最 終 報 告 書

（訂正版）

試験表題：Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた
経口投与による反復投与毒性･生殖発生毒性併合試験

試験番号：R-1089

作成日：2013 年 8 月 23 日

試験期間：2011 年 10 月 21 日~2012 年 3 月 28 日

試験施設
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1. 目次

1. 目次 2
2. 試験実施概要 7
2.1 試験計画書 7
2.2 試験目的 7
2.3 試験委託者 7
2.4 試験受託者 7
2.5 試験実施施設 7
2.6 被験物質 7
2.7 試験日程 7
2.8 試験責任者 8
2.9 試験担当者 8
2.10 試験成績の信頼性に影響を及ぼしたと思われる環境要因 8
2.11 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 8
2.12 資料保存 9
2.13 試験責任者の記名・なつ印 9
3. 要約 10
3.1 反復投与毒性 10
3.2 生殖発生毒性 10
4. 緒言 11
4.1 GLP 11
4.2 毒性試験ガイドライン 11
4.3 動物の福祉 11
5. 試験材料及び方法 12
5.1 被験物質及び媒体 12
5.1.1 被験物質 12
5.1.2 媒体 13
5.2 投与液の調製及び保存方法 13
5.2.1 媒体の調製及び保存 13
5.2.2 被験液の調製及び保存 13
5.2.3 被験液の安定性 14
5.2.4 被験液の濃度・均一性確認 14
5.3 試験動物種及び系統の選択理由 15
5.4 試験動物 15
5.5 飼育条件 16
5.6 動物の識別 16

5.7　投与経路、投与期間及び投与回数並びに回復期間とそれらの 選択理由 17
5.8　投与方法 17
5.9　投与量及び群構成 17
5.10　投与量の設定根拠 18
5.11　観察及び検査の方法 18
5.11.1　一般状態の観察 18
5.11.2　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定 18
5.11.3　体重測定 19
5.11.4　摂餌量測定 20
5.11.5　膣垢検査 20
5.11.6　交配方法 20
5.11.7　分娩及び哺育観察 20
5.11.8　尿検査（摂水量測定を含む） 22
5.11.9　血液学検査 23
5.11.10　血液化学検査 24
5.11.11　血中ホルモン測定 24
5.11.12　病理学検査 25
5.12　統計解析 26
5.12.1　パラメータの算出 26
5.12.2　検定 26
6.　試験結果 28
6.1　一般状態（Table 1-1~1-7、Appendix 1-1~1-22） 28
6.2　詳細な一般状態の観察、機能検査、握力測定及び自発運動量の測定（Fig. 1~5、Table 2-1~2-84、Appendix 2-1~2-258） 28
6.2.1　ホームケージ内観察（Table 2-1~2-23、Appendix 2-1~2-72） 28
6.2.2　手に持っての観察（Table 2-24~2-46、Appendix 2-73~2-144） 28
6.2.3　オープンフィールド内観察（Table 2-47~2-69、Appendix 2-145~2-216） 28
6.2.4　機能検査（Table 2-70~2-74、Appendix 2-217~2-230） 28
6.2.5　握力（Table 2-75~2-79、Appendix 2-231~2-244） 28
6.2.6　自発運動量（Fig. 1~5、Table 2-80~2-84、Appendix 2-245~2-258） 28
6.3　体重（Fig. 6~8、Table 3-1~3-7、Appendix 3-1~3-22） 29
6.4　摂餌量（Fig. 9~11、Table 4-1~4-7、Appendix 4-1~4-22） 29
6.5　尿検査（摂水量測定を含む）（Table 5-1~5-16、Appendix 5-1~5-30） 29
6.6　血液学検査（Table 6-1~6-10、Appendix 6-1~6-10） 29

6.7　血液化学検査（Table 7-1~7-10、Appendix 7-1~7-10）.....30
6.8　器官重量（Table 8-1~8-12、Appendix 8-1~8-42）.....30
6.9　剖検所見（Table 9-1~9-5、Appendix 9-1~9-116）.....31
6.10　病理組織学検査（Table 10-1~10-13、Appendix 9-1~9-116）.....31
6.11　性周期（Table 11、Appendix 10-1~10-4）.....31
6.12　交配成績（Table 12、Appendix 11-1~11-4）.....31
6.13　分娩成績（Table 13、Appendix 12-1~12-4）並びに分娩及び哺育状態（Table 1-3 及び 1-4、Appendix 1-9~1-16）.....32
6.14　出生児の生存率（Table 14、Appendix 13-1~13-4）.....32
6.15　出生児の性比（Table 15、Appendix 14-1~14-4）.....32
6.16　出生児の体重（Table 16、Appendix 15-1~15-4）.....32
6.17　出生児の生後 4 日肉眼観察所見（Table 17、Appendix 16-1~16-4）.....32
7.　考察.....33
7.1　反復投与毒性.....33
7.2　生殖発生毒性.....33
8.　文献.....34

添付資料

添付資料 1　試験成績書（被験物質の特性）
添付資料 2　試験成績書（被験物質の安定性）
添付資料 3　試験成績書（被験液中 Octadecanoic acid, 1,2-ethanediyl ester の均一性・安定性）
添付資料 4　被験液中の被験物質濃度・均一性分析結果（初回投与）
添付資料 5　被験液中の被験物質濃度・均一性分析結果（投与 6 週）
添付資料 6　Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）における所見
添付資料 7　検査成績書（ジステアリン酸エチレングリコール）
添付資料 8　試験成績書(Octadecanoic acid, 1,2-ethanediyl ester の純度)

図

Fig. 1~5　自発運動量
Fig. 6~8　体重
Fig. 9~11　摂餌量

表

Table 1-1~1-7　一般状態
Table 2-1~2-23　ホームケージ内観察

Table 2-24~2-46　手に持っての観察
Table 2-47~2-69　オープンフィールド内観察
Table 2-70~2-74　機能検査
Table 2-75~2-79　握力
Table 2-80~2-84　自発運動量
Table 3-1~3-7　体重
Table 4-1~4-7　摂餌量
Table 5-1~5-16　尿検査（含、摂水量）
Table 6-1~6-10　血液学検査
Table 7-1~7-10　血液化学検査
Table 8-1~8-12　器官重量
Table 9-1~9-5　剖検所見
Table 10-1~10-13　病理組織学検査
Table 11　性周期
Table 12　交配成績
Table 13　分娩成績
Table 14　出生児の生存率
Table 15　出生児の性比
Table 16　出生児の体重
Table 17　出生児の生後 4 日肉眼観察所見

個体別表

Appendix 1-1~1-22　一般状態
Appendix 2-1~2-72　ホームケージ内観察
Appendix 2-73~2-144　手に持っての観察
Appendix 2-145~2-216　オープンフィールド内観察
Appendix 2-217~2-230　機能検査
Appendix 2-231~2-244　握力
Appendix 2-245~2-258　自発運動量
Appendix 3-1~3-22　体重
Appendix 4-1~4-22　摂餌量
Appendix 5-1~5-30　尿検査（含、摂水量）
Appendix 6-1~6-10　血液学検査
Appendix 7-1~7-10　血液化学検査
Appendix 8-1~8-42　器官重量
Appendix 9-1~9-116　剖検所見及び病理組織学検査
Appendix 10-1~10-4　性周期
Appendix 11-1~11-4　交配成績

Appendix 12-1~12-4　分娩成績
Appendix 13-1~13-4　出生児の生存率
Appendix 14-1~14-4　出生児の性比
Appendix 15-1~15-4　出生児の体重
Appendix 16-1~16-4　出生児の生後 4 日肉眼観察所見

2. 試験実施概要

2.1 試験計画書

試験番号 : R-1089

試験表題 : Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験
（A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats）

2.2 試験目的

本試験は、動物に被験物質を一定期間反復投与したときに現れる被験物質の一般毒性及び生殖発生毒性を明らかにすることを目的とした。

2.3 試験委託者

厚生労働省　医薬食品局　審査管理課　化学物質安全対策室
〒100-8916　東京都千代田区霞が関 1-2-2

2.4 試験受託者

株式会社ボゾリサーチセンター
〒151-0065　東京都渋谷区大山町 36-7

2.5 試験実施施設

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〒412-0039　静岡県御殿場市かまど 1284

2.6 被験物質

製造者	:	株式会社ワコーケミカル
名称	:	Octadecanoic acid, 1,2-ethanediyl ester
別名	:	ジステアリン酸エチレングリコール
CAS 番号	:	627-83-8
官報公示整理番号	:	2-767、2-2492
入手日	:	2011 年 9 月 21 日

2.7 試験日程

試験開始日	:	2011 年 10 月 21 日
被験物質出庫日	:	2011 年 11 月 4 日

動物入荷日　　：　2011 年 10 月 24 日
実験開始日（投与開始日）
　　：　2011 年 11 月 10 日
交配開始日　　：　2011 年 11 月 24 日
分娩開始日　　：　2011 年 12 月 16 日
母動物剖検開始日　：　2011 年 12 月 21 日
投与終了剖検日　　：　2011 年 12 月 22 日　（雄及び非交配群）
回復開始日　　：　2011 年 12 月 22 日
回復終了剖検日　　：　2012 年　1 月　5 日
動物試験終了日　　：　2012 年　1 月　5 日
実験終了日（病理組織学検査終了日）
　　：　2012 年　2 月 21 日
試験終了日　　：　2012 年　3 月 28 日

2.8　試験責任者

株式会社ボゾリサーチセンター　御殿場研究所　研究部

[redacted]

2.9　試験担当者

試験主担当者　　：
被験物質保存責任者：

臨床検査責任者　　：
化学分析責任者　　：
病理検査責任者　　：
統計解析責任者　　：

[redacted]

2.10　試験成績の信頼性に影響を及ぼしたと思われる環境要因

本試験に関し、試験成績の信頼性に影響を及ぼしたと思われる環境要因はなかった。

2.11　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

投与 6 週の尿検査において動物番号 4012 の摂水量が同投与群の他個体に比べ著しい低値を示したことから、確認のため当該例について摂水量とともに尿検査の全項目の追加検査を実施した。その結果、追加検査における摂水量は初期値と同様であったため、追加検査で得られたデータは全て参考値とした。なお、本操作による試験成績へ及ぼす影響はなかった。

2.12　資料保存

株式会社ボゾリサーチセンターの保存方法に従い、試験計画書（試験計画書変更書を含む）原本、記録文書、生データ、報告書類（最終報告書は原本）及び標本（被験物質保存サンプルを含む）は株式会社ボゾリサーチセンター御殿場研究所の資料保存施設に最終報告書提出後 5 年間保存する。期間終了後の保存については、厚生労働省医薬食品局審査管理課化学物質安全対策室と株式会社ボゾリサーチセンター間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿、血清）及び膣垢標本については、試験終了までに廃棄した。また、死産児、死亡児及び生後 4 日生存児については、出生率及び生後 4 日生存率に被験物質投与の影響が認められなかったため試験終了までに廃棄した。

2.13　試験責任者の記名・なつ印

[redacted]　2013 年 8 月 23 日 [redacted]

3. 要約

Octadecanoic acid, 1,2-ethanediyl ester の 0（対照群：0.5 w/v%メチルセルロース溶液）、100、300 及び 1000 mg/kg を Sprague-Dawley 系 SPF ラット（交配群として雌雄各 12 匹/群、雌には非交配群として対照群及び 1000 mg/kg 投与群に各 10 匹を追加）の雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 投与群の一部の動物（交配群雄 5 匹と非交配群雌 5 匹）については非交配群雌及び雄ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。

検査は、親動物について一般状態の観察、詳細な一般状態の観察、機能検査、握力測定及び自発運動量の測定、体重、摂餌量、尿検査（摂水量測定を含む）、血液学検査、血液化学検査、器官重量、剖検所見及び病理組織学検査、更に性周期、交配及び分娩・哺育観察、児動物について出生時の外表観察、出生時及び生後 4 日の雌雄体重並びに性比、生後 4 日の生存率及び肉眼観察とした。

3.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、いずれの検査にも被験物質投与の影響は認められなかった。

3.2 生殖発生毒性

親動物及び児動物のいずれの検査においても、被験物質投与による影響は認められなかった。

これらの結果から、本試験条件下において、本被験物質の雌雄動物における反復投与毒性に対する無影響量及び無毒性量は雌雄ともに 1000 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量はいずれも 1000 mg/kg と判断した。

4. 緒言

厚生労働省医薬食品局審査管理課化学物質安全対策室の委託により、Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験を実施したので、その成績を報告する。

なお、本試験は以下の基準を遵守し、ガイドライン等に準拠して、株式会社ボゾリサーチセンターで実施した。また、本試験は動物実験委員会の承認を受けている（承認番号：G110148）。

4.1 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」
  （平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23・3・29 製局第 6 号、環保企発第 110331010 号）

4.2 毒性試験ガイドライン

- 「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）

4.3 動物の福祉

- 「動物の愛護及び管理に関する法律」
  （昭和 48 年 10 月 1 日法律第 105 号、最終改正平成 23 年 6 月 24 日法律第 74 号）
- 「実験動物の飼養及び保管並びに苦痛の軽減に関する基準」
  （平成 18 年 4 月 28 日環境省告示第 88 号）
- 「動物実験の適正な実施に向けたガイドライン」
  （日本学術会議 平成 18 年 6 月 1 日）

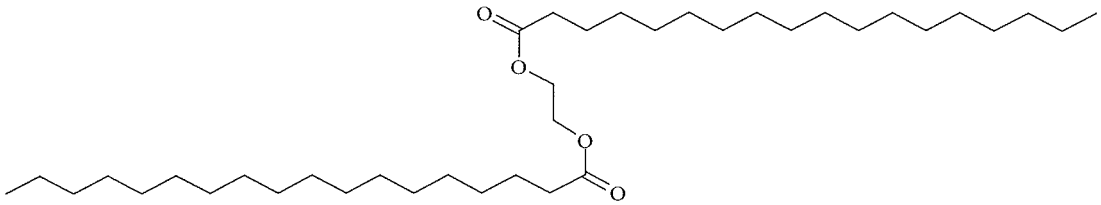
5. 試験材料及び方法

5.1 被験物質及び媒体

5.1.1 被験物質

Octadecanoic acid, 1,2-ethanediyl ester は[redacted]から以下の情報とともに購入した。また、試験開始前に赤外吸収スペクトルの測定により特性が確認されている（試験番号：A-2426、添付資料 1）。

製造者	:	株式会社ワコーケミカル
名称	:	Octadecanoic acid, 1,2-ethanediyl ester
別名	:	ジステアリン酸エチレングリコール
CAS 番号	:	627-83-8
官報公示整理番号	:	2-767、2-2492
構造式又は示性式	:	



分子式	:	$C_{38}H_{74}O_4$
分子量	:	594.99
常温における性状（外観）	:	白色のフレーク状
融点	:	約 63°C
沸点	:	73~79°C
引火点	:	248°C（クリーブランド開放式）
溶解性	:	アルコール、アセトン、エーテルに溶け、水に溶けにくい。
ロット番号	:	DCH0971
鹸化価(KOHmg/g)	:	201.6（添付資料 7）
純度	:	99.99%（Octadecanoic acid を主とする長鎖脂肪酸エステルの混合物としての固形分含量、添付資料 8）
入手量	:	1925 g
保存条件	:	密閉、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：2~8°C）に保存した。
保存場所	:	御殿場研究所被験物質保存室、第 2 研究棟 4 階被験物質調製室及び生化学部標準物質保存場所
安定性	:	投与期間終了後に株式会社ボゾリサーチセンター御殿場研究所において、残余被験物質の赤外吸収スペクト

