5	5	5	5	5	5
Mean	1.79	0.72	62.7	25.2	93.9	37.9	0.48	0.19
SD	0.17	0.04	9.7	3.2	24.3	9.7	0.05	0.04
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 36-3. Individual organ weights of female rats (recovery period)

Ethyl propionate group at 1000 mg/kg													
Animal No.	Body weight (g)	Brain		Thyroids		Thymus		Heart		Liver		Spleen	
		(g)	(g%)	(mg)	(mg%)	(g)	(g%)	(g)	(g%)	(g)	(g%)	(g)	(g%)
F04456	238	1.94	0.82	19.2	8.1	0.40	0.17	0.83	0.35	6.19	2.60	0.52	0.22
F04457	271	1.89	0.70	21.1	7.8	0.50	0.18	0.84	0.31	7.72	2.85	0.50	0.18
F04458	270	1.94	0.72	18.9	7.0	0.42	0.16	0.88	0.33	7.45	2.76	0.48	0.18
F04459	258	1.98	0.77	16.5	6.4	0.42	0.16	0.97	0.38	7.15	2.77	0.55	0.21
F04460	268	2.04	0.76	17.5	6.5	0.58	0.22	0.97	0.36	6.87	2.56	0.55	0.21
Number of animals	5	5	5	5	5	5	5	5	5	5	5	5	5
Mean	261	1.96	0.75	18.6	7.2	0.46	0.18	0.90	0.35	7.08	2.71	0.52	0.20
SD	14	0.06	0.05	1.8	0.8	0.08	0.02	0.07	0.03	0.59	0.12	0.03	0.02
Significance	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 36-3. (Continued) Individual organ weights of female rats (recovery period)

Ethyl propionate group at 1000 mg/kg								
Animal No.	Kidneys		Adrenals		Ovaries		Uterus	
	(g)	(g%)	(mg)	(mg%)	(mg)	(mg%)	(g)	(g%)
F04456	1.87	0.79	69.2	29.1	84.7	35.6	0.44	0.18
F04457	1.81	0.67	59.0	21.8	96.6	35.6	0.58	0.21
F04458	1.59	0.59	80.2	29.7	96.0	35.6	0.59	0.22
F04459	1.84	0.71	68.9	26.7	86.0	33.3	0.44	0.17
F04460	1.76	0.66	72.9	27.2	114.6	42.8	0.36	0.13
Number of animals	5	5	5	5	5	5	5	5
Mean	1.77	0.68	70.0	26.9	95.6	36.6	0.48	0.18
SD	0.11	0.07	7.7	3.1	12.0	3.6	0.10	0.04
Significance	NS	NS	NS	NS	NS	NS	NS	NS
Statistical method	DU	DU	DU	DU	DU	DU	DU	DU

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 37-1. Individual histopathological findings in male rats (administration period)

Control group		
Animal No.	Organ/Tissue	Finding
M01101	Prostate	Cellular infiltration, lymphoid cell: ±
	Other organs and tissues	No abnormality detected
M01102	Kidney	Cyst, left: ±
	Parathyroid	Missing
	Other organs and tissues	No abnormality detected
M01103	All organs and tissues	No abnormality detected
M01104	Jejunum	Mineralization, Peyer's patch: ±
	Kidney	Cyst, left: ±
	Eyeball	Retinal dysplasia, right: ±
	Other organs and tissues	No abnormality detected
M01105	All organs and tissues	No abnormality detected

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.

Examined the heart, lung, trachea, liver, pancreas, submandibular gland, stomach, duodenum, jejunum, ileum (including Peyer's patch), cecum, colon, rectum, thymus, spleen, mesenteric lymph node, axillary lymph node, kidney, urinary bladder, testis, epididymis, prostate, seminal vesicle, coagulation gland, skin, mammary gland, pituitary, adrenal, thyroid, parathyroid (except for M01102), cerebrum, cerebellum, pons, spinal cord (cervical, thoracic, and lumbar part), sciatic nerve, eyeball, Harderian gland, rectus femoris muscle, sternum (including bone marrow), and femur (including bone marrow).

Appendix 37-2. Individual histopathological findings in male rats (administration period)

Ethyl propionate group at 1000 mg/kg		
Animal No.	Organ/Tissue	Finding
M04401	Heart	Cellular infiltration, mononuclear cell, focal: ±
	Jejunum	Mineralization, Peyer's patch: ±
	Other organs and tissues	No abnormality detected
M04402	Jejunum	Mineralization, Peyer's patch: ±
	Prostate	Cellular infiltration, lymphoid cell: ±
	Pituitary	Cyst: ±
	Thyroid	Ectopic, thymic tissue: ±
	Ultimobranchial remnant: ±	
M04403	Other organs and tissues	No abnormality detected
	All organs and tissues	No abnormality detected
M04404	Testis	Degeneration/atrophy, seminiferous tubule, bilateral: 2+
	Epididymis	Decrease, sperm, bilateral: 3+
	Other organs and tissues	No abnormality detected
M04405	All organs and tissues	No abnormality detected

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.

Examined the heart, lung, trachea, liver, pancreas, submandibular gland, stomach, duodenum, jejunum, ileum (including Peyer's patch), cecum, colon, rectum, thymus, spleen, mesenteric lymph node, axillary lymph node, kidney, urinary bladder, testis, epididymis, prostate, seminal vesicle, coagulation gland, skin, mammary gland, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, pons, spinal cord (cervical, thoracic, and lumbar part), sciatic nerve, eyeball, Harderian gland, rectus femoris muscle, sternum (including bone marrow), and femur (including bone marrow).

Appendix 38-1. Individual histopathological findings in female rats (administration period)

Control group		
Animal No.	Organ/Tissue	Finding
F01151	Jejunum	Mineralization, Peyer's patch: ±
	Kidney	Cyst, left: ±
	Other organs and tissues	No abnormality detected
F01152	All organs and tissues	No abnormality detected
F01153	Pituitary	Cyst: ±
	Other organs and tissues	No abnormality detected
F01154	Jejunum	Mineralization, Peyer's patch: ±
	Other organs and tissues	No abnormality detected
F01155	Kidney	Infarct, left: ±
	Other organs and tissues	No abnormality detected

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.

Examined the heart, lung, trachea, liver, pancreas, submandibular gland, stomach, duodenum, jejunum, ileum (including Peyer's patch), cecum, colon, rectum, thymus, spleen, mesenteric lymph node, axillary lymph node, kidney, urinary bladder, ovary, uterus (including cervix of uterus), vagina, skin, mammary gland, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, pons, spinal cord (cervical, thoracic, and lumbar part), sciatic nerve, eyeball, Harderian gland, rectus femoris muscle, sternum (including bone marrow), and femur (including bone marrow).

Appendix 38-2. Individual histopathological findings in female rats (administration period)

Ethyl propionate group at 1000 mg/kg

Animal No.	Organ/Tissue	Finding
F04451	All organs and tissues	No abnormality detected
F04452	Eyeball	Retinal dysplasia, right: ±
	Other organs and tissues	No abnormality detected
F04453	Thyroid	Ultimobranchial remnant: ±
	Other organs and tissues	No abnormality detected
F04454	Jejunum	Mineralization, Peyer's patch: ±
	Other organs and tissues	No abnormality detected
F04455	All organs and tissues	No abnormality detected

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.

Examined the heart, lung, trachea, liver, pancreas, submandibular gland, stomach, duodenum, jejunum, ileum (including Peyer's patch), cecum, colon, rectum, thymus, spleen, mesenteric lymph node, axillary lymph node, kidney, urinary bladder, ovary, uterus (including cervix of uterus), vagina, skin, mammary gland, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, pons, spinal cord (cervical, thoracic, and lumbar part), sciatic nerve, eyeball, Harderian gland, rectus femoris muscle, sternum (including bone marrow), and femur (including bone marrow).

Appendix 39-1. Individual histopathological findings in male rats (recovery period)

Control group		
Animal No.	Organ/Tissue	Finding
M01106	Testis	No abnormality detected
	Epididymis	No abnormality detected

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.

Appendix 39-2. Individual histopathological findings in male rats (recovery period)

Ethyl propionate group at 300 mg/kg		
Animal No.	Organ/Tissue	Finding
M03306	Testis	Degeneration/atrophy, seminiferous tubule, bilateral: +
	Epididymis	Decrease, sperm, bilateral: 3+

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.

Attachment 1.

検査成績書

2023年10月31日

(株)日本バイオリサーチセンター 御中

プロピオン酸エチル

規格/等級		
Lot No.		
数量	500ml	
検査項目	検査成績	規格値
外観	無色透明の液体	無色透明の液体
密度(20°C)	0.890g/ml	0.889~0.894g/ml
屈折率 n ₂₀ /D	1.384	1.382~1.386
水分	0.0%	1.0%以下
酸(CH ₃ CH ₂ COOHとして)	0.05%以下	0.05%以下
含量(キャピラリーカラムGC)	99.9%	97.0%以上
検査年月日	2023/07/04	

判定	合格	検査責任者	
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(1/1)

成績書発行番号

9456857

Attachment 2.