ルを確認した結果、実験実施前に確認した参照スペクトルとほぼ同様であり安定性に問題はなかった（添付資料 2）。

取扱い上の注意　：　作業場の換気を十分に行い、マスク、保護眼鏡、保護手袋等の適切な保護具を着用し、直接の接触を防ぐ。取り扱い後は、手、顔等を良く洗い、うがいをする。

残量の処理　：　被験物質 5 g を保存試料（1.2 g を含水量及び純度測定に使用し、残りの 3.8 g を再保存）として御殿場研究所の資料保存施設に保存した。動物試験及び分析終了後の残量は全て焼却処分した。

5.1.2　媒体

名称　：　0.5 w/v%メチルセルロース溶液（略称：0.5 w/v%MC 溶液）

なお、媒体については、本試験に先立って実施した被験液中濃度測定法バリデーション及び均一性・安定性試験（試験番号：A-2426）[1]において、0.5 w/v%MC 溶液中での被験物質の安定性に良好な結果が得られていることから、0.5 w/v%MC 溶液を選択した。

5.2　投与液の調製及び保存方法

5.2.1　媒体の調製及び保存

メチルセルロース（METOLOSE SM-400、日本薬局方、信越化学工業株式会社、ロット番号：0055301）を注射用水（日本薬局方、株式会社大塚製薬工場、ロット番号：1C80、1C94）に溶解して 0.5 w/v%MC 溶液とした。調製した媒体は、調製当日に被験液の調製に使用した。また、被験液調製当日の被験物質を取り扱う前に対照群投与液として、必要量の媒体を褐色ガラス瓶に分注し、投与に使用するまで被験液と同様に保存した。

5.2.2　被験液の調製及び保存

濃度ごとに必要量の被験物質を正確に秤取した。媒体を少量ずつ添加し、乳鉢及び乳棒を用いて被験物質を媒体に懸濁させた。懸濁液をメスシリンダーに移すとともに、乳鉢及び乳棒を少量の媒体で数回洗い、その液もメスシリンダーに加えた。更に媒体をメスシリンダーに加えて規定量にメスアップし、所定の濃度液を調製した。調製は 5 日に 1 回以上の頻度で最大 5 日分を一括して行い、調製した被験液は褐色ガラス瓶に入れて冷所（冷蔵庫内、許容値：1~10°C、実測値：5~8°C）に保存し、安定性の確認された範囲内で投与に使用した。残液はポリ瓶に回収又はペーパータオル等に吸着させて焼却処分した。

5.2.3　被験液の安定性

本被験物質の 1.00 及び 200 mg/mL 懸濁液（媒体：0.5 w/v%MC 溶液）は、褐色ガラス瓶に入れ冷所（冷蔵庫内、許容値：1~10°C）で 8 日間、その後室温で 24 時間安定であることが株式会社ボゾリサーチセンターで確認されている（試験番号：A-2426、添付資料 3）[1]。

5.2.4　被験液の濃度・均一性確認

初回投与及び投与 6 週の 2 回、投与に用いる各濃度の被験液（上・中・下層より各 10 mL 採取）について、投与に使用する前に株式会社ボゾリサーチセンター御殿場研究所で GC により濃度及び均一性確認を実施した。初回投与の確認において 60 mg/mL 液の表示値に対する被験物質の割合が 114.7%となり許容範囲（濃度：表示値に対する割合；100.0±10.0%）を上回ったため再調製し、再確認を行った。その結果、各濃度液における表示値に対する被験物質の割合は 96.0~110.0%、変動係数は 5.6%以下であり、いずれも許容範囲内（濃度：表示値に対する割合；100.0±10.0%、均一性：CV10.0%以下）であった（添付資料 4、5）ことから、被験液の調製に問題はなかったと考えられた。なお、GC を用いた被験液中濃度測定法バリデーションは株式会社ボゾリサーチセンター御殿場研究所（試験番号：A-2426）[1]で実施された。分析法の概略を以下に示した。

[標準物質]

被験物質から一部分配したものを用いた。

名称	:	Octadecanoic acid, 1,2-ethanediyl ester
ロット番号	:	DCH0971
保存条件	:	密閉、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：2~8°C）に保存した。
保存場所	:	御殿場研究所　被験物質保存室及び生化学部標準物質保存場所

[測定実測試料の調製]

マグネチックスターラーで攪拌しながら各測定試料を任意の場所から n=1 で採取し、以下の表に従い、アセトンで溶解・希釈、シリンジフィルターでろ過（最初の 1 mL は使用せず、廃棄）した測定実測試料を用時調製した。なお、溶解しにくい場合は超音波処理を行った。

濃度 (mg/mL)	溶解		希釈		希釈率
	採取量 (mL)	定容量 (mL)	1 次希釈液採取量 (mL)	定容量 (mL)	
20	1	50	1	20	1000
60	0.5	100	2	30	3000
200	0.5	200	1	25	10000

溶媒：アセトン

[GC システム]

機器名及び型式		メーカー
GC	HP6890N	Agilent Technologies, Inc.
インジェクタ	G2613A	
オートサンプラトレイ	G2614A	
データ処理ソフト	GC ChemStation G2070AJ	

[GC 測定条件]

カラム	:	DB-1ht（0.32 mm I.D.×15 m、膜厚 0.1 μm、Agilent Technologies Inc.）
キャリアガス	:	He
流量モード	:	コンスタントフローモード
流量	:	5.0 mL/min
注入口	:	スプリットレス注入口
注入口温度	:	400°C
検出器	:	Flame ionization detector（FID）
検出器温度	:	400°C
H_2 流量	:	40 mL/min
Air 流量	:	450 mL/min
オーブン温度	:	150°C（Hold 0 分）→320°C（10°C/min、Hold 3 分）
注入量	:	1 μL

5.3 試験動物種及び系統の選択理由

毒性試験法ガイドラインによりげっ歯類を用いた試験が必要とされていることからラットを選択した。また、この試験に使用された系統のラットは一般毒性試験、生殖発生毒性試験に広く用いられ、かつ、その特性がよく知られており、背景資料が豊富であることから選択した。

5.4 試験動物

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、厚木飼育センター〕の雄 62 匹及び雌 83 匹をそれぞれ 8 週齢で入手[注)]し、入荷日を馴化 1 日と起算して、3 日間の検疫期間を含む 17 日間の馴化飼育を行った。その間、一般状態の観察（1 回/日）、体重測定（馴化 1、3、10 及び 17 日の 4 回）、詳細な一般状態の観察（群分け前日の馴化 16 日に 1 回）を実施した。更に、雄について馴化終了日に陰嚢内の精巣の触診及び陰茎亀頭の観察を実施し、雌については膣垢を検疫期間終了後群分け日まで採取して性周期を調べた。その結果、性周期の異常が 2 例（耳標番号：521 及び 582）にみられ、不正咬合が雄 1 例（耳標番号：465）、陰茎突出が 1 例（耳標番号：470）にみられた。それらの異常例を除き、検疫・馴化期間中の一般状態、詳細な一般状態、体重推移、精巣の触診結果及び性周期（検疫期間終了後 13 日間）に異常がなく、性成熟に達した陰茎亀頭であり、健康と思われる雄 60 匹中 48

匹及び雌 81 匹中 68 匹を選択し、10 週齢で投与に使用した。投与開始時（10 週齢）の体重の変動範囲は雄で 380~446 g（平均体重：405 g）、雌は 222~285 g（平均体重：250 g）であり、雌雄それぞれ平均体重の±20%以内であった。

なお、動物は検疫・馴化期間中の体重増加量（入荷日~群分け時）により選別後、群分け当日（投与開始の前日）の体重に基づいて、非交配群も含め各群の平均体重ができるだけ均等となるよう各群に割付けた。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組み合わせ（ブロック配置法で必要な群を構成し、試験群及び群内の個体番号を無作為に割当てた）により行った。供試個体の選択条件を満たして余剰となった雌は無処置動物として継続飼育し、使用しなかった無処置動物は交配期間終了後に試験から除外した。その他の雌雄残余動物は投与開始後に試験から除外した。なお、試験から除外された動物は、有効利用を目的として動物管理責任者に移管した。

注）：試験計画書に従い、動物発注数は雄 60 匹及び雌 80 匹であったが、実際には雄 62 匹及び雌 83 匹が納入された。

5.5　飼育条件

動物は、温度 23±3°C（実測値：22~25°C）、相対湿度 50±20%（実測値：40~55 %）、換気回数 10~15 回/h、照明 12 時間/日（07:00~19:00）の動物飼育室（飼育室番号：905 号室）でブラケット式金属製網ケージ（W254×D350×H170 mm：リードエンジニアリング株式会社）に交配中を除いて個別に収容した。なお、妊娠 17 日から授乳 4 日までは、床敷（ホワイトフレーク：日本チャールス・リバー株式会社、ロット番号：2011-2）を入れたプラスチック製エコンケージ（W340×D400×H185 mm：日本クレア株式会社）に 1 腹単位で収容した。

飼料は NMF 固形（放射線滅菌、オリエンタル酵母工業株式会社、ロット番号：110714、110817）をステンレス製給餌器により自由に摂取させた。

飲料水は御殿場市営水道水を自動給水装置（ブラケット式金属製網ケージでの飼育時）又は給水瓶（プラスチック製エコンケージでの飼育時）により自由に摂取させた。

飼料及び床敷中の混入物質の分析に関しては、使用したロットについて Eurofins Scientific Analytics で実施した分析結果を入手した。また、飲料水については、水道法に準拠した施設全体の水質の分析を定期的（年 4 回）に芝浦セムテック株式会社に依頼して得られたデータを入手した。これらのデータにより飼料、床敷及び飲料水中の混入物質が試験成績に影響を与える可能性のないことを確認し、分析報告書の写しを保存した。

5.6　動物の識別

動物は番号（雄：446~507、雌：508~590）が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000 の位は群（対照群、低、中及び高用量の順）、100 の位は性別（0 番を雄、1 番を雌）、10 と 1 の位は個体番号を示す 4 桁の動物番

号を設定した。各飼育ケージに投与量（群）ごとに色分けしたケージラベルを付け、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日（雄及び非交配群の雌）、交尾成立日（交配群の雌雄）及び分娩日（交配群の雌）を明記した。

5.7 投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間は雄では 42 日間（交配前 14 日間、交配期間 14 日間、その後 14 日間）、交配群の雌では 41~46 日間（交配前 14 日間、交配期間及び妊娠期間を通して授乳 4 日まで）、非交配群の雌では 42 日間とした。また、不妊であった動物（動物番号：3111）については 40 日間とした。回復期間は投与終了後 14 日間とし、その間投与を行わなかった。投与回数は反復投与試験で一般的に行われている 1 回/日（7 回/週）とした。

5.8 投与方法

投与方法は、げっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は 5 mL/kg 体重とし、フレキシブル胃ゾンデを用いて投与液を 1 日 1 回、08:38~12:18 の間に強制経口投与した。ただし、投与時に分娩中であった動物は分娩終了を待って、14:20~14:48 の間に投与した。対照群には媒体のみを同様に投与した。個体ごとの投与液量は（表示単位：0.1 mL）、直近の体重を基準に算出した。

5.9 投与量及び群構成

投与量は 100、300 及び 1000 mg/kg の 3 用量とし、試験群はこれらの用量群に媒体を投与する対照群を加え 4 群構成とした。1 群当たりの動物数は交配を行う交配群として各群で雌雄各 12 匹、交配しない非交配群として対照群及び高用量群で雌各 10 匹とした。なお、対照群及び高用量群における雄の群内番号 8 番以降、雌の群内番号 18 番以降の各 5 匹は、最終投与終了日以降、回復動物とした。群構成を表 1-1.及び 1-2.に示した。

表 1-1.群構成表（雄）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群	
				動物数	動物番号
対照群	0	0	5	12	1001~1012 注1
低用量群	100	20	5	12	2001~2012
中用量群	300	60	5	12	3001~3012
高用量群	1000	200	5	12	4001~4012 注1

注 1： 群内番号 8 番以降の 5 匹は、最終投与終了日以降、回復動物とした。

表 1-2.群構成表（雌）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群		非交配群	
				動物数	動物番号	動物数	動物番号
対照群	0	0	5	12	1101~1112	10	1113~1122 注2
低用量群	100	20	5	12	2101~2112	—	—
中用量群	300	60	5	12	3101~3112	—	—
高用量群	1000	200	5	12	4101~4112	10	4113~4122 注2

注 2： 群内番号 18 番以降の 5 匹は、最終投与終了日以降、回復動物とした。

5.10 投与量の設定根拠

本試験の投与量は、先に実施した「Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）、株式会社ボゾリサーチセンター、試験番号：N-R029、投与量：250、500 及び 1000 mg/kg/day」[2]の結果（添付資料 6）を参考に設定した。投与量設定試験では、高用量の 1000 mg/kg 投与群においても死亡例はみられず、一般状態、体重、摂餌量及び剖検所見に被験物質投与の影響はみられなかった。しかし、1000 mg/kg 投与群では、雄で総たん白質の低値、心臓相対重量の高値、雌でヘマトクリット値及び総たん白質の高値が認められた。250 及び 500 mg/kg 投与群では、いずれも雄で総たん白質の低値が認められた。したがって、本試験では毒性試験法ガイドラインに示されている限度試験の最高投与量である 1000 mg/kg を高用量とし、以下公比約 3 で除して 300 及び 100 mg/kg をそれぞれ中及び低用量に設定した。

5.11 観察及び検査の方法

試験日の起算は、投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与期間終了の翌日）を回復 1 日、回復 1 日から 7 日を回復 1 週、交尾成立日を妊娠 0 日、分娩終了日を授乳 0 日、出産日（出生日）を哺育 0 日（生後 0 日）とし、以下に示す項目について、それぞれ記載の時期に観察及び検査を実施した。

5.11.1 一般状態の観察

全個体について、検疫・馴化期間中は毎日 1 回、投与期間中は毎日 3 回（投与前、投与直後及び投与後 1~3 時間）、回復期間中は毎日 1 回（午前中）、それぞれ生死、身体の外観、姿勢、行動及び排泄物（尿、糞）などの一般状態における異常の有無を観察した。なお、投与 2 週以降の動物のハンドリングを伴った定期的な観察は、詳細な一般状態の観察と兼ねて行った。

5.11.2 詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について行った。投与開始前（馴化期間中）に 1 回、また、雄及び非交配群は投与期間中及び回復期間中毎週 1 回、交配群雌は交配前投与期間中毎週 1 回、妊娠期間中及び授乳期間中は指定された日（交尾動物は妊娠 1、7、

14 及び 20 日、分娩動物は授乳 4 日）にそれぞれ行った。

機能検査、握力測定及び自発運動量の測定は、各群の 5 匹（雄の群内番号 8~12 番、交配群雌の各群の分娩順で動物番号が若い順[注]、非交配群の群内番号 18~22 番）について行った。投与期間中は交配群の雌で授乳 4 日（投与 41~43 日）に、その他は投与期間終了週（投与 6 週、投与 41 日）に、回復期間中は、対照群及び高用量群の雌雄で回復期間終了週（回復 2 週、雌雄ともに回復 13 日）に行った。

上記の観察、検査及び測定は、動物をランダムに配置し、観察者に対して投与量などの情報を制限（ブラインド化）した状態で行った。ただし、自発運動量の測定に関しては、ブラインド化を行わなかった。なお、詳細な一般状態の観察及び機能検査の観察・検査結果について、実数データ以外はスコア化した評点法を用いて記録した。

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対 照 群	1101、1102、1104、1105、1107
低用量群	2103、2107、2110、2111、2112
中用量群	3101、3104、3107、3108、3110
高用量群	4104、4106、4109、4111、4112

1) 詳細な一般状態の観察

ケージ内観察として姿勢、痙攣、異常行動、手に持っての観察としてケージからの取り出し易さ、被毛・皮膚の状態、眼・鼻の分泌物、眼球突出、眼瞼閉鎖状態、可視粘膜、自律神経機能（流涙、流涎、立毛、瞳孔径、異常呼吸）、ハンドリングに対する反応、ハンドリング時の発声、オープンフィールド内観察として覚醒状態、痙攣、異常行動、常同行動、歩行、姿勢、身繕い、立ち上がり回数、排泄物（排糞数、排尿）について観察した。

2) 機能検査

聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅について検査した。

3) 握力測定

機能検査に引き続き、CPU ゲージ MODEL-RX-5（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測定した。

4) 自発運動量の測定

握力測定に引き続き、実験動物用自発運動センサーNS-AS01（株式会社ニューロサイエンス）を用いて自発運動量を測定した。測定時間は 1 時間とし、10 分間隔及び 0~60 分の測定値を集計した。

5.11.3 体重測定

全個体について、馴化 1、3、10 及び 17 日に体重を測定した。交配群の雄及び非交配群の雌は投与 1、8、15、22、29、36、42 日及び剖検日に、回復動物は更に回復 1、

8、14 日及び剖検日に、交配群の雌は投与 1、8、15 日、妊娠 0、7、14 及び 20 日、授乳 0 及び 4 日並びに剖検日に体重を測定した。なお、午後の分娩観察時に分娩の終了が確認された個体の授乳 0 日の体重測定（14:03~17:02 の間）を除き、測定当日の投与前、08:18~11:21 の間に体重測定を行った。剖検日には、前日から約 16 時間絶食させた後、相対器官重量算出に備えて体重を 07:33~11:03 の間に測定した。また、妊娠 25 日未分娩動物については、搬出前に体重を測定した。

5.11.4　摂餌量測定

全個体について、交配群の雄及び非交配群の雌は投与 1、8、15、30、36 及び 42 日に、回復動物は更に回復 1、8 及び 14 日に、交配群の雌は投与 1、8 及び 15 日、妊娠 1、7、14 及び 20 日並びに授乳 2 及び 4 日に残餌量を測定し、前日の給餌量との差から 1 匹当たりの 1 日摂餌量を算出した。給餌量及び残餌量の測定は測定当日の投与前、08:19~11:25 の間に行った。

5.11.5　膣垢検査

馴化期間中は雌全個体について検疫期間終了後から群分け日まで毎日膣垢を採取し、性周期異常の有無について調べた。

交配前投与期間中は交配群の雌の全個体について、投与開始日から交尾成立まで毎日膣垢を採取し、多数の角化上皮細胞から成る膣垢像を発情の指標とし、発情回数及び発情期から次の発情期までの日数（性周期）を調べた。

交配期間中は膣垢内の精子の有無を調べるとともに膣垢像を発情前期、発情期、発情後期及び発情休止期に分類した。

非交配群については、剖検時における性周期ステージを調べるため、剖検 6 日前から剖検日まで毎日膣垢を採取し、鏡検した。なお、鏡検結果については、解剖日の性周期の判別のための参考データとした。

5.11.6　交配方法

交配前投与期間終了後、交配群の同じ投与群の雌雄を 1:1 で終夜同居させ、翌朝、膣栓形成あるいは膣垢中に精子を確認したものを交尾成立とみなした。交配開始日を 0 日と起算して交尾までに要した日数を調べた。同一雌雄による同居期間は最長 5 日間であった。

5.11.7　分娩及び哺育観察

1)　母動物の観察

交尾の確認された雌動物は妊娠 21 日から妊娠 25 日の午前中まで 1 日 2 回（午前・午後、妊娠 25 日は午前に 1 回）分娩の有無並びにその終了を確認するとともに分娩状態の異常の有無を観察した。分娩が 17 時までに終了していた場合、その日を授乳 0 日とした。交尾成立から分娩終了までを妊娠期間とし、妊娠期間を 0.5 日単位で算出、

1日単位で集計した。

分娩が終了した母動物は授乳4日まで出生児を哺育させ、児集め、営巣及び授乳を指標として哺育状態を観察し、授乳5日に病理学検査に供した。なお、妊娠25日の10時までに分娩が終了しなかった300 mg/kg投与群の1例（動物番号：3111）は、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、病理学検査に供した。妊娠の有無を確認した結果、着床が認められなかったため不妊とみなした。

2) 出生児の観察

生後0日に出生児数及び死産児数を数え、それぞれ外表異常の有無を観察[注)]し、性別を判定して体重を測定した。出生児は体重を個体別に測定した後、母動物に哺育させた。死産児はブアン液で固定して保存した。

生後4日まで毎日1回、死亡児の有無を確認した。死亡児は肉眼による異常の有無を観察した後、ブアン液で固定して保存した。

生後4日に全生存児の性別を判定し、個体別に体重を測定後、肉眼による異常の有無を観察した後、イソフルラン深麻酔下でブアン液に浸漬し、固定して保存した。

注）：頭部の陥没や裂、顔面の鼻吻や上下顎、口唇のゆがみや裂、眼瞼や耳介の大きさ、形状、左右のバランス、胸胴部のゆがみや大きさ、内部臓器の突出、尾部の長さ、形状、数、欠損、四肢部の長さ、形状、指の数、欠損及び左右のバランスに注意して観察し、正常と異なる場合を異常とした。

5.11.8　尿検査（摂水量測定を含む）

投与期間終了週（投与 6 週、投与 36~37 日）及び回復期間終了週（回復 2 週、回復 8~9 日）に検査を実施した。投与期間中は検査当日の投与後に、雄では群内番号 8~12 番、非交配群では群内番号 18~22 番の各群それぞれ 5 匹を、回復期間中は回復動物の全個体を、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で 4 時間尿を、次いで自由摂食・自由摂水下でその後の 20 時間尿を採取した。検査項目を表 2. に示した。採取した最初の 4 時間尿について pH 以下沈渣までの検査と尿量を、その後に得られた 20 時間尿について浸透圧及び電解質（ナトリウム、カリウム、塩素）と尿量の測定を行った。尿量は 4 時間の尿量と 20 時間の尿量を合計して 1 日量を算出した。電解質は 20 時間尿について濃度を測定し、測定濃度と 24 時間の尿量から 1 日当たりの排泄量を算出した。摂水量は、採尿器をセットしたケージに収容した状態で前日からの 1 日の摂取量を、給水瓶を用いて測定した。

表 2.尿検査の項目、測定法及び使用機器など

検査項目	測定方法
pH	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
たん白質	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
ケトン体	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
グルコース	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
潜血	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
ビリルビン	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
ウロビリノーゲン	ﾏﾙﾃｨｽﾃｨｯｸｽ試験紙［ｼｰﾒﾝｽﾍﾙｽｹｱ・ﾀﾞｲｱｸﾞﾉｽﾃｨｸｽ株式会社］ a)
色調	肉眼観察
沈渣	鏡検法
尿量（4 時間量）	目盛付スピッツ管を用いた容量測定（単位：mL）
浸透圧	氷点降下法 b)（単位：mOsm/kg）
ナトリウム	イオン選択電極法 c)（単位：mmol/24h）
カリウム	イオン選択電極法 c)（単位：mmol/24h）
塩素	イオン選択電極法 c)（単位：mmol/24h）
尿量（20 時間量）	メスシリンダーを用いた容量測定（単位：mL）
摂水量（24 時間量）	重量測定

使用測定機器
a)：クリニテック 500（Siemens Healthcare Diagnostics Inc., Illinois, USA）
b)：自動浸透圧測定装置 オートアンドスタット OM-6030（アークレイ株式会社）
c)：臨床化学自動分析装置　TBA-120FR 形（東芝メディカルシステムズ株式会社）

5.11.9　血液学検査

全例について剖検前日（最終投与日あるいは回復 14 日）から一夜（16~21 時間）絶食させた。各群雌雄各 5 匹（動物番号が若い順、但し、交配群雌は分娩順の 5 匹注）について、イソフルラン麻酔下に開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液（約 1 mL）を採取した。得られた血液について、次の表 3.-1)に記載した項目及び方法により検査した。また、3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取した血液（0.9 mL）を遠心分離（3,000 rpm、1,600×g、10 分間）し、得られた血漿について表 3.-2)に記載の項目及び方法により検査した。妊娠 25 日未分娩動物についても採血し同様に検査した。なお、採血した全例について、May-Grünwald-Giemsa 染色法による血液塗抹標本を作製した。

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1101、1102、1104、1105、1107
低用量群	2103、2107、2110、2111、2112
中用量群	3101、3104、3107、3108、3110
高用量群	4104、4106、4109、4111、4112

表 3.血液学検査の項目、測定法及び使用機器など

1）EDTA-2K 加血液についての検査		
検査項目	測定方法	単位
赤血球数(RBC)	2 角度レーザーフローサイトメトリー法 a)	10^4/μL
ヘモグロビン量(Hb)	シアンメトヘモグロビン変法 a)	g/dL
ヘマトクリット値(Ht)	赤血球数及び平均赤血球容積から算出 a)	%
平均赤血球容積(MCV)	2 角度レーザーフローサイトメトリー法 a)	fL
平均赤血球血色素量(MCH)	赤血球数及びヘモグロビン量から算出 a)	pg
平均赤血球血色素濃度(MCHC)	ヘモグロビン量及びヘマトクリット値から算出 a)	g/dL
網赤血球率(Reticulocyte)	RNA 染色によるレーザーフローサイトメトリー法 a)	%
血小板数(Platelet)	2 角度レーザーフローサイトメトリー法 a)	10^4/μL
白血球数(WBC)	2 角度レーザーフローサイトメトリー法 a)	10^2/μL
白血球百分率注)	ペルオキシダーゼ染色によるフローサイトメトリー法 +2 角度レーザーフローサイトメトリー法 a)	%
白血球各細胞の絶対数注)	ペルオキシダーゼ染色によるフローサイトメトリー法 +2 角度レーザーフローサイトメトリー法 a)	10^2/μL
2）クエン酸ナトリウム加血液から分離した血漿についての検査		
検査項目	測定方法	単位
プロトロンビン時間(PT)	クロット法 b)	s
活性化部分トロンボプラスチン時間(APTT)	クロット法 b)	s
フィブリノーゲン量(Fibrinogen)	トロンボプラスチン法 b)	mg/dL
使用測定機器 a)：総合血液学検査装置　アドヴィア 120（Siemens Healthcare Diagnostics Inc., Illinois, USA） b)：血液凝固自動分析装置　ACL Elite Pro（Instrumentation Laboratory, MA, USA）		
注）：好中球(Neut.)、好酸球(Eosino.)、好塩基球(Baso.)、リンパ球(Lymph.)、単球(Mono.)及び大型非染色球(LUC)		

5.11.10　血液化学検査

血液学検査用試料と同時に採取した血液（約 6 mL）を凝固促進剤入り試験管（ベノジェクト II-オートセップ:テルモ株式会社）に採り、遠心分離（3,000 rpm、1,670×g、10 分間）し、得られた血清について表 4.-1)に記載の項目及び方法により検査した。また、ヘパリン加試験管（血液 1 mL 当たり約 20 単位のヘパリン）に採取した血液（約 2 mL）を遠心分離（3,000 rpm、1,600×g、10 分間）して得られた血漿について表 4.-2)に記載の項目及び方法により検査した。妊娠 25 日未分娩動物についても同様に検査した。血清の一部は血中ホルモン測定に備え、約 0.5 mL×3 本をサンプルチューブに分注し、–80°C の冷凍庫（許容範囲：–70°C 以下）に保存した。

表 4.血液化学検査の項目、測定法及び使用機器など

1）分離した血清についての検査		
検査項目	測定方法	単位
ALP	Bessey-Lowry 法 a)	IU/L
総胆汁酸（TBA）	3α-ヒドロキシステロイドデヒドロゲナーゼ a)	μmol/L
総コレステロール(T.cho)	CEH-COD-POD 法 a)	mg/dL
トリグリセライド(TG)	LPL-GK-GPO-POD 法 a)	mg/dL
リン脂質(PL)	PLD-ChOD-POD 法 a)	mg/dL
総ビリルビン(T.bilirubin)	ビリルビンオキシダーゼ法 a)	mg/dL
グルコース(Glucose)	グルコースデヒドロゲナーゼ法 a)	mg/dL
尿素窒素(BUN)	Urease-LEDH 法 a)	mg/dL
クレアチニン(Creatinine)	Creatininase-creatinase-sarcosine oxidase-POD 法 a)	mg/dL
ナトリウム(Na)	イオン選択電極法 a)	mmol/L
カリウム(K)	イオン選択電極法 a)	mmol/L
塩素(Cl)	イオン選択電極法 a)	mmol/L
カルシウム(Ca)	OCPC 法 a)	mg/dL
無機リン(P)	モリブデン酸法 a)	mg/dL
総たん白質(TP)	Biuret 法 a)	g/dL
アルブミン(Albumin)	BCG 法 a)	g/dL
A/G 比	総たん白質及びアルブミンから算出	
2）ヘパリン加血液から分離した血漿についての検査		
検査項目	測定方法	単位
AST(GOT)	UV-rate 法 a)	IU/L
ALT(GPT)	UV-rate 法 a)	IU/L
LDH	UV-rate 法 a)	IU/L
γ-GTP	L-γ-グルタミル-3-カルボキシ-4-ニトロアニリド法 a)	IU/L
使用測定機器		
a)：臨床化学自動分析装置　TBA-120FR 形（東芝メディカルシステムズ株式会社）		

5.11.11　血中ホルモン測定

他の観察及び検査結果から下垂体-甲状腺系への影響が認められなかったため 6.11.10 で得られた血清について血中ホルモン（T_3、T_4 及び TSH）測定は実施しなかった。

5.11.12　病理学検査

1)　剖検及び器官重量測定

最終投与翌日及び回復期間終了日に全ての生存動物について、採血した動物は採血後に、その他の動物はイソフルラン麻酔下で、腹大動脈切断により放血致死させ、それぞれ体外表並びに頭部、胸部及び腹部の器官・組織の肉眼検査を行った。なお、母動物については剖検時に黄体数及び着床痕数を数えた。次いで、全例について、以下に示す器官の重量を測定した。それら器官重量（絶対重量）と剖検時の体重から体重100 g当たりの相対重量を算出した。なお、*印をつけた両側性の器官については左右別々に測定し、その合計値で評価した。妊娠 25 日未分娩動物については、採血して放血致死させた後、同様に剖検を行い器官の重量を測定した。