検査成績書

(株) 日本バイオリサーチセンター 御中

2023年10月27日
富士フイルム和光純薬株式会社

Code No.032-17016

コーン油



規格/等級	生化学用	
Lot No.	WTF5137	
数量	500ml	
検査項目	検査成績	規格値
外観	黄色澄明の液体	無色～黄褐色、澄明の液体
密度(20°C)	0.919g/ml	0.912～0.920g/ml
酸価	0.1	0.2以下
よう素価	123	103～130
検査年月日	2022/11/18	

判定	合格	検査責任者	
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(1/1)

成績書発行番号

9455124

Attachment 3-1.

プロピオン酸エチル測定法

1. 標準物質（被験物質）

名称 : プロピオン酸エチル
 英語名称 : Ethyl propionate
 CAS No. : 105-37-3
 ロット番号 : ██████████ (Attachment 1)
 性状 : 無色澄明の液体
 含量 : 99.9% (規格値 : 97.0%以上)
 分子量 : 102.13
 保管条件 : 室温 (1.0~30.0°C), 遮光
 保管場所 : 試験施設の被験物質保管室 (保管庫 : FMU-404I, 福島工業株式会社)
 製造元 : ████████████████████
 取扱い注意事項 : 直接手に触れない様に取り扱う。取扱い時には適切な保護具 (保護メガネ, マスク, ゴム手袋) を着用する。

2. 使用機器及び器具

機器名	型式	販売元
ガスクロマトグラフ	GC-2010	株式会社島津製作所
オートサンプラー	AOC-20s	株式会社島津製作所
オートインジェクター	AOC-20i Plus	株式会社島津製作所
データ処理装置	Labsolutions	株式会社島津製作所
シェーカー	レシプロシェーカー SR-2s	タイテック株式会社
遠心機	CF16RX	日立工機株式会社
マイクロピペット	マイクロマン	Gilson Inc.

3. 使用試薬

試薬名	グレード	販売元
エタノール	HPLC 用	富士フイルム和光純薬株式会社

Attachment 3-2.

4. GC 条件

検出器 : 水素炎イオン化検出器 (FID)
 カラム : DB-1 (0.53 mm×15 m, 膜厚 1.5 μm)
 カラム温度 : 40°C
 注入部温度 : 200°C
 検出器温度 : 250°C
 キャリアガス : ヘリウム, 5 mL/min
 スプリット比 : 1/20
 注入量 : 1 μL
 分析時間 : 5 分

5. 標準溶液の調製

調製量は同比で適宜変更する.

5.1. 標準原液 (ST : 1000 μg/mL)

プロピオン酸エチル約 1 g を精密に量り, エタノールに溶解し正確に 20 mL とする. この液 1 mL をエタノールで正確に 50 mL とする.

5.2. 標準溶液

以下の表に従い, 標準原液及び標準溶液をエタノールで希釈する.

標準溶液	調製濃度 (μg/mL)	採取標準液	採取量 (mL)	定容量 (mL)
St5	500	ST	5	10
St4	200	ST	2	10
St3	100	ST	1	10
St2	50	St5	1	10
St1	20	St4	1	10

Attachment 3-3.

6. 測定試料の調製**6.1. 被験物質の安定性確認用測定試料**

プロピオン酸エチル約1gを精密に量り、エタノールに溶解し正確に20mLとする。この液1mLをエタノールで正確に100mLとする。この溶液を測定試料とする。この調製を3回行う。ブランク試料はエタノールとする。

6.2. 投与検体の濃度及び安定性確認用測定試料**6.2.1. 33 mg/mL 測定試料**

33 mg/mL 投与検体 200 μ L を正確に量り、エタノール 5 mL を加え、10 分間振とう後、遠心分離 (1600 \times g, 5 分, 4 $^{\circ}$ C) する。上層から 1.5 mL を正確にとり、エタノールで正確に 20 mL とする。この溶液を測定試料とする。この調製を 3 回行う。

6.2.2. 100 mg/mL 測定試料

100 mg/mL 投与検体 200 μ L を正確に量り、エタノール 5 mL を加え、10 分間振とう後、遠心分離 (1600 \times g, 5 分, 4 $^{\circ}$ C) する。上層から 2.5 mL を正確にとり、エタノールで正確に 100 mL とする。この溶液を測定試料とする。この調製を 3 回行う。

6.2.3. 333 mg/mL 測定試料

333 mg/mL 投与検体 200 μ L を正確に量り、エタノール 5 mL を加え、10 分間振とう後、遠心分離 (1600 \times g, 5 分, 4 $^{\circ}$ C) する。上層から 1.5 mL を正確にとり、エタノールで正確に 20 mL とする。さらにこの液 1 mL を正確にとり、エタノールで正確に 10 mL とする。この溶液を測定試料とする。この調製を 3 回行う。

6.3. システム適合性

標準溶液 (S3) もしくは被験物質の安定性確認用測定試料を 3 回連続で注入し、プロピオン酸エチルのピーク面積及び保持時間の変動係数 (CV%) が 3.0%以下であることを確認する。

Attachment 3-4.

7. データ処理方法

各測定試料はそれぞれ1回測定し、ピークの同定は溶出時間に基づく。各パラメータの算出は表計算ソフト Excel (Microsoft) を用いて算出する。

7.1. 被験物質中のプロピオン酸エチル含量の算出

被験物質の安定性確認用測定試料を測定した時のクロマトグラム中のブランク試料由来のピークを除いた全ピーク面積に対する、プロピオン酸エチルのピーク面積の割合の平均値を被験物質含量 (%) とする。

7.2. 投与検体中のプロピオン酸エチル濃度の算出

投与検体中のプロピオン酸エチル濃度 (mg/mL) = $(Y - b) / a \times \text{希釈係数} / 1000$

Y : ピーク面積, a : 傾き, b : y-切片

希釈係数 : 33 mg/mL 投与検体 (1000/3), 100 mg/mL 投与検体 (1000),
333 mg/mL 投与検体 (10000/3)

7.3. 対表示濃度の算出

対表示濃度 (%) = 測定濃度の平均値 / 設定濃度 $\times 100$

7.4. 変動係数の算出

変動係数 (CV%) = 標準偏差 / 平均値 $\times 100$

7.5. 残存率の算出

被験物質の残存率 (%) = $\frac{\text{回復群の投与期間終了後の被験物質含量}}{\text{投与群投与開始日目の被験物質含量}} \times 100$

投与検体の残存率 (%) = $\frac{\text{保管後の投与検体の被験物質濃度の平均値}}{\text{調製直後の投与検体の被験物質濃度の平均値}} \times 100$

Attachment 3-5.

8. 数値の取り扱い

ピーク面積	実測値
回帰式の傾き, y-切片	四捨五入して有効数字4桁
相関係数	切り捨てして小数点以下4桁
平均値	四捨五入して該当するパラメータと同じ桁数
標準偏差	四捨五入して平均値と同じ桁
濃度 (mg/mL)	四捨五入して有効数字4桁
被験物質含量 (%)	四捨五入して小数点以下1桁
変動係数 (CV%)	四捨五入して小数点以下1桁
残存率 (%)	四捨五入して小数点以下1桁

Attachment 4-1.

Certificate of Analysis (1)

Test article: Ethyl propionate
Lot No.: XXXXXXXXXX
Date of analysis: November 16, 2023
Method: GC
Study period: Initial
Test facility: Hashima Laboratory, Nihon Bioresearch Inc.
Study No.: 430157

Test Item	Result
Content	100.0%

GLP:

Good Laboratory Practice for Test Facilities Conducting Tests of New Chemical Substances etc. (Notification 0331 No. 8 of the Pharmaceutical and Food Safety Bureau dated March 31, 2011, Notification No. 6 of the Manufacturing Industries Bureau dated March 29, 2011, Notification No. 110331010 of the Environmental Health Policy Planning and Management Division)

Attachment 4-2.

Certificate of Analysis (2)

Test article: Ethyl propionate
Lot No.: XXXXXXXXXX
Date of analysis: January 5, 2024
Method: GC
Study period: Final
Test facility: Hashima Laboratory, Nihon Bioresearch Inc.
Study No.: 430157

Test Item	Result
Content	100.0%
Stability ¹⁾	100.0%

1) Acceptable range: within 100.0% ± 10.0% of the initial content.

GLP:

Good Laboratory Practice for Test Facilities Conducting Tests of New Chemical Substances etc. (Notification 0331 No. 8 of the Pharmaceutical and Food Safety Bureau dated March 31, 2011, Notification No. 6 of the Manufacturing Industries Bureau dated March 29, 2011, Notification No. 110331010 of the Environmental Health Policy Planning and Management Division)

Attachment 5-1.