脳、下垂体、甲状腺*（上皮小体を含む）、副腎*、胸腺、脾臓、心臓、肝臓、腎臓*、精巣*、精巣上体*、前立腺、精嚢（凝固腺を含む）、卵巣*、子宮

2)　病理組織学検査

全ての個体について、以下に示す全検査対象器官/組織をリン酸緩衝 10 vol%ホルマリン液で固定し、保存した。固定時に肺にはリン酸緩衝 10 vol%ホルマリン液を注入した。ただし、眼球、視神経はリン酸緩衝液で調製した 3 vol%グルタルアルデヒド・2.5 vol%ホルマリン液で固定後、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10 vol%ホルマリン液に置換し保存した。次いで、パラフィン包埋した後、切片とし（下線を施した器官・組織は固定・保存のみとした）、ヘマトキシリン・エオジン（H・E）染色標本を作製した。鏡検は、まず投与終了時剖検群における対照群及び高用量群の採血を行った動物及び妊娠 25 日未分娩動物の全検査対象器官/組織について行った。両側性の器官については両側を摘出し、坐骨神経、眼球、甲状腺、上皮小体、副腎、顎下腺、腎臓、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、精巣、卵巣、精巣上体及び精嚢（凝固腺含む）は両側並びに子宮は両角部を鏡検した。なお、舌下腺及び視神経は H･E 染色標本作製までとし、病理組織学検査は実施しなかった。その結果、高用量群の雌雄ともに被験物質投与によると考えられる変化はみられなかったため、中及び低用量群については鏡検しなかった。ただし、回復期間終了時の器官重量測定において 1000 mg/kg 投与群の精巣上体重量に対照群と比べ有意な低値が認められたことから、回復動物の精巣及び精巣上体の病理組織学検査を実施した。

大脳、小脳（橋を含む）、坐骨神経、脊髄（胸部）、眼球、視神経、<u>ハーダー腺</u>、下垂体、甲状腺、上皮小体、副腎、胸腺、脾臓、顎下リンパ節、腸間膜リンパ節、心臓、<u>胸大動脈</u>、気管、肺（気管支を含む）、<u>舌</u>、<u>喉頭</u>、<u>食道</u>、胃、十二指腸、空腸、回腸（パイエル板を含む）、盲腸、結腸、直腸、顎下腺、舌下腺、肝臓、膵臓、腎臓、膀胱、精巣、卵巣、精巣上体、子宮、腟、前立腺、精嚢（凝固腺を含む）、<u>皮膚（鼠径部）</u>、<u>乳腺（鼠径部）</u>、<u>胸骨（骨髄を含む）</u>、大腿骨（骨髄

を含む）、大腿部骨格筋、個体識別部（耳標を装着した耳介）

5.12　統計解析

5.12.1　パラメータの算出

以下の式により交尾率、授精率、受胎率及び出産率を群ごとに、妊娠期間、着床率、死産児率、外表異常率、出生率、生後 4 日生存率、生後 0 及び 4 日の出生児の性比を母動物ごとに算出した。なお、出生児の体重については母動物ごと雌雄別に平均値を求めた。

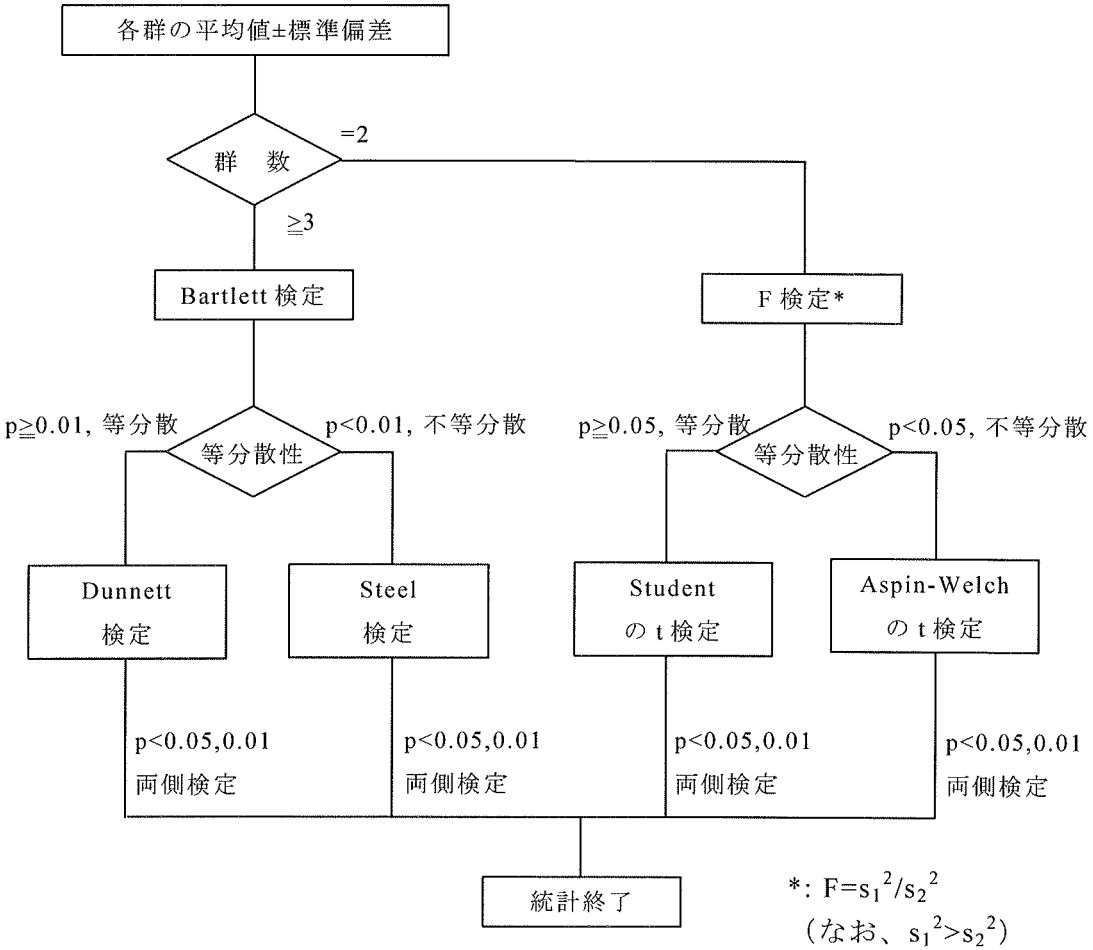
交尾率(%) =（交尾動物数/同居動物数）×100
授精率(%) =（雌を妊娠させた雄の数/交尾した雄の数）×100
受胎率(%) =（妊娠した雌の数/交尾した雌の数）×100
出産率(%) =（出生児出産雌数/妊娠雌数）×100
妊娠期間(日) = 妊娠 0 日から分娩した日までの日数
着床率(%) =（着床痕数/黄体数）×100
死産児率(%) =（死産児数/出生児数及び死産児数）×100
外表異常率(%) =（外表異常児数/出生児数及び死産児数）×100
出生率(%) =（出生児数/着床痕数）×100
生後 4 日生存率(%) =（生後 4 日の生存児数/出生児数）×100
生後 0 日の性比 = 雄出生児数/出生児数
生後 4 日の性比 = 生後 4 日の雄生存児数/生後 4 日の生存児数

5.12.2　検定

対照群と各用量群との差について以下の手法により統計学的有意性の検定を行った。

体重、体重増加量（雄及び非交配群雌：投与 1~42 日及び回復 1~14 日、交配群雌：投与 1~15 日、妊娠 0~20 日及び授乳 0~4 日、出生児：生後 0~4 日）、摂餌量、摂水量、発情期像発現回数、性周期（発情周期）、交尾までに要した日数、妊娠期間、黄体数、着床痕数、生存児数、出生児の性比（生後 0 及び 4 日）、オープンフィールド内観察（排糞数、立ち上がり回数）、機能検査（着地開脚幅）、握力及び自発運動量、尿検査の定量的項目、血液学検査、血液化学検査及び器官重量（含、剖検時体重）は、群ごとに平均値及び標準偏差を求め、次に示す模式図の方法に従って検定した[3][4][5]。

なお、不妊と判断された雌の交配開始後の交配成績を除くデータは統計解析より除外した。



着床率、死産児率、外表異常率、出生率及び生後 4 日生存率については、群ごとに平均値及び標準偏差を求め、Steel 検定（有意水準 0.05 及び 0.01、両側）を行った[5]。

交尾率、授精率、受胎率、出産率、聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射は、各群の交尾動物数、雌を妊娠させた雄動物数、妊娠雌動物数、出生児出産雌動物数、正常反射のみられた動物数より算出し、期待度数が 5 以下のセルがみられたため Fisher の直接確率計算法により検定（有意水準 0.05 及び 0.01、両側）を行った[6]。

6. 試験結果

6.1 一般状態（Table 1-1~1-7、Appendix 1-1~1-22）

いずれの投与群においても死亡動物はみられず、いずれの動物にも投与期間及び回復期間を通じて哺育状態を含め異常はみられなかった。

6.2 詳細な一般状態の観察、機能検査、握力測定及び自発運動量の測定（Fig. 1~5、Table 2-1~2-84、Appendix 2-1~2-258）

6.2.1 ホームケージ内観察（Table 2-1~2-23、Appendix 2-1~2-72）

いずれの動物にも異常はみられなかった。

6.2.2 手に持っての観察（Table 2-24~2-46、Appendix 2-73~2-144）

いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。

6.2.3 オープンフィールド内観察（Table 2-47~2-69、Appendix 2-145~2-216）

いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。また、立ち上がり回数及び排糞の個数には対照群と各被験物質投与群との間に有意差は認められなかった。

6.2.4 機能検査（Table 2-70~2-74、Appendix 2-217~2-230）

1) 投与期間終了週検査

いずれの動物にも聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射に異常はみられず、着地開脚幅には対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週検査

いずれの動物にも聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射に異常はみられず、着地開脚幅には対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

6.2.5 握力（Table 2-75~2-79、Appendix 2-231~2-244）

1) 投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

6.2.6 自発運動量（Fig. 1~5、Table 2-80~2-84、Appendix 2-245~2-258）

1) 投与期間終了週測定

交配群雌の 1000 mg/kg 投与群で 0-10 分の運動量に対照群と比べ有意な低値が認められたが、軽微な差であり以降の期間及び総運動量に異常はないことから、偶発性と判断した。

雄及び非交配群雌では対照群と被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

6.3 体重（Fig. 6~8、Table 3-1~3-7、Appendix 3-1~3-22）

1) 投与期間

雄の 300 mg/kg 投与群で体重増加量に対照群と比べて有意な高値が認められたが、用量に依存性のない変化であった。その他には各被験物質投与群と対照群との間に有意差は認められなかった。

交配群雌及び非交配群雌では交配前、妊娠及び授乳の各期間中、各被験物質投与群ともに対照群と同様な体重推移を示し、有意差は認められなかった。

2) 回復期間

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

6.4 摂餌量（Fig. 9~11、Table 4-1~4-7、Appendix 4-1~4-22）

1) 投与期間

交配群雌では 300 及び 1000 mg/kg 投与群の投与 8 日に対照群と比べ有意な低値が認められたが、非交配群の同時点には異常はないことから、対照群の一過性の軽微な高値に伴う相対的な低値と考えられ、偶発性と判断した。

雄及び非交配群雌では各被験物質投与群ともに対照群と比べ有意差は認められなかった。

2) 回復期間

対照群と 1000 mg/kg 投与群との間に有意差は認められなかった。

6.5 尿検査（摂水量測定を含む）（Table 5-1~5-16、Appendix 5-1~5-30）

1) 投与期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

定量項目については、いずれの検査項目においても被験物質投与群と対照群との間に有意差は認められなかった。

2) 回復期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

定量項目については、いずれの検査項目においても 1000 mg/kg 投与群と対照群との間に有意差は認められなかった。

6.6 血液学検査（Table 6-1~6-10、Appendix 6-1~6-10）

1) 投与期間終了時検査

雄では 100 mg/kg 投与群で対照群と比べ赤血球数の有意な高値、平均赤血球容積及び平均赤血球血色素量の有意な低値が認められたが、用量に依存性のない変化であった。

交配群雌では 1000 mg/kg 投与群でフィブリノーゲン量に対照群と比べ有意な低値が認められたが、軽微な変化であり他の血液凝固系パラメータに変動はないことから偶発性と判断した。その他に 100 mg/kg 投与群で白血球分画における好塩基球比率に有意な低値、300 mg/kg 投与群で白血球数並びに好中球比率及び絶対数に有意な低値が認められたが、用量に依存性のない変化であった。また、100 mg/kg 以上の投与群で好塩基球数に有意な低値が認められたが、白血球に占める割合の少ない分画におけるわずかな変動であり白血球数等の関連項目に異常はないことから偶発性と判断した。

非交配群雌の 1000 mg/kg 投与群で、対照群と比べ平均赤血球容積、平均赤血球血色素量、フィブリノーゲン量及び好酸球数に有意な低値が認められたが、いずれも軽微な変化であり生理的変動範囲内と判断した。

2) 回復期間終了時検査

1000 mg/kg 投与群の雌雄ではいずれの検査項目においても対照群との間に有意差は認められなかった。

6.7 血液化学検査（Table 7-1~7-10、Appendix 7-1~7-10）

1) 投与期間終了時検査

雄ではいずれの検査項目においても各被験物質投与群と対照群との間に有意差は認められなかった。

交配群雌では 300 mg/kg 投与群で対照群と比べ塩素の有意な高値が認められたが、用量に依存性のない変化であった。

非交配群雌の 1000 mg/kg 投与群で ALT に対照群と比べ有意な高値が認められたが、軽微な変化であり生理的変動範囲内と判断した。

2) 回復期間終了時検査

1000 mg/kg 投与群の雄ではいずれの検査項目においても対照群との間に有意差は認められなかった。

1000 mg/kg 投与群の雌で ALP に対照群と比べ有意な低値が認められたが、軽微な変化であり投与期間終了時検査に異常がみられないことから生理的変動範囲内と判断した。

6.8 器官重量（Table 8-1~8-12、Appendix 8-1~8-42）

1) 投与期間終了時検査

雄及び非交配群雌ではいずれの器官重量にも各被験物質投与群と対照群との間に有意差は認められなかった。

交配群雌では 100 mg/kg 投与群で脳、肝臓及び卵巣の絶対重量に対照群と比べ有意な低値が認められたが、用量に依存性のない変化であった。

2) 回復期間終了時検査

1000 mg/kg 投与群の雄で精巣上体の絶対及び相対重量に対照群と比べ有意な低値が認められた。

1000 mg/kg 投与群の雌ではいずれの器官重量にも対照群との間に有意差は認められなかった。

6.9　剖検所見（Table 9-1~9-5、Appendix 9-1~9-116）

1)　投与期間終了時検査

雄では肉眼的異常はみられなかった。

交配群及び非交配群雌で腺胃に暗赤色巣がみられたが、その発現状況あるいは病理学的性状から偶発性変化と考えられた。

妊娠 25 日未分娩（不妊）であった 300 mg/kg 投与群の 1 例（動物番号：3111）では肉眼的異常はみられなかった。

2)　回復期間終了時検査

対照群の雌雄の腺胃に暗赤色巣がみられたが、その発現状況から偶発性変化と考えられた。

6.10　病理組織学検査（Table 10-1~10-13、Appendix 9-1~9-116）

1)　投与期間終了時検査

いずれの器官/組織にも被験物質投与に起因する考えられる変化はみられなかった。

なお、いくつかの器官/組織に組織学的変化がみられたが、その発現状況あるいは病理学的性状から被験物質投与と関係しない偶発性変化と判断した。

妊娠 25 日未分娩（不妊）であった 300 mg/kg 投与群の 1 例では腟粘膜の粘液変性がみられ不妊との関連性も考えられたが、詳細は不明であった。不妊は中用量群の 1 例のみであり、偶発性にも発現しうることから、被験物質投与による影響は否定した。

2)　回復期間終了時検査

回復期間終了時、1000 mg/kg 投与群の精巣上体重量が対照群と比べて有意な低値を示したことから、対照群及び 1000 mg/kg 投与群の精巣上体及び精巣について病理組織学検査を実施した。その結果、精巣に軽微な精細管萎縮が対照群の 1 例にみられた以外、特記すべき組織学的変化はみられず、精巣上体重量減少の原因は不明であった。

6.11　性周期（Table 11、Appendix 10-1~10-4）

観察期間中に発情期像の発現が 1 回もみられず性周期が算出出来なかった対照群の 1 例（動物番号：1102）を除き性周期異常の動物はみられず、発情期像発現回数及び平均性周期日数には対照群と各被験物質投与群との間に有意差は認められなかった。

6.12　交配成績（Table 12、Appendix 11-1~11-4）

交配 5 日までに全例の交尾が成立し、交尾までに要した日数、交尾率、授精率及び受胎率には対照群と各被験物質投与群との間に有意差は認められなかった。

6.13　分娩成績（Table 13、Appendix 12-1~12-4）並びに分娩及び哺育状態（Table 1-3 及び 1-4、Appendix 1-9~1-16）

出産率、妊娠期間、黄体数、着床痕数、着床率、死産児率、出生児数、外表異常率及び出生率には対照群と各被験物質投与群との間に有意差は認められなかった。

妊娠動物の分娩状態では妊娠 21 又は 22 日に全例が分娩し、胎盤及び羊膜の処理は正常に行われ、哺育状態ではいずれの母動物にも児集め、営巣及び授乳行動に異常はみられなかった。

6.14　出生児の生存率（Table 14、Appendix 13-1~13-4）

生後 4 日の生存率には対照群と各被験物質投与群との間に有意差は認められなかった。

6.15　出生児の性比（Table 15、Appendix 14-1~14-4）

生後 0 及び 4 日の性比には対照群と各被験物質投与群との間に有意差は認められなかった。

6.16　出生児の体重（Table 16、Appendix 15-1~15-4）

生後 0 及び 4 日の雌雄体重並びに生後 0~4 日の間の体重増加量には対照群と各被験物質投与群との間に有意差は認められなかった。

6.17　出生児の生後 4 日肉眼観察所見（Table 17、Appendix 16-1~16-4）

いずれの出生児にも肉眼的異常はみられなかった。

7. 考察

Octadecanoic acid, 1,2-ethanediyl ester の 0（対照群：0.5 w/v%MC 溶液）、100、300 及び 1000mg/kg を、Sprague-Dawley 系 SPF ラットの雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 1000 mg/kg 投与群の一部の動物については雌雄ともに 42 日間投与した後、14 日間の回復期間を設け、毒性変化の可逆性を検討した。

7.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、一般状態、詳細な一般状態、機能検査、握力、自発運動量、体重、摂餌量、尿検査（摂水量を含む）、血液学検査、血液化学検査、器官重量、剖検及び病理組織学検査には被験物質投与の影響は認められなかった。なお、投与量設定試験において、1000 mg/kg 投与群の雄で総たん白質に低値、心臓相対重量に高値、雌でヘマトクリット値及び総たん白質に高値が認められ、250 及び 500 mg/kg 投与群の雄で総たん白質に低値が認められていたが、本試験では投与期間の延長にも関わらず同様の変化はみられなかった。投与量設定試験の投与期間は 2 週間であることから、変化は投与初期にみられ、その後回復した可能性が考えられた。

7.2 生殖発生毒性

性周期、交尾までに要した日数、交尾率、授精率及び受胎率には被験物質投与の影響は認められなかった。更に、出産率、妊娠期間、黄体数、着床痕数、着床率、死産児率、死産児の外表観察、出生児数及び出生率に被験物質投与の影響は認められず、授乳期間中の哺育状態にも異常が認められないことから、1000 mg/kg 投与群においても雌雄動物の交尾能、授精能及び受胎能、母動物の妊娠維持、分娩及び哺育行動などの生殖機能への影響はないと判断した。

出生児では、生後 0 日の外表観察、生後 0 及び 4 日の雌雄体重並びに性比、生後 4 日の生存率及び肉眼観察所見に被験物質投与による影響は認められなかった。

これらの結果から、本試験条件下で Octadecanoic acid, 1,2-ethanediyl ester を反復経口投与することにより、被験物質に起因すると考えられる変化はみられなかった。したがって、本被験物質の雌雄動物における反復投与毒性に対する無影響量及び無毒性量は雌雄ともに 1000 mg/kg と判断した。また、雌雄親動物と児動物における生殖発生毒性に対する無影響量及び無毒性量はいずれも 1000 mg/kg と判断した。

8. 文献

[1] [redacted] Octadecanoic acid, 1,2-ethanediyl ester の GC を用いた被験液中濃度測定法バリデーション及び均一性・安定性試験（媒体：0.5 w/v%メチルセルロース溶液）並びに IR を用いた特性及び安定性試験（株式会社ボゾリサーチセンター御殿場研究所、試験番号：A-2426、2011 年）

[2] [redacted] Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）（株式会社ボゾリサーチセンター、試験番号：N-R029、2011 年）

[3] Snedecor GW, Cochran WG. Statistical methods. 8th ed. Ames: Iowa State University Press; 1989.

[4] Dunnett, CW. New tables for multiple comparisons with a control. Biometrics 1964; 20: 482-91.

[5] Steel RGD. A multiple comparison rank sum test: Treatments versus control. Biometrics 1959; 15: 560-72.

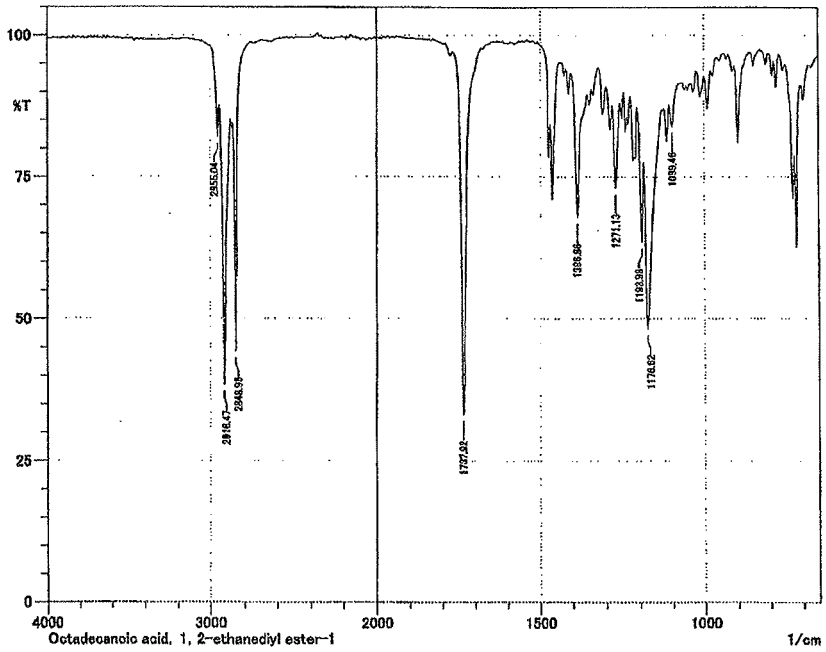
[6] 佐久間昭（1981）：薬効評価－計画と分析–II, pp.23-27, 387-389, 東京大学出版会, 東京.

R-1089
添付資料 1

試験番号：A-2426

試験成績書
[Octadecanoic acid, 1,2-ethanediyl ester の特性]

ステージ	:	実験の実施前
測定日	:	2011 年 10 月 1 日
被験物質	:	Octadecanoic acid, 1,2-ethanediyl ester （ロット番号 DCH0971）
試験項目	:	赤外吸収スペクトルの確認（ATR 法）
結果	:	赤外吸収スペクトルを以下に示す。



基準　：　「新規化学物質等に係る試験を実施する試験施設に関する基準」（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）

[redacted]　2011 年　11 月　19 日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

測定成績書
（被験物質の安定性）

試験番号	:	R-1089
被験物質	:	Octadecanoic acid,1,2-ethanediyl ester （ロット番号：DCH0971）
測定項目	:	赤外吸収スペクトルの確認（ATR 法）
ステージ	:	投与期間終了後
測定日	:	2012 年 1 月 6 日
判定基準	:	参照スペクトル [1)]と同一波数のところに同様な強度の吸収を認める。 1) [redacted] Octadecanoic acid,1,2-ethanediyl ester の GC を用いた被験液中濃度測定法バリデーション及び均一性・安定性試験（媒体：0.5 w/v%メチルセルロース溶液）並びに IR を用いた特性及び安定性試験（株式会社ボゾリサーチセンター御殿場研究所、試験番号：A-2426）
結果	:	参照スペクトルと同一波数のところに同様な強度の吸収を認めた。 なお、赤外吸収スペクトルは次のページに示す。
判定	:	適
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（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）

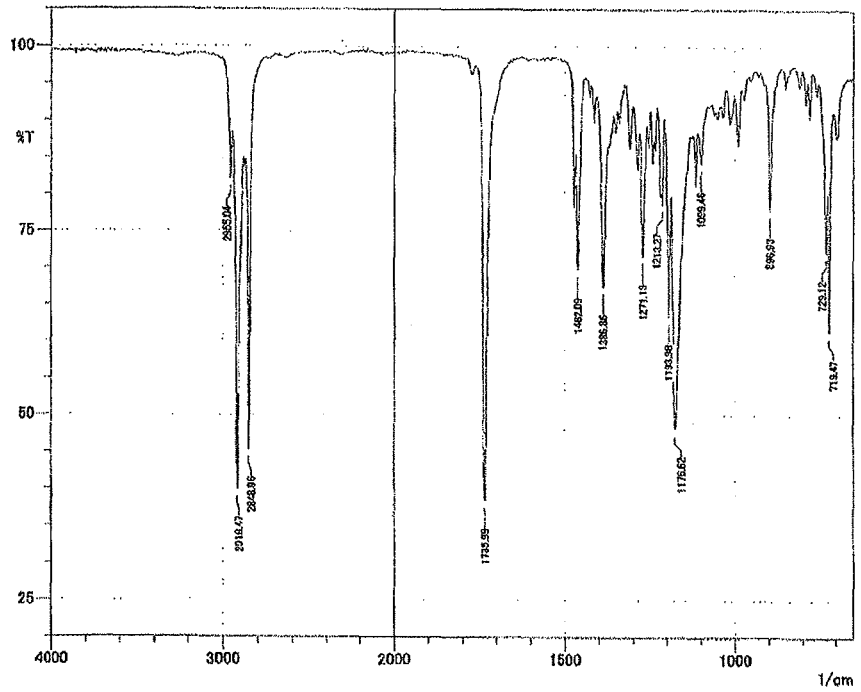
[redacted] 2012 年 1 月 13 日

化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

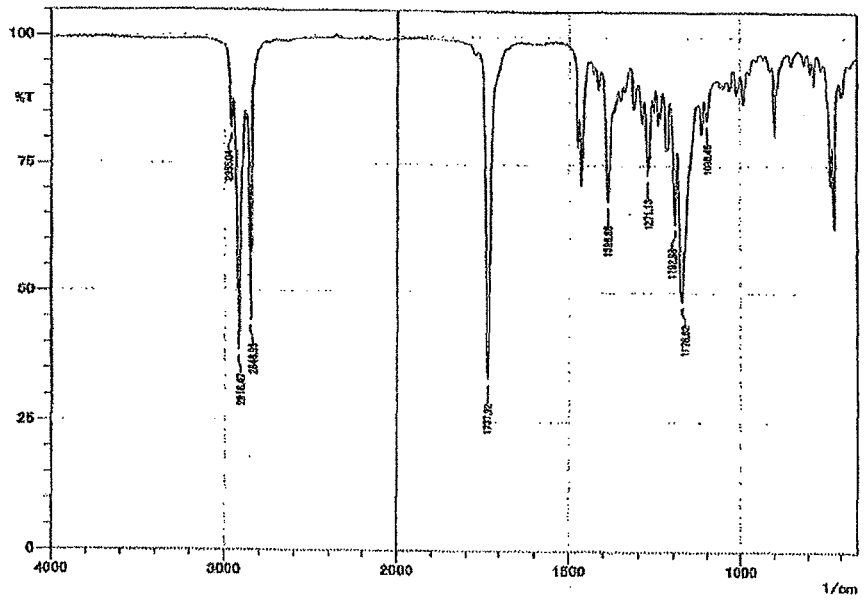
R-1089
添付資料２（2/2）

試験番号：R-1089
(2/2)

結果　　：　赤外吸収スペクトル



（投与期間終了後）



（参照スペクトル）

R-1089
添付資料 3

試験番号：A-2426（訂正版）

試験成績書

[被験液中 Octadecanoic acid, 1,2-ethanediyl ester の均一性・安定性]

被験物質　：　Octadecanoic acid, 1,2-ethanediyl ester
（ロット番号：DCH0971）

形態（媒体）　：　懸濁液（0.5 w/v%メチルセルロース溶液）

評価基準

安定性　：　残存率｛調製直後の測定濃度の平均値 (100) に対する保存後の測定濃度の平均値の割合｝が 100.0 ± 10.0%以内。

均一性　：　変動係数が 10.0%以下。

結果：

調製濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	
		調製直後	冷所 8 日間 + 室温 24 時間保存後
1.00	上	0.981	0.989
	中	1.010	1.003
	下	0.990	1.003
平均値 ± 標準偏差		0.994 ± 0.015	0.998 ± 0.008
残存率 (%)		100	100.4
変動係数(%)		1.5	0.8

調製濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	
		調製直後	冷所 8 日間 + 室温 24 時間保存後
200	上	211	211
	中	217	203
	下	227	199
平均値± 標準偏差		218 ± 8	204 ± 6
残存率 (%)		100	93.6
変動係数(%)		3.7	2.9

判定　：　被験液中の Octadecanoic acid, 1,2-ethanediyl ester は、褐色ガラスビン中で冷所 8 日間 + 室温 24 時間保存後の均一性及び安定性が確認された。

基準　：　「新規化学物質等に係る試験を実施する試験施設に関する基準」（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）

[redacted]　2011年 12月 16日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

R-1089
添付資料 4

分析結果

試験番号　：　R-1089
測定項目　：　濃度・均一性
ステージ　：　初回投与
分析日　：　2011 年 11 月 7 日（20, 200 mg/mL）
2011 年 11 月 8 日（60 mg/mL）

測定試料
被験物質　：　Octadecanoic acid, 1,2-ethanediyl ester
（ロット番号；DCH0971）
形態（媒体）　：　懸濁液（0.5 w/v%メチルセルロース溶液）
調製日　：　2011 年 11 月 7 日（20, 200 mg/mL）
2011 年 11 月 8 日（60 mg/mL）

評価基準
濃度　：　表示値に対する割合；100.0±10.0%
均一性　：　変動係数（CV）；10.0%以下

結果：

濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	平均値±標準偏差	表示値に対する割合 (%)	変動係数 (%)
20	上層	21.4	21.4±0.2	107.0	0.9
	中層	21.6			
	下層	21.3			
60	上層	63.6	63.3±0.4	105.5	0.6
	中層	62.8			
	下層	63.5			
200	上層	218	220±10	110.0	4.5
	中層	231			
	下層	211			