Concentrations of ethyl propionate in dosing preparations (1)

Test article: Ethyl propionate (Lot No. XXXXXXXXXX)
 Vehicle: Corn oil
 Form: Solution
 Analyte: Ethyl propionate
 Method: GC
 Date of preparation: November 16, 2023
 Date of analysis: November 16, 2023
 Test facility: Hashima Laboratory, Nihon Bioresearch Inc.
 Study No. 430157

Results

Concentration of analyte (mg/mL)	Measured concentration (mg/mL)				Recovery rate ¹⁾ (%)
	1st	2nd	3rd	Mean	
33	30.59	30.62	30.44	30.55	92.6
100	93.59	93.52	93.98	93.70	93.7
333	315.9	316.2	316.3	316.1	94.9

1) Acceptable range: within 100.0% ± 10.0% of the prescribed concentration.

GLP:

Good Laboratory Practice for Test Facilities Conducting Tests of New Chemical Substances etc.
 (Notification 0331 No. 8 of the Pharmaceutical and Food Safety Bureau dated March 31, 2011,
 Notification No. 6 of the Manufacturing Industries Bureau dated March 29, 2011, Notification No.
 110331010 of the Environmental Health Policy Planning and Management Division)

Attachment 5-2.

Concentrations of ethyl propionate in dosing preparations (2)

Test article: Ethyl propionate (Lot No. XXXXXXXXXX)
 Vehicle: Corn oil
 Form: Solution
 Analyte: Ethyl propionate
 Method: GC
 Date of preparation: December 20, 2023
 Date of analysis: December 20, 2023
 Test facility: Hashima Laboratory, Nihon Bioresearch Inc.
 Study No. 430157

Results

Concentration of analyte (mg/mL)	Measured concentration (mg/mL)				Recovery rate ¹⁾ (%)
	1st	2nd	3rd	Mean	
33	30.88	30.84	31.01	30.91	93.7
100	95.26	94.87	95.65	95.26	95.3
333	322.1	320.3	321.5	321.3	96.5

1) Acceptable range: within 100.0% ± 10.0% of the prescribed concentration.

GLP:

Good Laboratory Practice for Test Facilities Conducting Tests of New Chemical Substances etc.
 (Notification 0331 No. 8 of the Pharmaceutical and Food Safety Bureau dated March 31, 2011,
 Notification No. 6 of the Manufacturing Industries Bureau dated March 29, 2011, Notification No.
 110331010 of the Environmental Health Policy Planning and Management Division)

Attachment 6.

Stability of ethyl propionate in dosing preparations

Test article (Lot No.) : Ethyl propionate (Lot No. ██████████)
 Vehicle : Corn oil
 Form : Solution
 Analyte : Ethyl propionate
 Method : GC
 Date of preparation : November 16, 2023
 Date of analysis : November 16 and 17, 2023
 Storage conditions : Stored in amber glass containers at room temperature (1.0°C - 30.0°C) and protected from light for 24 hours.
 Test facility : Hashima Laboratory, Nihon Bioresearch Inc.
 Study No. : 430157

Results

Concentration of analyte (mg/mL)	Measurement period	Concentration (mg/mL)				Stability ¹⁾ (%)
		1st	2nd	3rd	Mean	
33	Initial	30.59	30.62	30.44	30.55	-
	After storage	30.94	30.65	30.97	30.85	101.0
100	Initial	93.59	93.52	93.98	93.70	-
	After storage	94.59	94.94	94.95	94.83	101.2
333	Initial	315.9	316.2	316.3	316.1	-
	After storage	316.0	315.2	317.3	316.2	100.0

1) Acceptable range: within 100.0% ± 10.0% of the initial concentration.

GLP:

Good Laboratory Practice for Test Facilities Conducting Tests of New Chemical Substances etc. (Notification 0331 No. 8 of the Pharmaceutical and Food Safety Bureau dated March 31, 2011, Notification No. 6 of the Manufacturing Industries Bureau dated March 29, 2011, Notification No. 110331010 of the Environmental Health Policy Planning and Management Division).

Attachment 7-1. General signs in male rats during quarantine and acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period						Acclimatization period		
		15-Nov-23 Day 0	16-Nov-23 Day 1	17-Nov-23 Day 2	18-Nov-23 Day 3	19-Nov-23 Day 4	20-Nov-23 Day 5	21-Nov-23 Day 1	22-Nov-23 Day 2	23-Nov-23 Day 3 #
M00001	M01103	N	N	N	N	N	N	N	N	N
M00002	M01101	N	N	N	N	N	N	N	N	N
M00003	EG, MA	N	N	N	N	N	N	N	N	N
M00004	M04405	N	N	N	N	N	N	N	N	N
M00005	M01102	N	N	N	N	N	N	N	N	N
M00006	M03303	N	N	N	N	N	N	N	N	N
M00007	M03304	N	N	N	N	N	N	N	N	N
M00008	M04404	N	N	N	N	N	N	N	N	N
M00009	EG, MA	N	N	N	N	N	N	N	N	N
M00010	M02205	N	N	N	N	N	N	N	N	N
M00011	M01104	N	N	N	N	N	N	N	N	N
M00012	EG	N	N	N	N	N	N	N	N	N
M00013	M03302	N	N	N	N	N	N	N	N	N
M00014	M01105	N	N	N	N	N	N	N	N	N
M00015	M03301	N	N	N	N	N	N	N	N	N
M00016	M03305	N	N	N	N	N	N	N	N	N
M00017	M04402	N	N	N	N	N	N	N	N	N
M00018	M04401	N	N	N	N	N	N	N	N	N
M00019	M02201	N	N	N	N	N	N	N	N	N
M00020	M02203	N	N	N	N	N	N	N	N	N
M00021	M02204	N	N	N	N	N	N	N	N	N
M00022	M02202	N	N	N	N	N	N	N	N	N
M00023	M04403	N	N	N	N	N	N	N	N	N

#: Day of grouping.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

N: Normal.

Attachment 7-2. General signs in male rats during quarantine and acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period						Acclimatization period			
		22-Nov-23 Day 0	23-Nov-23 Day 1	24-Nov-23 Day 2	25-Nov-23 Day 3	26-Nov-23 Day 4	27-Nov-23 Day 5	28-Nov-23 Day 1	29-Nov-23 Day 2	30-Nov-23 Day 3	1-Dec-23 Day 4 #
M00024	M03308	N	N	N	N	N	N	N	N	N	N
M00025	M03307	N	N	N	N	N	N	N	N	N	N
M00026	M03309	N	N	N	N	N	N	N	N	N	N
M00027	M01109	N	N	N	N	N	N	N	N	N	N
M00028	M04407	N	N	N	N	N	N	N	N	N	N
M00029	M01107	N	N	N	N	N	N	N	N	N	N
M00030	M04409	N	N	N	N	N	N	N	N	N	N
M00031	M04406	N	N	N	N	N	N	N	N	N	N
M00032	M03306	N	N	N	N	N	N	N	N	N	N
M00033	M01106	N	N	N	N	N	N	N	N	N	N
M00034	M01108	N	N	N	N	N	N	N	N	N	N
M00035	M03310	N	N	N	N	N	N	N	N	N	N
M00036	M01110	N	N	N	N	N	N	N	N	N	N
M00037	EG	N	N	N	N	N	N	N	N	N	N
M00038	EG	N	N	N	N	N	N	N	N	N	N
M00039	M04408	N	N	N	N	N	N	N	N	N	N
M00040	M04410	N	N	N	N	N	N	N	N	N	N

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

N: Normal.

Attachment 8-1. General signs in female rats during quarantine and acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period						Acclimatization period		
		15-Nov-23 Day 0	16-Nov-23 Day 1	17-Nov-23 Day 2	18-Nov-23 Day 3	19-Nov-23 Day 4	20-Nov-23 Day 5	21-Nov-23 Day 1	22-Nov-23 Day 2	23-Nov-23 Day 3 #
F00001	F04452	N	N	N	N	N	N	N	N	N
F00002	EG	N	N	N	N	N	N	N	N	N
F00003	F02254	N	N	N	N	N	N	N	N	N
F00004	F01152	N	N	N	N	N	N	N	N	N
F00005	F01153	N	N	N	N	N	N	N	N	N
F00006	F02255	N	N	N	N	N	N	N	N	N
F00007	F04455	N	N	N	N	N	N	N	N	N
F00008	F03351	N	N	N	N	N	N	N	N	N
F00009	EG	N	N	N	N	N	N	N	N	N
F00010	EG	N	N	N	N	N	N	N	N	N
F00011	F03352	N	N	N	N	N	N	N	N	N
F00012	F01154	N	N	N	N	N	N	N	N	N
F00013	F04451	N	N	N	N	N	N	N	N	N
F00014	F02251	N	N	N	N	N	N	N	N	N
F00015	F04453	N	N	N	N	N	N	N	N	N
F00016	F04454	N	N	N	N	N	N	N	N	N
F00017	F01155	N	N	N	N	N	N	N	N	N
F00018	F01151	N	N	N	N	N	N	N	N	N
F00019	F03354	N	N	N	N	N	N	N	N	N
F00020	F03353	N	N	N	N	N	N	N	N	N
F00021	F03355	N	N	N	N	N	N	N	N	N
F00022	F02252	N	N	N	N	N	N	N	N	N
F00023	F02253	N	N	N	N	N	N	N	N	N

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

N: Normal.