判定　：　適

R-1089
添付資料 5

分析結果

試験番号 : R-1089
測定項目 : 濃度・均一性
ステージ : 投与 6 週
分析日 : 2011 年 12 月 16 日

測定試料
被験物質 : Octadecanoic acid, 1,2-ethanediyl ester
（ロット番号；DCH0971）
形態（媒体） : 懸濁液（0.5 w/v%MC 溶液）
調製日 : 2011 年 12 月 15 日

評価基準
濃度 : 表示値に対する割合；100.0±10.0%
均一性 : 変動係数（CV）；10.0%以下

結果：

濃度 (mg/mL)	採取層	測定濃度 (mg/mL)	平均値±標準偏差	表示値に対する割合 (%)	変動係数 (%)
20	上層	19.3	19.2±0.2	96.0	1.0
	中層	19.2			
	下層	19.0			
60	上層	61.9	60.2±3.4	100.3	5.6
	中層	62.3			
	下層	56.3			
200	上層	210	208±5	104.0	2.4
	中層	211			
	下層	202			

判定 : 適

R-1089
添付資料 6

Octadecanoic acid, 1,2-ethanediyl ester のラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）における所見

試験番号：N-R029

被験物質		媒体 a)	Octadecanoic acid, 1,2-ethanediyl ester		
投与量(mg/kg)		0	250	500	1000
投与容量(mL/kg)		5	5	5	5
使用動物数 (♂/♀)		5/5	5/5	5/5	5/5
死亡動物数 (♂/♀)		0/0	0/0	0/0	0/0
死亡発現時期		—	—	—	—
一般状態	生存	—	—	—	—
	死亡	/	/	/	/
体重		/	—	—	—
摂餌量		/	—	—	—
血液学検査		/	—	—	Ht：↑(♀)
血液化学検査		/	TP：↓(♂)	TP：↓(♂)	TP：↓↓(♂)、↑(♀)
器官重量	絶対	/	腎臓：↑(♂)	—	—
	相対	/	—	—	心臓：↑(♂)
剖検	生存	胃(腺胃)：暗赤色巣(♀1/5)	—	胃(腺胃)：暗赤色巣(♂1/5、♀1/5)	胃(腺胃)：暗赤色巣(♀1/5)
	死亡	/	/	/	/

a) ：0.5w/v%メチルセルロース水溶液
– ：著変なし
/ ：データなし又は判別不明あるいは検定不能
↑又は↓；$p<0.05$，↑↑又は↓↓；$p<0.01$，(対照群との間に有意差あり)

R-1089
添付資料 7

検査成績書

2012年12月27日
株式会社 ワコーケミカル
宮崎県宮崎市清武町[redacted]

株式会社ボゾリサーチセンター 御中

Code No.329-27665
ジステアリン酸エチレングリコール

規格／等級	
Lot No.	DCH0971
数量	500g

検査項目	検査成績	規格値
外観	白色のフレーク状	白色～微黄色、粉末またはフレーク状
けん化価(KOHmg/g)	201.6	190.0～210.0
検査年月日	2011/01/19	

判 定	合格	検査責任者	[redacted]

成績書発行番号 9948152

R-1089
添付資料 8

A-2579

試験番号：A-2579 (1/1)

試験成績書
(Octadecanoic acid, 1,2-ethanediyl ester の純度)

測定日	:	2013 年 7 月 10 日
被験物質	:	Octadecanoic acid, 1,2-ethanediyl ester （ロット番号；DCH0971）
試験項目	:	純度測定及び水分測定（電量滴定法）
評価基準	:	なし
結果	:	純度；99.99% 水分；0.01%（0.01%, 0.01%, 0.02%）
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（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）

[redacted] 2013 年 7 月 17 日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

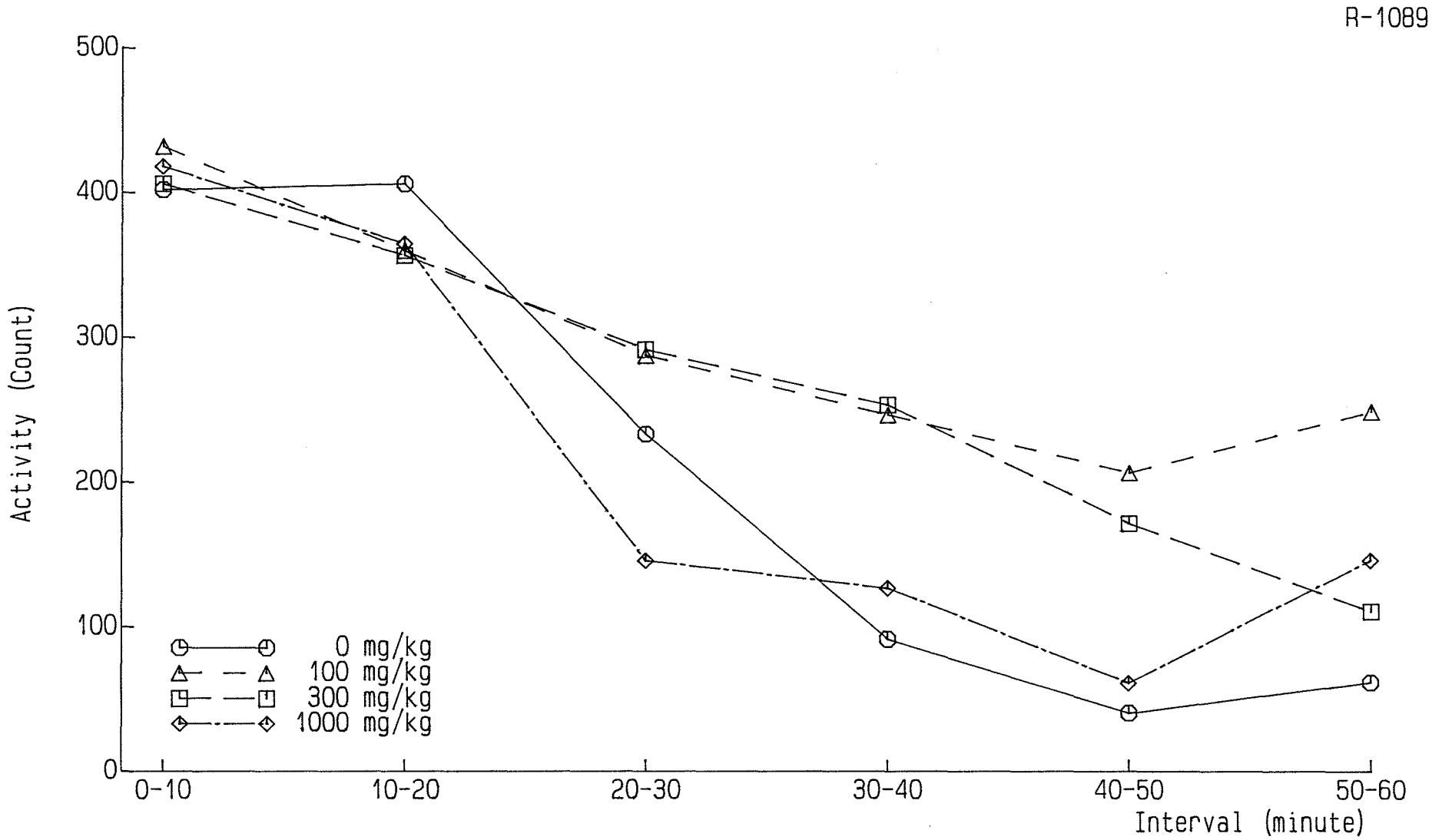


Fig.1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of male rats (Week 6 of administration)

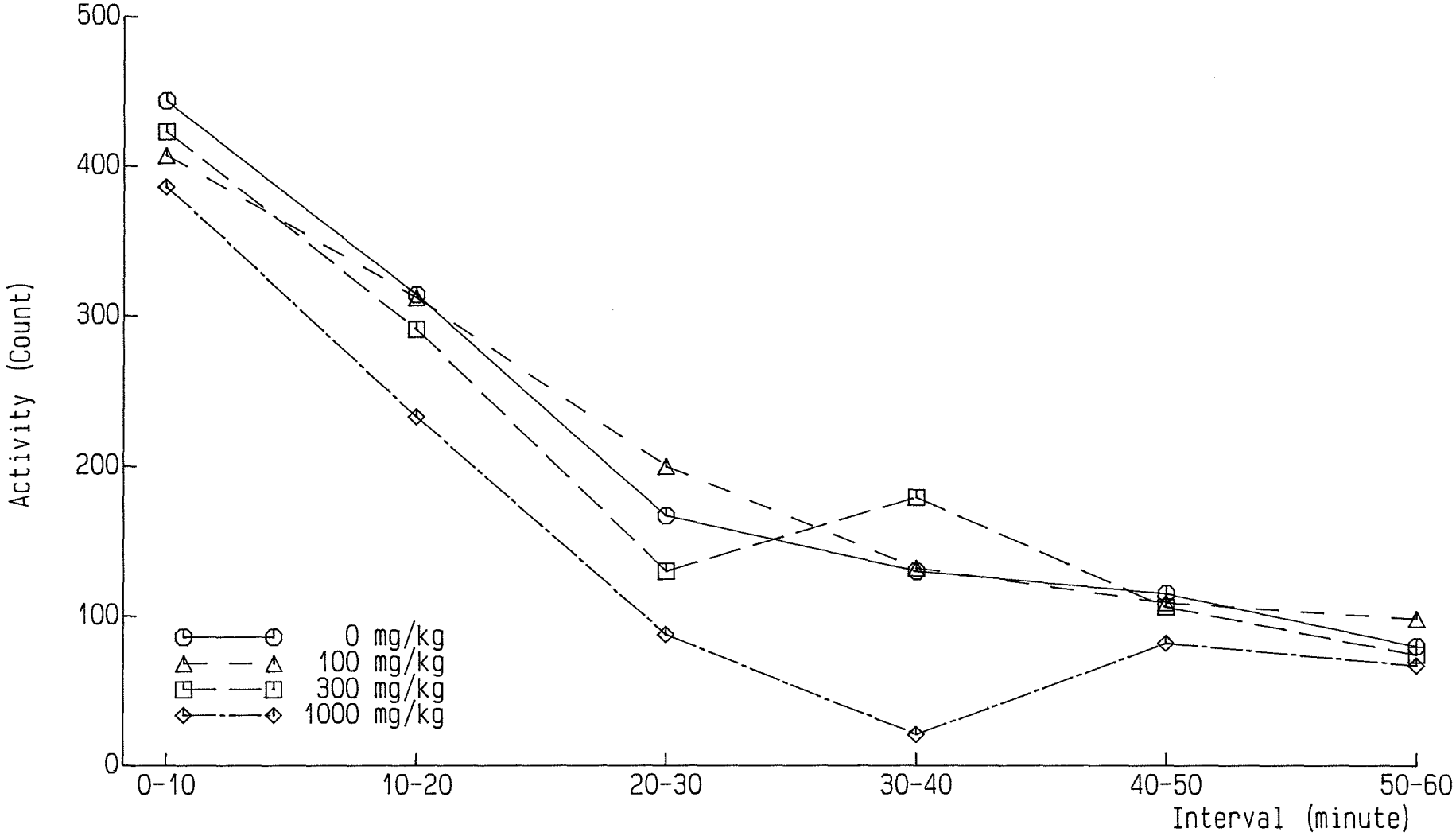


Fig.2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of female rats (Main group, Lactation day 4)

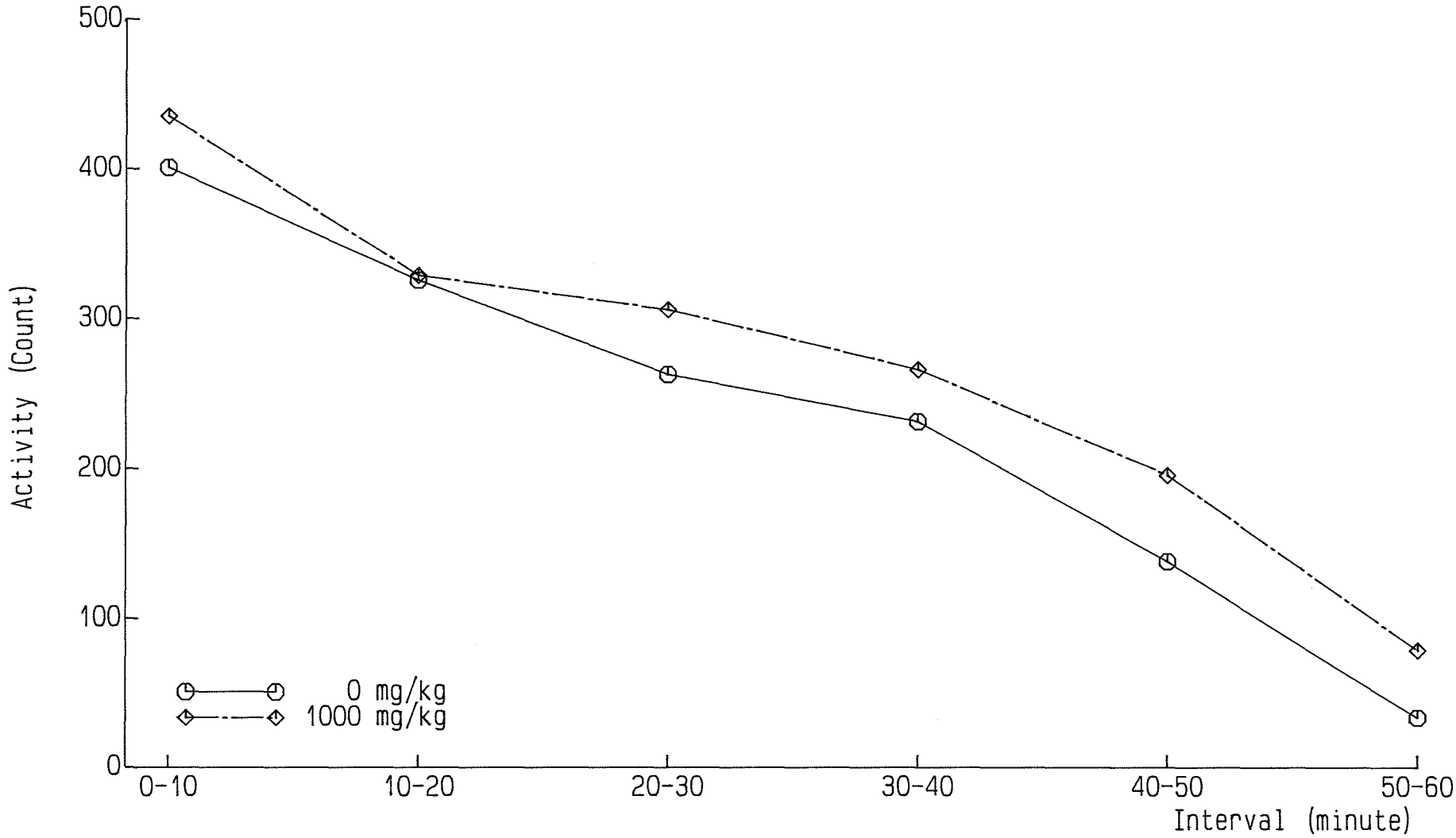


Fig.3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of female rats (Satellite group, Week 6 of administration)

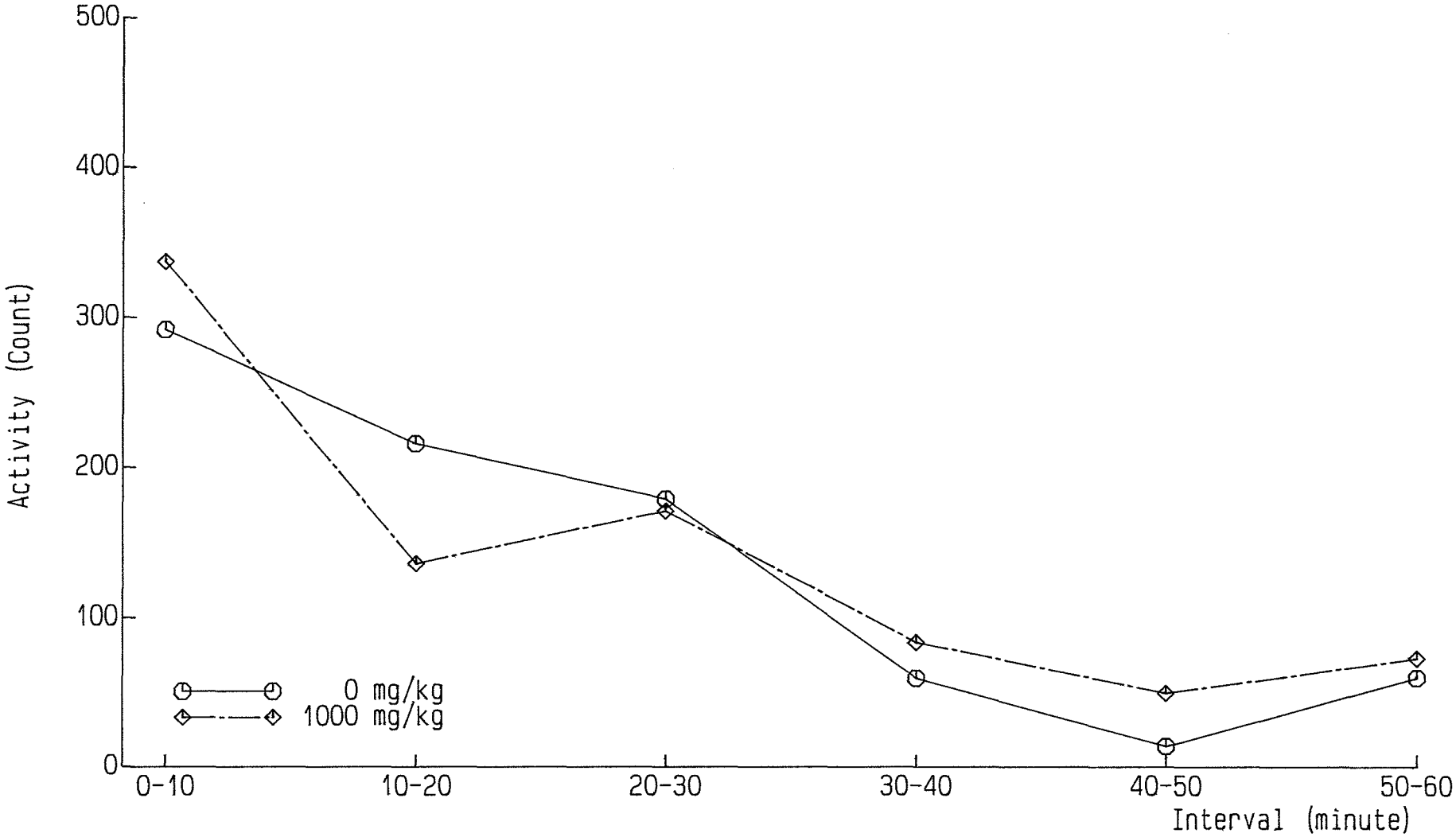


Fig.4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

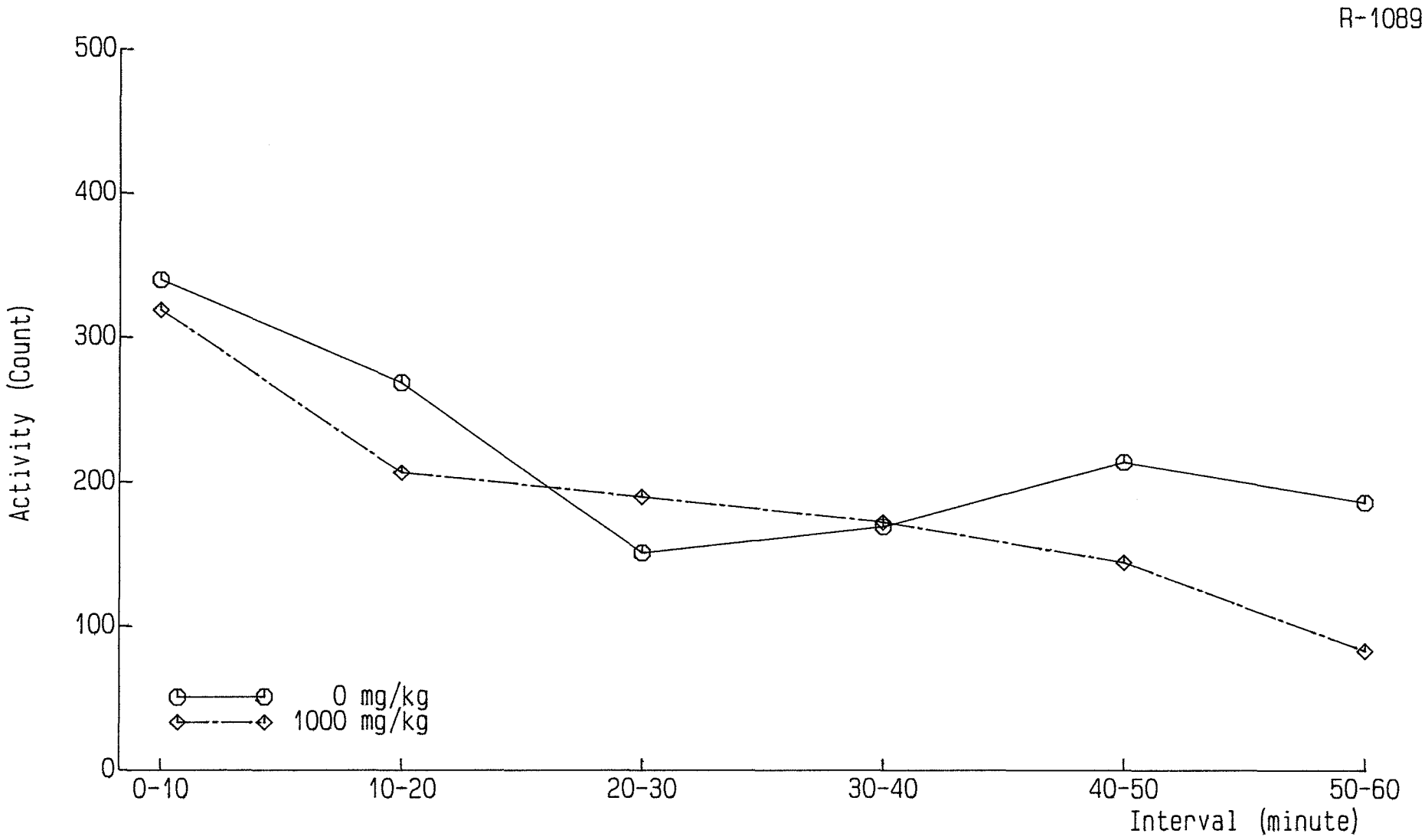


Fig.5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

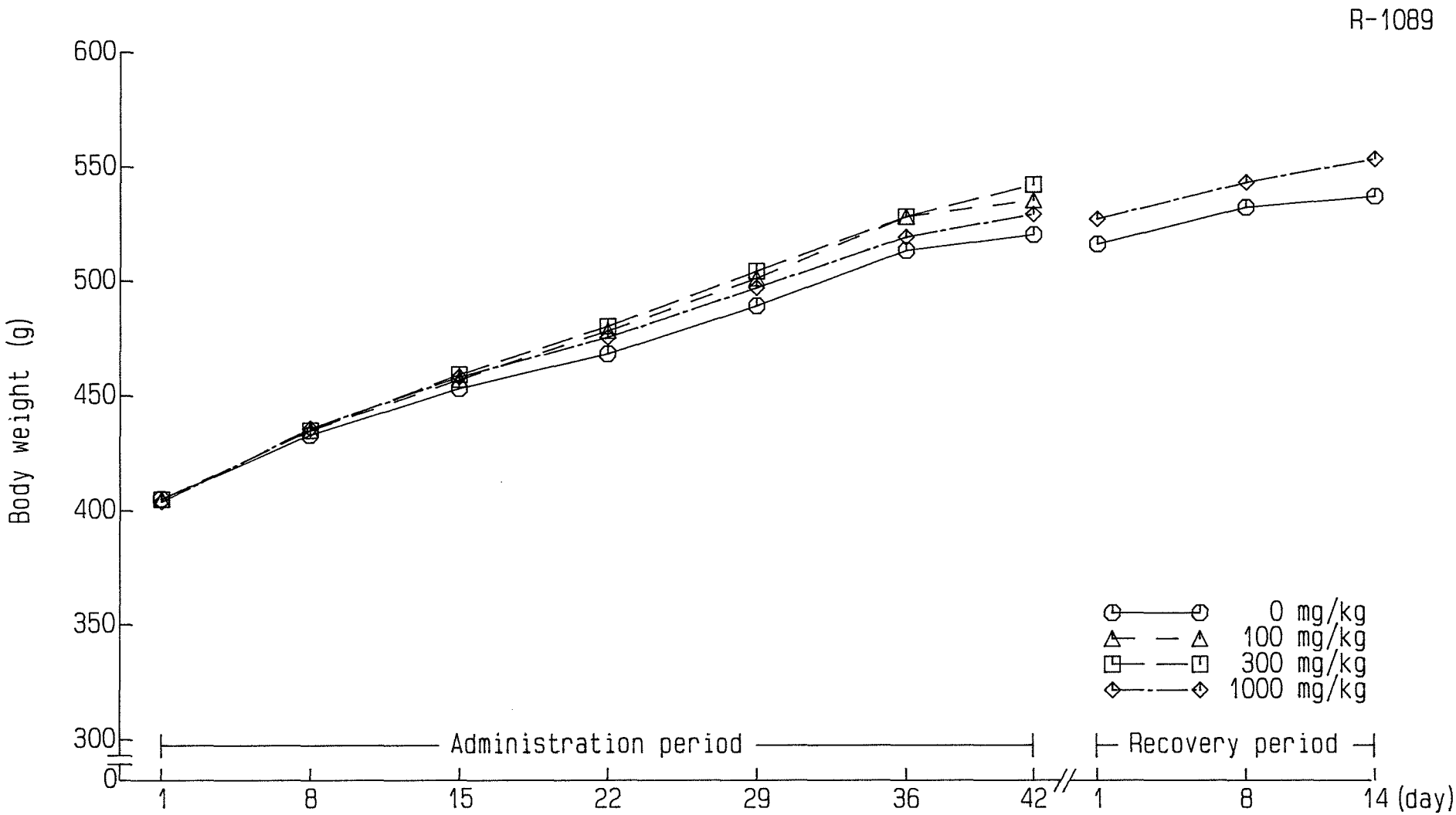


Fig.6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of male rats

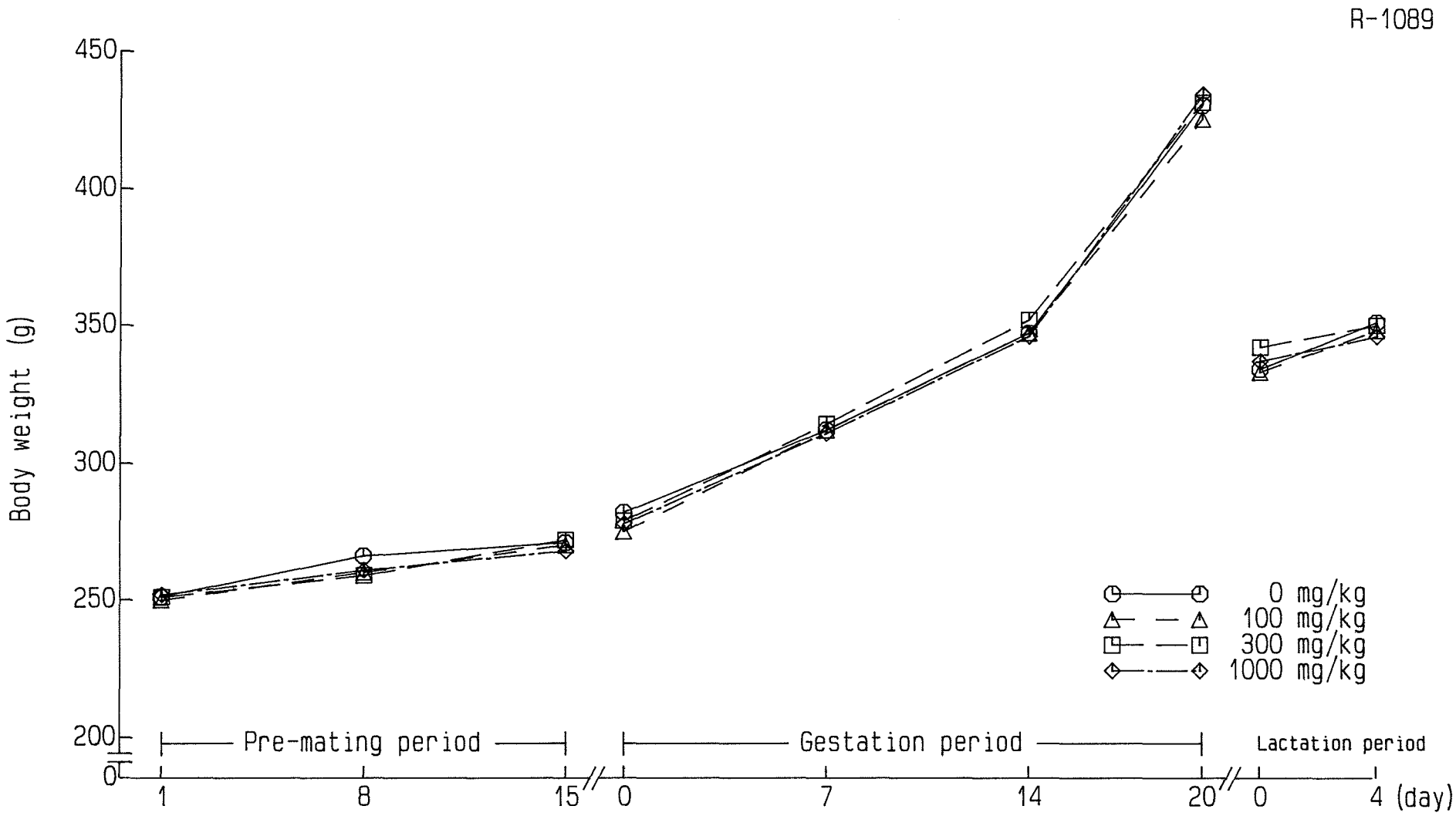


Fig.7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of female rats (Main group)