Attachment 8-2. General signs in female rats during quarantine and acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period						Acclimatization period			
		22-Nov-23 Day 0	23-Nov-23 Day 1	24-Nov-23 Day 2	25-Nov-23 Day 3	26-Nov-23 Day 4	27-Nov-23 Day 5	28-Nov-23 Day 1	29-Nov-23 Day 2	30-Nov-23 Day 3	1-Dec-23 Day 4 #
F00024	F01156	N	N	N	N	N	N	N	N	N	N
F00025	F03359	N	N	N	N	N	N	N	N	N	N
F00026	F01157	N	N	N	N	N	N	N	N	N	N
F00027	F03358	N	N	N	N	N	N	N	N	N	N
F00028	F04460	N	N	N	N	N	N	N	N	N	N
F00029	F04457	N	N	N	N	N	N	N	N	N	N
F00030	F03357	N	N	N	N	N	N	N	N	N	N
F00031	F04459	N	N	N	N	N	N	N	N	N	N
F00032	F04456	N	N	N	N	N	N	N	N	N	N
F00033	F01159	N	N	N	N	N	N	N	N	N	N
F00034	F01160	N	N	N	N	N	N	N	N	N	N
F00035	F03356	N	N	N	N	N	N	N	N	N	N
F00036	F03360	N	N	N	N	N	N	N	N	N	N
F00037	EG	N	N	N	N	N	N	N	N	N	N
F00038	EG	N	N	N	N	N	N	N	N	N	N
F00039	F04458	N	N	N	N	N	N	N	N	N	N
F00040	F01158	N	N	N	N	N	N	N	N	N	N

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

N: Normal.

Attachment 9-1. Body weights of male rats during quarantine and acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period		Acclimatization period
		16-Nov-23	20-Nov-23	23-Nov-23
		Day 1	Day 5	Day 3 #
M00001	M01103	87	123	153
M00002	M01101	100	140	169
M00003	EG, MA	105	145	177
M00004	M04405	102	141	175
M00005	M01102	98	135	168
M00006	M03303	98	136	164
M00007	M03304	106	146	176
M00008	M04404	96	129	158
M00009	EG, MA	98	130	152
M00010	M02205	98	130	158
M00011	M01104	101	139	172
M00012	EG	95	126	147
M00013	M03302	99	134	169
M00014	M01105	97	135	164
M00015	M03301	92	128	159
M00016	M03305	88	127	157
M00017	M04402	97	137	169
M00018	M04401	96	132	162
M00019	M02201	100	140	170
M00020	M02203	90	131	161
M00021	M02204	98	140	174
M00022	M02202	100	139	168
M00023	M04403	96	132	161

Unit: g

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

Attachment 9-2. Body weights of male rats during quarantine and acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period		Acclimatization period
		23-Nov-23	27-Nov-23	1-Dec-23
		Day 1	Day 5	Day 4 #
M00024	M03308	90	126	170
M00025	M03307	97	132	175
M00026	M03309	93	129	164
M00027	M01109	92	128	164
M00028	M04407	100	140	185
M00029	M01107	97	137	180
M00030	M04409	92	127	165
M00031	M04406	96	132	174
M00032	M03306	95	130	174
M00033	M01106	98	134	176
M00034	M01108	98	134	176
M00035	M03310	102	143	185
M00036	M01110	99	139	173
M00037	EG	98	141	195
M00038	EG	99	139	188
M00039	M04408	98	138	169
M00040	M04410	96	139	174

Unit: g

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 10-1. Body weights of female rats during quarantine and acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period		Acclimatization period
		16-Nov-23	20-Nov-23	23-Nov-23
		Day 1	Day 5	Day 3 #
F00001	F04452	100	131	157
F00002	EG	102	138	163
F00003	F02254	95	121	143
F00004	F01152	94	120	138
F00005	F01153	96	125	144
F00006	F02255	92	117	138
F00007	F04455	100	131	153
F00008	F03351	97	127	145
F00009	EG	95	117	130
F00010	EG	101	138	164
F00011	F03352	96	124	144
F00012	F01154	101	124	148
F00013	F04451	97	130	150
F00014	F02251	100	131	152
F00015	F04453	99	125	141
F00016	F04454	94	122	140
F00017	F01155	95	129	153
F00018	F01151	98	129	157
F00019	F03354	100	131	151
F00020	F03353	97	130	140
F00021	F03355	98	133	159
F00022	F02252	94	133	156
F00023	F02253	92	131	150

Unit: g

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 10-2. Body weights of female rats during quarantine and acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Quarantine period		Acclimatization period
		23-Nov-23	27-Nov-23	1-Dec-23
		Day 1	Day 5	Day 4 #
F00024	F01156	102	126	148
F00025	F03359	99	128	154
F00026	F01157	104	139	162
F00027	F03358	102	131	160
F00028	F04460	101	135	163
F00029	F04457	99	130	156
F00030	F03357	102	137	169
F00031	F04459	101	135	158
F00032	F04456	98	127	148
F00033	F01159	101	132	166
F00034	F01160	102	132	160
F00035	F03356	91	124	150
F00036	F03360	99	131	157
F00037	EG	98	122	141
F00038	EG	103	138	174
F00039	F04458	103	136	167
F00040	F01158	93	127	155

Unit: g

#: Day of grouping

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-1. Detailed clinical signs by FOB in male rats during acclimatization (administrarion group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages			
		Posture	Palpebral closure	Excessive grooming	Repetitive circling
M00001	M01103	2	1	1	1
M00002	M01101	2	1	1	1
M00003	EG, MA	2	1	1	1
M00004	M04405	2	1	1	1
M00005	M01102	2	1	1	1
M00006	M03303	2	1	1	1
M00007	M03304	2	1	1	1
M00008	M04404	2	1	1	1
M00009	EG, MA	2	1	1	1
M00010	M02205	2	1	1	1
M00011	M01104	2	1	1	1
M00012	EG	2	1	1	1
M00013	M03302	2	1	1	1
M00014	M01105	2	1	1	1
M00015	M03301	2	1	1	1
M00016	M03305	2	1	1	1
M00017	M04402	2	1	1	1
M00018	M04401	2	1	1	1
M00019	M02201	2	1	1	1
M00020	M02203	2	1	1	1
M00021	M02204	2	1	1	1
M00022	M02202	2	1	1	1
M00023	M04403	2	1	1	1

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

(Continued)

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages		
		Biting behavior	Clonic convulsions	Tonic convulsions
M00001	M01103	1	1	1
M00002	M01101	1	1	1
M00003	EG, MA	1	1	1
M00004	M04405	1	1	1
M00005	M01102	1	1	1
M00006	M03303	1	1	1
M00007	M03304	1	1	1
M00008	M04404	1	1	1
M00009	EG, MA	1	1	1
M00010	M02205	1	1	1
M00011	M01104	1	1	1
M00012	EG	1	1	1
M00013	M03302	1	1	1
M00014	M01105	1	1	1
M00015	M03301	1	1	1
M00016	M03305	1	1	1
M00017	M04402	1	1	1
M00018	M04401	1	1	1
M00019	M02201	1	1	1
M00020	M02203	1	1	1
M00021	M02204	1	1	1
M00022	M02202	1	1	1
M00023	M04403	1	1	1

Findings were graded as follows;

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

(Continued)

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Ease of removal from cage	Ease of handling	Muscle tone	Fur conditions
M00001	M01103	2	2	2	1
M00002	M01101	2	2	2	1
M00003	EG, MA	2	2	2	1
M00004	M04405	2	2	2	1
M00005	M01102	2	2	2	1
M00006	M03303	2	2	2	1
M00007	M03304	2	2	2	1
M00008	M04404	2	2	2	1
M00009	EG, MA	2	2	2	1
M00010	M02205	2	2	2	1
M00011	M01104	2	2	2	1
M00012	EG	2	2	2	1
M00013	M03302	2	2	2	1
M00014	M01105	2	2	2	1
M00015	M03301	2	2	2	1
M00016	M03305	2	2	2	1
M00017	M04402	2	2	2	1
M00018	M04401	2	2	2	1
M00019	M02201	2	2	2	1
M00020	M02203	2	2	2	1
M00021	M02204	2	2	2	1
M00022	M02202	2	2	2	1
M00023	M04403	2	2	2	1

Findings were graded as follows;

(Continued)

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Mucous membranes	Lacrimation	Salivation	Piloerection
M00001	M01103	1	1	1	1
M00002	M01101	1	1	1	1
M00003	EG, MA	1	1	1	1
M00004	M04405	1	1	1	1
M00005	M01102	1	1	1	1
M00006	M03303	1	1	1	1
M00007	M03304	1	1	1	1
M00008	M04404	1	1	1	1
M00009	EG, MA	1	1	1	1
M00010	M02205	1	1	1	1
M00011	M01104	1	1	1	1
M00012	EG	1	1	1	1
M00013	M03302	1	1	1	1
M00014	M01105	1	1	1	1
M00015	M03301	1	1	1	1
M00016	M03305	1	1	1	1
M00017	M04402	1	1	1	1
M00018	M04401	1	1	1	1
M00019	M02201	1	1	1	1
M00020	M02203	1	1	1	1
M00021	M02204	1	1	1	1
M00022	M02202	1	1	1	1
M00023	M04403	1	1	1	1

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

(Continued)

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm	
		Pupil size	Respiration
M00001	M01103	2	1
M00002	M01101	2	1
M00003	EG, MA	2	1
M00004	M04405	2	1
M00005	M01102	2	1
M00006	M03303	2	1
M00007	M03304	2	1
M00008	M04404	2	1
M00009	EG, MA	2	1
M00010	M02205	2	1
M00011	M01104	2	1
M00012	EG	2	1
M00013	M03302	2	1
M00014	M01105	2	1
M00015	M03301	2	1
M00016	M03305	2	1
M00017	M04402	2	1
M00018	M04401	2	1
M00019	M02201	2	1
M00020	M02203	2	1
M00021	M02204	2	1
M00022	M02202	2	1
M00023	M04403	2	1

Findings were graded as follows;

(Continued)

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Frequency of urination (during a 2-minute period)	Frequency of defecation (during a 2-minute period)	Frequency of rearing (during a 2-minute period)	Frequency of grooming (during a 2-minute period)
M00001	M01103	2	2	3	0
M00002	M01101	1	2	3	0
M00003	EG, MA	2	2	6	0
M00004	M04405	0	0	6	0
M00005	M01102	0	1	15	0
M00006	M03303	0	4	7	0
M00007	M03304	0	1	8	0
M00008	M04404	0	0	4	0
M00009	EG, MA	0	1	7	0
M00010	M02205	1	2	1	0
M00011	M01104	2	1	7	0
M00012	EG	1	3	3	0
M00013	M03302	0	0	6	0
M00014	M01105	0	0	12	0
M00015	M03301	1	3	13	0
M00016	M03305	1	2	3	1
M00017	M04402	0	3	4	0
M00018	M04401	1	0	6	0
M00019	M02201	0	1	8	0
M00020	M02203	1	0	9	1
M00021	M02204	0	2	7	0
M00022	M02202	1	0	1	0
M00023	M04403	2	0	2	0

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

(Continued)

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Gait	Palpebral closure	Consciousness	Behavioral abnormalities
M00001	M01103	1	1	2	1
M00002	M01101	1	1	2	1
M00003	EG, MA	1	1	2	1
M00004	M04405	1	1	2	1
M00005	M01102	1	1	2	1
M00006	M03303	1	1	2	1
M00007	M03304	1	1	2	1
M00008	M04404	1	1	2	1
M00009	EG, MA	1	1	2	1
M00010	M02205	1	1	2	1
M00011	M01104	1	1	2	1
M00012	EG	1	1	2	1
M00013	M03302	1	1	2	1
M00014	M01105	1	1	2	1
M00015	M03301	1	1	2	1
M00016	M03305	1	1	2	1
M00017	M04402	1	1	2	1
M00018	M04401	1	1	2	1
M00019	M02201	1	1	2	1
M00020	M02203	1	1	2	1
M00021	M02204	1	1	2	1
M00022	M02202	1	1	2	1
M00023	M04403	1	1	2	1

Findings were graded as follows;

(Continued)

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

Attachment 11-1. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test	
		Righting reflex	
M00001	M01103		1
M00002	M01101		1
M00003	EG, MA		1
M00004	M04405		1
M00005	M01102		1
M00006	M03303		1
M00007	M03304		1
M00008	M04404		1
M00009	EG, MA		1
M00010	M02205		1
M00011	M01104		1
M00012	EG		1
M00013	M03302		1
M00014	M01105		1
M00015	M03301		1
M00016	M03305		1
M00017	M04402		1
M00018	M04401		1
M00019	M02201		1
M00020	M02203		1
M00021	M02204		1
M00022	M02202		1
M00023	M04403		1

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

Attachment 11-2. Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages			
		Posture	Palpebral closure	Excessive grooming	Repetitive circling
M00024	M03308	2	1	1	1
M00025	M03307	2	1	1	1
M00026	M03309	2	1	1	1
M00027	M01109	2	1	1	1
M00028	M04407	2	1	1	1
M00029	M01107	2	1	1	1
M00030	M04409	2	1	1	1
M00031	M04406	2	1	1	1
M00032	M03306	2	1	1	1
M00033	M01106	2	1	1	1
M00034	M01108	2	1	1	1
M00035	M03310	2	1	1	1
M00036	M01110	2	1	1	1
M00037	EG	2	1	1	1
M00038	EG	2	1	1	1
M00039	M04408	2	1	1	1
M00040	M04410	2	1	1	1

Findings were graded as follows;

(Continued)

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages		
		Biting behavior	Clonic convulsions	Tonic convulsions
M00024	M03308	1	1	1
M00025	M03307	1	1	1
M00026	M03309	1	1	1
M00027	M01109	1	1	1
M00028	M04407	1	1	1
M00029	M01107	1	1	1
M00030	M04409	1	1	1
M00031	M04406	1	1	1
M00032	M03306	1	1	1
M00033	M01106	1	1	1
M00034	M01108	1	1	1
M00035	M03310	1	1	1
M00036	M01110	1	1	1
M00037	EG	1	1	1
M00038	EG	1	1	1
M00039	M04408	1	1	1
M00040	M04410	1	1	1

Findings were graded as follows;

(Continued)

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Ease of removal from cage	Ease of handling	Muscle tone	Fur conditions
M00024	M03308	2	2	2	1
M00025	M03307	2	2	2	1
M00026	M03309	2	2	2	1
M00027	M01109	2	2	2	1
M00028	M04407	2	2	2	1
M00029	M01107	2	2	2	1
M00030	M04409	2	2	2	1
M00031	M04406	2	2	2	1
M00032	M03306	2	2	2	1
M00033	M01106	2	2	2	1
M00034	M01108	2	2	2	1
M00035	M03310	2	2	2	1
M00036	M01110	2	2	2	1
M00037	EG	2	2	2	1
M00038	EG	2	2	2	1
M00039	M04408	2	2	2	1
M00040	M04410	2	2	2	1

Findings were graded as follows;

(Continued)

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Mucous membranes	Lacrimation	Salivation	Piloerection
M00024	M03308	1	1	1	1
M00025	M03307	1	1	1	1
M00026	M03309	1	1	1	1
M00027	M01109	1	1	1	1
M00028	M04407	1	1	1	1
M00029	M01107	1	1	1	1
M00030	M04409	1	1	1	1
M00031	M04406	1	1	1	1
M00032	M03306	1	1	1	1
M00033	M01106	1	1	1	1
M00034	M01108	1	1	1	1
M00035	M03310	1	1	1	1
M00036	M01110	1	1	1	1
M00037	EG	1	1	1	1
M00038	EG	1	1	1	1
M00039	M04408	1	1	1	1
M00040	M04410	1	1	1	1

Findings were graded as follows;

(Continued)

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm	
		Pupil size	Respiration
M00024	M03308	2	1
M00025	M03307	2	1
M00026	M03309	2	1
M00027	M01109	2	1
M00028	M04407	2	1
M00029	M01107	2	1
M00030	M04409	2	1
M00031	M04406	2	1
M00032	M03306	2	1
M00033	M01106	2	1
M00034	M01108	2	1
M00035	M03310	2	1
M00036	M01110	2	1
M00037	EG	2	1
M00038	EG	2	1
M00039	M04408	2	1
M00040	M04410	2	1

Findings were graded as follows;

(Continued)

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Frequency of urination (during a 2-minute period)	Frequency of defecation (during a 2-minute period)	Frequency of rearing (during a 2-minute period)	Frequency of grooming (during a 2-minute period)
M00024	M03308	0	1	6	0
M00025	M03307	0	0	6	0
M00026	M03309	0	0	4	0
M00027	M01109	1	0	12	0
M00028	M04407	2	4	1	0
M00029	M01107	0	1	5	0
M00030	M04409	0	0	8	0
M00031	M04406	2	4	4	0
M00032	M03306	0	0	6	0
M00033	M01106	0	0	5	0
M00034	M01108	0	0	7	0
M00035	M03310	1	0	9	0
M00036	M01110	0	0	11	0
M00037	EG	0	0	4	0
M00038	EG	1	2	7	0
M00039	M04408	2	1	5	0
M00040	M04410	2	4	3	0

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Gait	Palpebral closure	Consciousness	Behavioral abnormalities
M00024	M03308	1	1	2	1
M00025	M03307	1	1	2	1
M00026	M03309	1	1	2	1
M00027	M01109	1	1	2	1
M00028	M04407	1	1	2	1
M00029	M01107	1	1	2	1
M00030	M04409	1	1	2	1
M00031	M04406	1	1	2	1
M00032	M03306	1	1	2	1
M00033	M01106	1	1	2	1
M00034	M01108	1	1	2	1
M00035	M03310	1	1	2	1
M00036	M01110	1	1	2	1
M00037	EG	1	1	2	1
M00038	EG	1	1	2	1
M00039	M04408	1	1	2	1
M00040	M04410	1	1	2	1

Findings were graded as follows;

(Continued)

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 11-2. (Continued) Detailed clinical signs by FOB in male rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test	
		Righting reflex	
M00024	M03308		1
M00025	M03307		1
M00026	M03309		1
M00027	M01109		1
M00028	M04407		1
M00029	M01107		1
M00030	M04409		1
M00031	M04406		1
M00032	M03306		1
M00033	M01106		1
M00034	M01108		1
M00035	M03310		1
M00036	M01110		1
M00037	EG		1
M00038	EG		1
M00039	M04408		1
M00040	M04410		1

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-1. Detailed clinical signs by FOB in female rats during acclimatization (administrarion group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages			
		Posture	Palpebral closure	Excessive grooming	Repetitive circling
F00001	F04452	2	1	1	1
F00002	EG	2	1	1	1
F00003	F02254	2	1	1	1
F00004	F01152	2	1	1	1
F00005	F01153	2	1	1	1
F00006	F02255	2	1	1	1
F00007	F04455	2	1	1	1
F00008	F03351	2	1	1	1
F00009	EG	2	1	1	1
F00010	EG	2	1	1	1
F00011	F03352	2	1	1	1
F00012	F01154	2	1	1	1
F00013	F04451	2	1	1	1
F00014	F02251	2	1	1	1
F00015	F04453	2	1	1	1
F00016	F04454	2	1	1	1
F00017	F01155	2	1	1	1
F00018	F01151	2	1	1	1
F00019	F03354	2	1	1	1
F00020	F03353	2	1	1	1
F00021	F03355	2	1	1	1
F00022	F02252	2	1	1	1
F00023	F02253	2	1	1	1

Findings were graded as follows;

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages		
		Biting behavior	Clonic convulsions	Tonic convulsions
F00001	F04452	1	1	1
F00002	EG	1	1	1
F00003	F02254	1	1	1
F00004	F01152	1	1	1
F00005	F01153	1	1	1
F00006	F02255	1	1	1
F00007	F04455	1	1	1
F00008	F03351	1	1	1
F00009	EG	1	1	1
F00010	EG	1	1	1
F00011	F03352	1	1	1
F00012	F01154	1	1	1
F00013	F04451	1	1	1
F00014	F02251	1	1	1
F00015	F04453	1	1	1
F00016	F04454	1	1	1
F00017	F01155	1	1	1
F00018	F01151	1	1	1
F00019	F03354	1	1	1
F00020	F03353	1	1	1
F00021	F03355	1	1	1
F00022	F02252	1	1	1
F00023	F02253	1	1	1

Findings were graded as follows;

(Continued)

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Ease of removal from cage	Ease of handling	Muscle tone	Fur conditions
F00001	F04452	2	2	2	1
F00002	EG	2	2	2	1
F00003	F02254	2	2	2	1
F00004	F01152	2	2	2	1
F00005	F01153	2	2	2	1
F00006	F02255	2	2	2	1
F00007	F04455	2	2	2	1
F00008	F03351	2	2	2	1
F00009	EG	2	2	2	1
F00010	EG	2	2	2	1
F00011	F03352	2	2	2	1
F00012	F01154	2	2	2	1
F00013	F04451	2	2	2	1
F00014	F02251	2	2	2	1
F00015	F04453	2	2	2	1
F00016	F04454	2	2	2	1
F00017	F01155	2	2	2	1
F00018	F01151	2	2	2	1
F00019	F03354	2	2	2	1
F00020	F03353	2	2	2	1
F00021	F03355	2	2	2	1
F00022	F02252	2	2	2	1
F00023	F02253	2	2	2	1

Findings were graded as follows;

(Continued)

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Mucous membranes	Lacrimation	Salivation	Piloerection
F00001	F04452	1	1	1	1
F00002	EG	1	1	1	1
F00003	F02254	1	1	1	1
F00004	F01152	1	1	1	1
F00005	F01153	1	1	1	1
F00006	F02255	1	1	1	1
F00007	F04455	1	1	1	1
F00008	F03351	1	1	1	1
F00009	EG	1	1	1	1
F00010	EG	1	1	1	1
F00011	F03352	1	1	1	1
F00012	F01154	1	1	1	1
F00013	F04451	1	1	1	1
F00014	F02251	1	1	1	1
F00015	F04453	1	1	1	1
F00016	F04454	1	1	1	1
F00017	F01155	1	1	1	1
F00018	F01151	1	1	1	1
F00019	F03354	1	1	1	1
F00020	F03353	1	1	1	1
F00021	F03355	1	1	1	1
F00022	F02252	1	1	1	1
F00023	F02253	1	1	1	1

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm	
		Pupil size	Respiration
F00001	F04452	2	1
F00002	EG	2	1
F00003	F02254	2	1
F00004	F01152	2	1
F00005	F01153	2	1
F00006	F02255	2	1
F00007	F04455	2	1
F00008	F03351	2	1
F00009	EG	2	1
F00010	EG	2	1
F00011	F03352	2	1
F00012	F01154	2	1
F00013	F04451	2	1
F00014	F02251	2	1
F00015	F04453	2	1
F00016	F04454	2	1
F00017	F01155	2	1
F00018	F01151	2	1
F00019	F03354	2	1
F00020	F03353	2	1
F00021	F03355	2	1
F00022	F02252	2	1
F00023	F02253	2	1

Findings were graded as follows;

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Frequency of urination (during a 2-minute period)	Frequency of defecation (during a 2-minute period)	Frequency of rearing (during a 2-minute period)	Frequency of grooming (during a 2-minute period)
F00001	F04452	0	0	10	0
F00002	EG	1	3	1	0
F00003	F02254	0	0	10	0
F00004	F01152	1	0	5	0
F00005	F01153	0	1	8	0
F00006	F02255	1	0	15	0
F00007	F04455	0	0	6	1
F00008	F03351	1	0	5	0
F00009	EG	0	0	9	1
F00010	EG	1	0	7	0
F00011	F03352	0	0	1	0
F00012	F01154	1	0	9	0
F00013	F04451	0	0	4	0
F00014	F02251	1	0	2	0
F00015	F04453	1	0	5	0
F00016	F04454	1	0	6	0
F00017	F01155	3	2	4	0
F00018	F01151	0	0	9	0
F00019	F03354	1	0	3	0
F00020	F03353	0	0	6	0
F00021	F03355	2	2	4	0
F00022	F02252	2	1	3	0
F00023	F02253	0	0	6	0

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Gait	Palpebral closure	Consciousness	Behavioral abnormalities
F00001	F04452	1	1	2	1
F00002	EG	1	1	2	1
F00003	F02254	1	1	2	1
F00004	F01152	1	1	2	1
F00005	F01153	1	1	2	1
F00006	F02255	1	1	2	1
F00007	F04455	1	1	2	1
F00008	F03351	1	1	2	1
F00009	EG	1	1	2	1
F00010	EG	1	1	2	1
F00011	F03352	1	1	2	1
F00012	F01154	1	1	2	1
F00013	F04451	1	1	2	1
F00014	F02251	1	1	2	1
F00015	F04453	1	1	2	1
F00016	F04454	1	1	2	1
F00017	F01155	1	1	2	1
F00018	F01151	1	1	2	1
F00019	F03354	1	1	2	1
F00020	F03353	1	1	2	1
F00021	F03355	1	1	2	1
F00022	F02252	1	1	2	1
F00023	F02253	1	1	2	1

Findings were graded as follows;

(Continued)

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-1. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (administration group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test	
		Righting reflex	
F00001	F04452		1
F00002	EG		1
F00003	F02254		1
F00004	F01152		1
F00005	F01153		1
F00006	F02255		1
F00007	F04455		1
F00008	F03351		1
F00009	EG		1
F00010	EG		1
F00011	F03352		1
F00012	F01154		1
F00013	F04451		1
F00014	F02251		1
F00015	F04453		1
F00016	F04454		1
F00017	F01155		1
F00018	F01151		1
F00019	F03354		1
F00020	F03353		1
F00021	F03355		1
F00022	F02252		1
F00023	F02253		1

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-2. Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages			
		Posture	Palpebral closure	Excessive grooming	Repetitive circling
F00024	F01156	2	1	1	1
F00025	F03359	2	1	1	1
F00026	F01157	2	1	1	1
F00027	F03358	2	1	1	1
F00028	F04460	2	1	1	1
F00029	F04457	2	1	1	1
F00030	F03357	2	1	1	1
F00031	F04459	2	1	1	1
F00032	F04456	2	1	1	1
F00033	F01159	2	1	1	1
F00034	F01160	2	1	1	1
F00035	F03356	2	1	1	1
F00036	F03360	2	1	1	1
F00037	EG	2	1	1	1
F00038	EG	2	1	1	1
F00039	F04458	2	1	1	1
F00040	F01158	2	1	1	1

Findings were graded as follows;

(Continued)

Posture: 1: Prone or recumbent position, 2: resting normally (normal score), 3: moving or running about, 4: jumping.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Excessive grooming: 1: Not observed (normal score), 2: observed.

Repetitive circling: 1: Not observed (normal score), 2: observed.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals in cages		
		Biting behavior	Clonic convulsions	Tonic convulsions
F00024	F01156	1	1	1
F00025	F03359	1	1	1
F00026	F01157	1	1	1
F00027	F03358	1	1	1
F00028	F04460	1	1	1
F00029	F04457	1	1	1
F00030	F03357	1	1	1
F00031	F04459	1	1	1
F00032	F04456	1	1	1
F00033	F01159	1	1	1
F00034	F01160	1	1	1
F00035	F03356	1	1	1
F00036	F03360	1	1	1
F00037	EG	1	1	1
F00038	EG	1	1	1
F00039	F04458	1	1	1
F00040	F01158	1	1	1

Findings were graded as follows;

(Continued)

Biting behavior: 1: Not observed (normal score), 2: observed.

Clonic convulsions: 1: Not observed (normal score), 2: jaw convulsions, 3: tremor.

Tonic convulsions: 1: Not observed (normal score), 2: tonic extension, 3: opisthotonus convulsions,
4: saltatory convulsions, 5: asphyxial convulsions.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Ease of removal from cage	Ease of handling	Muscle tone	Fur conditions
F00024	F01156	2	2	2	1
F00025	F03359	2	2	2	1
F00026	F01157	2	2	2	1
F00027	F03358	2	2	2	1
F00028	F04460	2	2	2	1
F00029	F04457	2	2	2	1
F00030	F03357	2	2	2	1
F00031	F04459	2	2	2	1
F00032	F04456	2	2	2	1
F00033	F01159	2	2	2	1
F00034	F01160	2	2	2	1
F00035	F03356	2	2	2	1
F00036	F03360	2	2	2	1
F00037	EG	2	2	2	1
F00038	EG	2	2	2	1
F00039	F04458	2	2	2	1
F00040	F01158	2	2	2	1

Findings were graded as follows;

(Continued)

Ease of removal from cage: 1: Docile and allowing itself to be handled, 2: rearing or cowering (normal score), 3: running about; hard to catch.

Ease of handling: 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing (normal score), 3: struggling and trying to bite observer's hand.

Muscle tone: 1: Decreased, 2: normal (normal score), 3: increased.

Fur conditions: 1: Normal (normal score), 2: slightly soiled, 3: markedly soiled.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm			
		Mucous membranes	Lacrimation	Salivation	Piloerection
F00024	F01156	1	1	1	1
F00025	F03359	1	1	1	1
F00026	F01157	1	1	1	1
F00027	F03358	1	1	1	1
F00028	F04460	1	1	1	1
F00029	F04457	1	1	1	1
F00030	F03357	1	1	1	1
F00031	F04459	1	1	1	1
F00032	F04456	1	1	1	1
F00033	F01159	1	1	1	1
F00034	F01160	1	1	1	1
F00035	F03356	1	1	1	1
F00036	F03360	1	1	1	1
F00037	EG	1	1	1	1
F00038	EG	1	1	1	1
F00039	F04458	1	1	1	1
F00040	F01158	1	1	1	1

Findings were graded as follows;

Mucous membranes: 1: Normal (normal score), 2: brown, 3: hemorrhage, 4: swelling.

Lacrimation: 1: None (normal score), 2: mild, 3: marked.

Salivation: 1: None (normal score), 2: mild, 3: marked.

Piloerection: 1: None (normal score), 2: mild, 3: marked.

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Observation of animals on observer's palm	
		Pupil size	Respiration
F00024	F01156	2	1
F00025	F03359	2	1
F00026	F01157	2	1
F00027	F03358	2	1
F00028	F04460	2	1
F00029	F04457	2	1
F00030	F03357	2	1
F00031	F04459	2	1
F00032	F04456	2	1
F00033	F01159	2	1
F00034	F01160	2	1
F00035	F03356	2	1
F00036	F03360	2	1
F00037	EG	2	1
F00038	EG	2	1
F00039	F04458	2	1
F00040	F01158	2	1

Findings were graded as follows;

(Continued)

Pupil size: 1: Mydriasis, 2: normal (normal score), 3: miosis.

Respiration: 1: Normal (normal score), 2: bradypnea, 3: dyspnea.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Frequency of urination (during a 2-minute period)	Frequency of defecation (during a 2-minute period)	Frequency of rearing (during a 2-minute period)	Frequency of grooming (during a 2-minute period)
F00024	F01156	0	0	16	0
F00025	F03359	0	1	8	0
F00026	F01157	0	0	5	0
F00027	F03358	1	0	8	0
F00028	F04460	1	1	13	0
F00029	F04457	0	0	13	0
F00030	F03357	0	0	4	0
F00031	F04459	1	0	7	0
F00032	F04456	0	0	6	0
F00033	F01159	0	0	20	0
F00034	F01160	0	0	10	0
F00035	F03356	0	0	9	0
F00036	F03360	0	0	14	0
F00037	EG	0	0	14	0
F00038	EG	0	0	18	0
F00039	F04458	0	0	18	0
F00040	F01158	1	0	6	0

EG: Excluded from grouping because body weight was extremely different from the mean.

(Continued)

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test			
		Gait	Palpebral closure	Consciousness	Behavioral abnormalities
F00024	F01156	1	1	2	1
F00025	F03359	1	1	2	1
F00026	F01157	1	1	2	1
F00027	F03358	1	1	2	1
F00028	F04460	1	1	2	1
F00029	F04457	1	1	2	1
F00030	F03357	1	1	2	1
F00031	F04459	1	1	2	1
F00032	F04456	1	1	2	1
F00033	F01159	1	1	2	1
F00034	F01160	1	1	2	1
F00035	F03356	1	1	2	1
F00036	F03360	1	1	2	1
F00037	EG	1	1	2	1
F00038	EG	1	1	2	1
F00039	F04458	1	1	2	1
F00040	F01158	1	1	2	1

Findings were graded as follows;

(Continued)

Gait: 1: Normal (normal score), 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure: 1: Eyelids open normally (normal score), 2: eyelids half-closed, 3: eyelids closed.

Consciousness: 1: Comatose; no response, 2: exploring behavior (normal score), 3: excited and moving spasmodically.

Behavioral abnormalities: 1: Not observed (normal score), 2: straub's tail reaction, 3: moving backward, 4: writhing, 5: self-biting.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 12-2. (Continued) Detailed clinical signs by FOB in female rats during acclimatization (recovery group)

Quarantine/ acclimatization animal No.	Animal No.	Open-field test	
		Righting reflex	
F00024	F01156		1
F00025	F03359		1
F00026	F01157		1
F00027	F03358		1
F00028	F04460		1
F00029	F04457		1
F00030	F03357		1
F00031	F04459		1
F00032	F04456		1
F00033	F01159		1
F00034	F01160		1
F00035	F03356		1
F00036	F03360		1
F00037	EG		1
F00038	EG		1
F00039	F04458		1
F00040	F01158		1

Findings were graded as follows;

Righting reflex: 1: Righting itself immediately (normal score),

2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

EG: Excluded from grouping because body weight was extremely different from the mean.

Attachment 13.

Background Data

Crl:CD(SD) Female Rats
9 - 11 weeks

Urinalysis

Exam.item	Unit	N	Value			
			Mean ± SD	Min.	Max.	Range of 2SD
UV	mL	84	11.0 ± 4.7	4.2	29.0	1.6 - 20.4
S.G.		84	1.050 ± 0.015	1.012	1.080	1.020 - 1.080
Na	mEq/L	55	131.1 ± 50.7	15.8	252	29.7 - 232.5
K	mEq/L	55	261.3 ± 83.4	91.5	422.6	94.5 - 428.1
Cl	mEq/L	55	181.3 ± 68.8	48.1	338.4	43.7 - 318.9
Na	mEq/day	55	1.26 ± 0.39	0.13	1.96	0.48 - 2.04
K	mEq/day	55	2.51 ± 0.62	0.64	3.82	1.27 - 3.75
Cl	mEq/day	55	1.74 ± 0.53	0.21	2.74	0.68 - 2.80

N: Number of animals

Hashima Laboratory, Nihon Bioresearch Inc.

Data collected between March 2017 and March 2023.

Data compiled in April 2023.

Attachment 14.

Background Data

CrI:CD(SD) Female Rats
9 - 11 weeks

Exam.item	Unit	N	Mean \pm SD	Min.	Max.	Range of 2SD
AST	U/L	54	91.3 \pm 18.6	59.5	165.7	54.1 - 128.5
ALT	U/L	54	24.6 \pm 6.3	17.7	62.3	12.0 - 37.2
ALP	U/L	34	94.3 \pm 22.4	55.1	155.8	49.5 - 139.1
T-Cho	mg/dL	54	57.7 \pm 13.0	32.2	86.9	31.7 - 83.7
TG	mg/dL	54	15.4 \pm 7.7	7.6	48.0	0.0 - 30.8
T-Bil	mg/dL	54	0.11 \pm 0.02	0.09	0.16	0.07 - 0.15
UN	mg/dL	54	16.4 \pm 2.8	11.1	28.7	10.8 - 22.0
CRE	mg/dL	54	0.37 \pm 0.04	0.30	0.47	0.29 - 0.45
IP	mg/dL	54	7.4 \pm 0.8	5.7	9.1	5.8 - 9.0
Ca	mg/dL	54	9.8 \pm 0.3	9.2	10.5	9.2 - 10.4
Glu	mg/dL	54	125.0 \pm 12.8	92.7	160.8	99.4 - 150.6
Na	mEq/L	54	142.7 \pm 1.7	139.8	150.6	139.3 - 146.1
K	mEq/L	54	3.98 \pm 0.22	3.48	4.55	3.54 - 4.42
Cl	mEq/L	54	106.7 \pm 2.2	95.5	109.7	102.3 - 111.1
TP	g/dL	54	5.65 \pm 0.34	4.98	6.81	4.97 - 6.33
A/G		54	1.06 \pm 0.11	0.84	1.27	0.84 - 1.28
alb	%	54	51.3 \pm 2.6	45.6	56.0	46.1 - 56.5
α_1 -glb	%	54	19.2 \pm 1.9	14.3	23.1	15.4 - 23.0
α_2 -glb	%	54	8.4 \pm 0.8	6.8	10.0	6.8 - 10.0
β -glb	%	54	15.9 \pm 1.2	13.2	18.5	13.5 - 18.3
γ -glb	%	54	5.2 \pm 1.4	3.0	9.1	2.4 - 8.0
Alb	g/dL	54	2.90 \pm 0.23	2.48	3.65	2.44 - 3.36

N: Number of animals

Hashima Laboratory, Nihon Bioresearch Inc.
Data collected between June 2021 and November 2022.

Data compiled in April 2023.

Attachment 15.

Background Data

Organ weights		Ctrl: CD(SD) Male Rats 9-11 weeks						
Organ	Unit	N	Mean	±	S.D.	Min.	Max.	Range of 2S.D.
Body weight	(g)	50	346	±	34	269	420	278 ~ 414
Brain	(g)	50	2.07	±	0.09	1.87	2.26	1.89 ~ 2.25
	(g%)	50	0.60	±	0.05	0.48	0.74	0.50 ~ 0.70
Thymus	(g)	50	0.55	±	0.12	0.34	0.81	0.31 ~ 0.79
	(g%)	50	0.16	±	0.04	0.09	0.24	0.08 ~ 0.24
Heart	(g)	50	1.23	±	0.13	0.89	1.44	0.97 ~ 1.49
	(g%)	50	0.36	±	0.03	0.28	0.41	0.30 ~ 0.42
Liver	(g)	50	9.91	±	1.07	7.74	12.54	7.77 ~ 12.05
	(g%)	50	2.86	±	0.18	2.54	3.49	2.50 ~ 3.22
Spleen	(g)	50	0.74	±	0.12	0.53	0.99	0.50 ~ 0.98
	(g%)	50	0.21	±	0.03	0.15	0.29	0.15 ~ 0.27
Kidneys	(g)	50	2.72	±	0.23	2.03	3.32	2.26 ~ 3.18
	(g%)	50	0.79	±	0.06	0.64	0.92	0.67 ~ 0.91
Adrenals	(mg)	50	58.8	±	8.4	46.9	84.7	42.0 ~ 75.6
	(mg%)	50	17.1	±	2.3	12.2	22.1	12.5 ~ 21.7
Testes	(g)	50	3.09	±	0.34	2.34	3.98	2.41 ~ 3.77
	(g%)	50	0.90	±	0.11	0.71	1.14	0.68 ~ 1.12
Epididymides	(g)	40	0.87	±	0.14	0.60	1.13	0.59 ~ 1.15
	(g%)	40	0.25	±	0.03	0.19	0.33	0.19 ~ 0.31

N: Number of animals

Hashima Laboratory, Nihon Bioresearch Inc.

Data collected between March 2021 and March 2023.

Data compiled in April 2023.

信 頼 性 保 証 陳 述 書

試験番号：430157

表 題：プロピオン酸エチルのラットを用いた 28 日間反復投与毒性試験

当試験が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（薬食発 0331 第 8 号，平成 23・03・29 製局第 6 号，環保企発第 110331010 号，平成 23 年 3 月 31 日）に従って実施され，この最終報告書には試験の方法が正確に記載され，かつ生データが正確に反映されていることを保証する。

調査については別紙 1, 2 のとおり実施し，調査結果を運営管理者及び試験責任者へ報告した。

2024 年 3 月 22 日

株式会社日本バイオリサーチセンター 羽島研究所

信頼性保証部門責任者



別紙 1

調 査 項 目	調査実施日	運営管理者及び試験責任者への報告日
1. 試験計画書	2023年11月14日	2023年11月15日
2. 動物の受け入れ	2023年11月15日	2023年11月15日
3. コンピュータプロトコール	2023年11月15日	2023年11月15日
4. 被験物質の安定性確認	2023年11月16日	2023年11月16日
5. 投与検体の濃度及び安定性の確認	2023年11月16日	2023年11月16日
6. 試験計画書変更書 (No.1)	2023年11月22日	2023年11月24日
7. 被験物質の管理	2023年11月24日	2023年11月24日
8. 投与検体の調製	2023年11月24日	2023年11月24日
9. 投与	2023年11月24日	2023年11月24日
10. 一般状態観察	2023年11月24日	2023年11月24日
11. 動物飼育管理	2023年11月24日	2023年11月24日
12. 行動機能 (FOB) 観察	2023年11月29日	2023年12月 1日
13. 体重測定	2023年11月30日	2023年12月 1日
14. 摂餌量測定	2023年11月30日	2023年12月 1日
15. 群分け及び個体識別	2023年12月 1日	2023年12月 1日
16. 尿検査	2023年12月15日	2023年12月21日
17. 自発運動量測定	2023年12月18日	2023年12月21日
18. 感覚反応検査	2023年12月19日	2023年12月21日
19. 握力測定	2023年12月19日	2023年12月21日
20. 膣垢検査	2023年12月21日	2023年12月21日
21. 剖検・採血・器官重量測定 (投与期間終了時)	2023年12月21日	2023年12月21日
22. 血液学的検査 (血漿分取、測定) (投与期間終了時)	2023年12月21日	2023年12月21日
23. 血液生化学的検査 (血清分取、測定、保存用血清の保管) (投与期間終了時)	2023年12月21日	2023年12月21日
24. 試験計画書変更書 (No.2)	2023年12月28日	2023年12月28日
25. 標本作製 (病理: 切り出し)	2024年 1月 4日	2024年 1月 4日
26. 試験計画書変更書 (No.3)	2024年 1月 9日	2024年 1月 9日
27. 尿検査	2024年 1月10日	2024年 1月10日
28. 標本作製 (病理: 薄切)	2024年 1月16日	2024年 1月16日
29. 病理組織学的検査	2024年 2月14日	2024年 2月14日

別紙 2

調 査 項 目	調査実施日	運営管理者及び試験 責任者への報告日
30. 生データ	2024年 3月 1日 ～ 3月 6日	2024年 3月 7日
31. 最終報告書（一次案）	2024年 3月 1日 ～ 3月 7日	2024年 3月 7日
32. 標本	2024年 3月 6日	2024年 3月 7日
33. 生データ（再調査）	2024年 3月 11日	2024年 3月 11日
34. 最終報告書（一次案）（再調査）	2024年 3月 11日	2024年 3月 11日
35. 生データ	2024年 3月 22日	2024年 3月 22日
36. 最終報告書	2024年 3月 22日	2024年 3月 22日