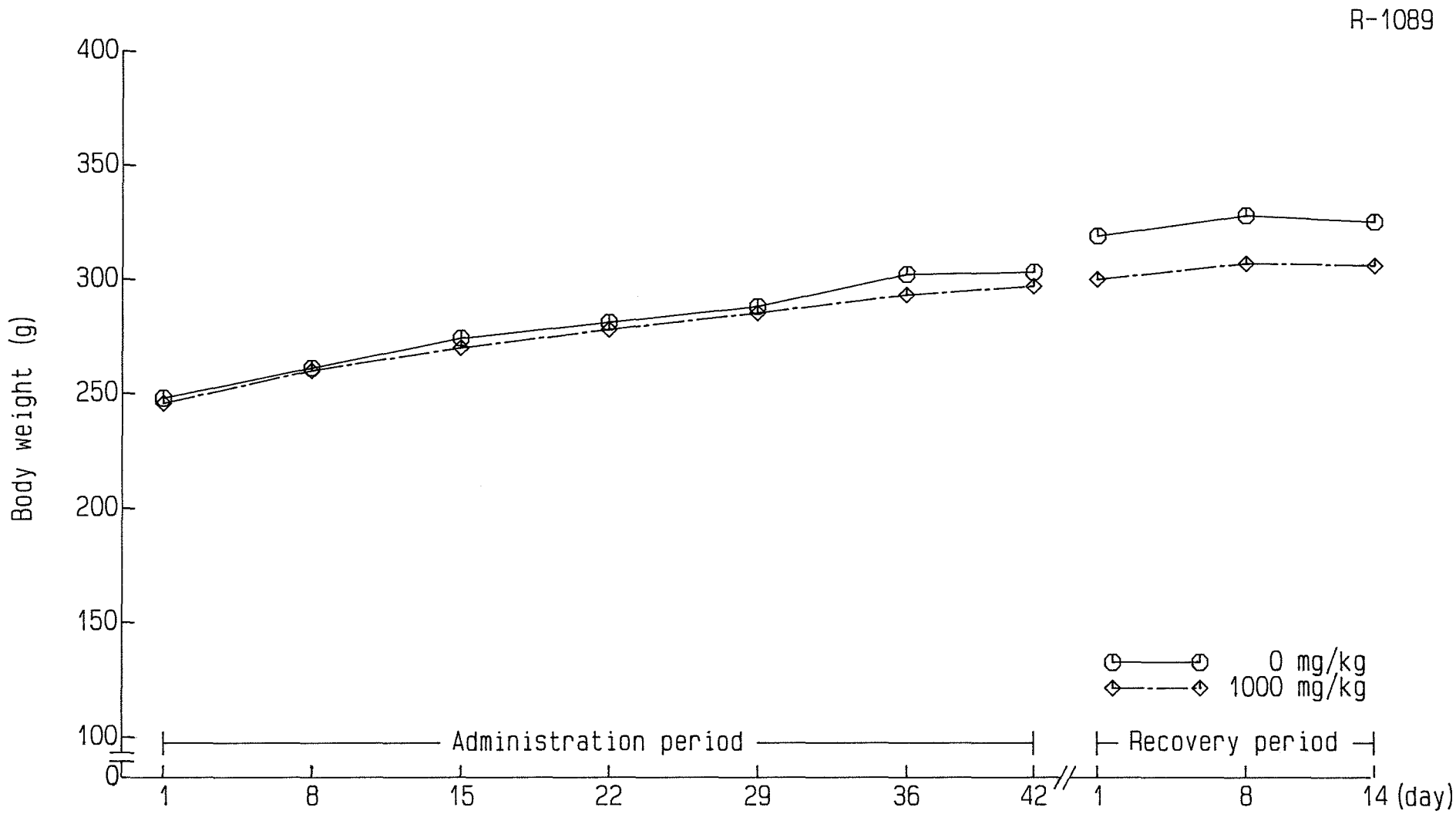


Fig.8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of female rats (Satellite group)

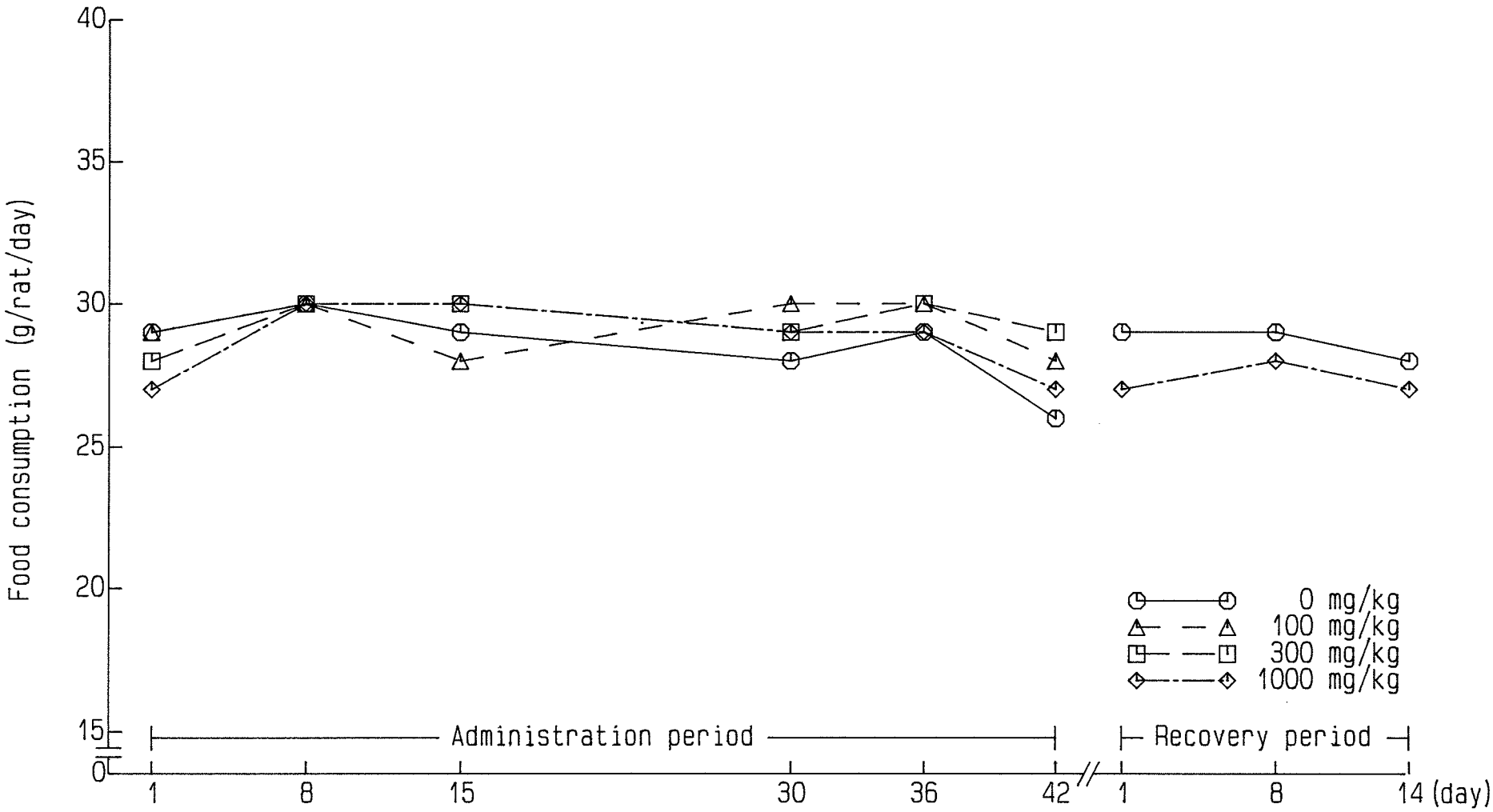


Fig.9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of male rats

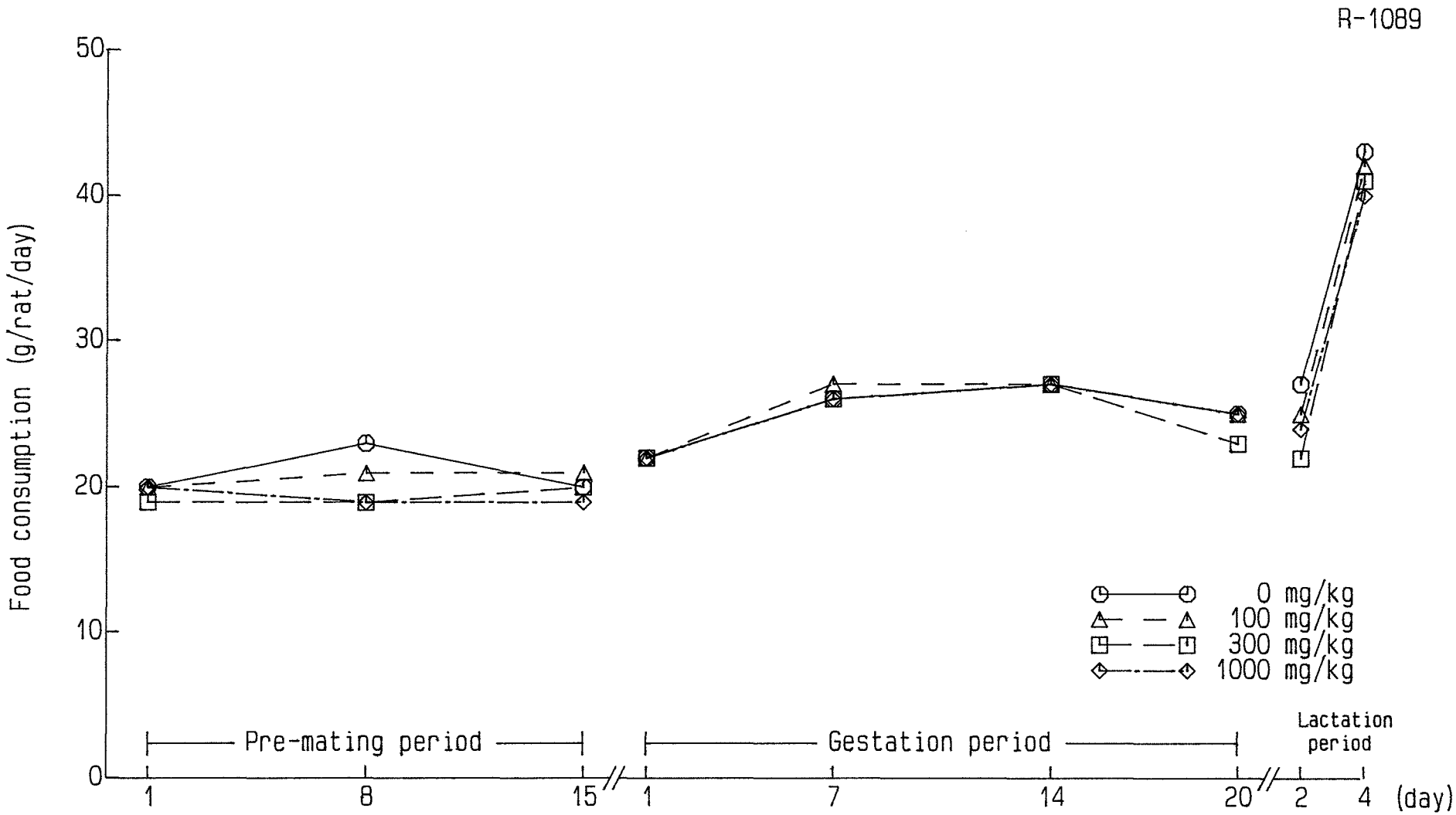


Fig.10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of female rats (Main group)

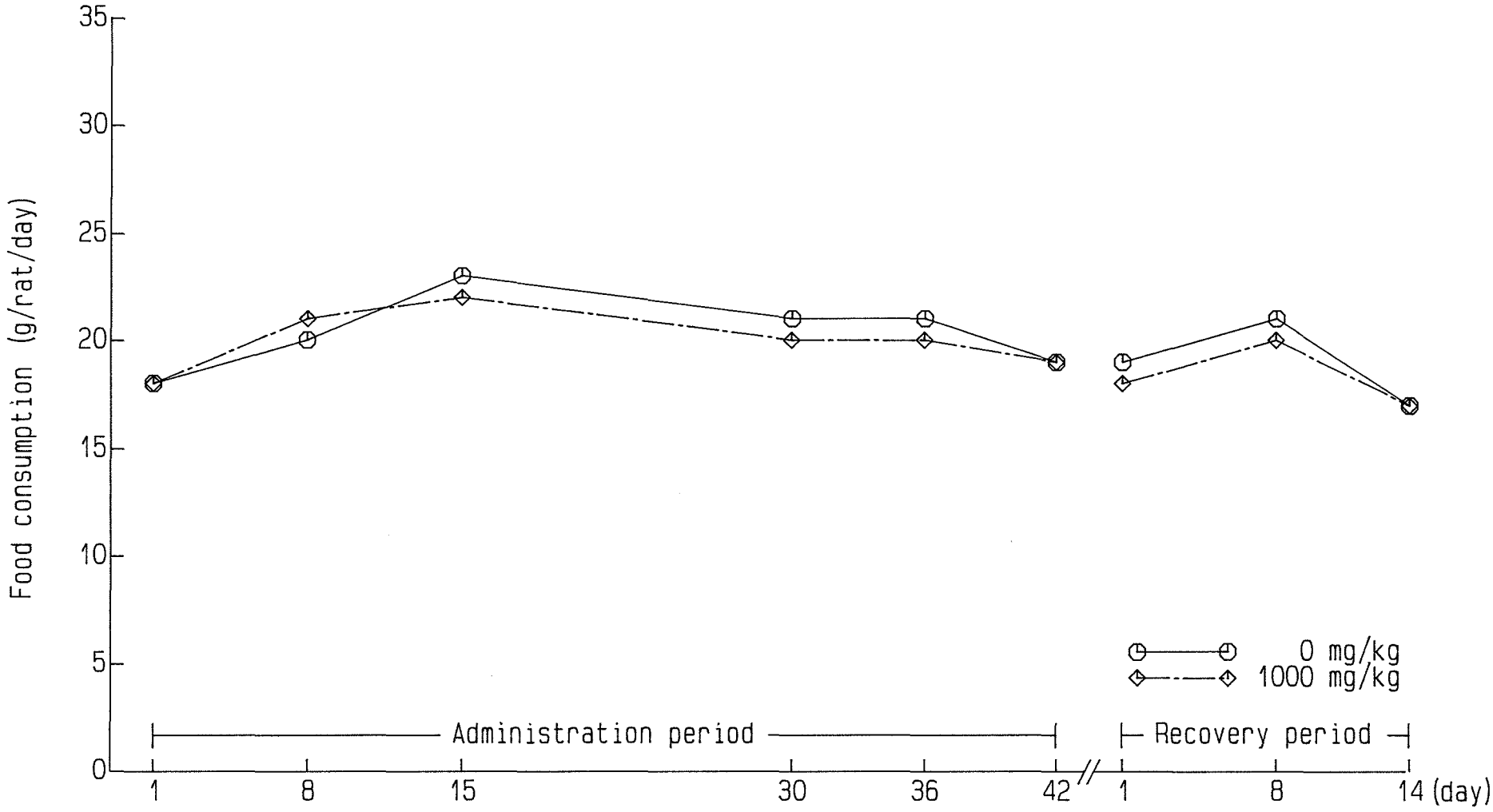


Fig.11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of female rats (Satellite group)

Table 1-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in male rats (Administration period)

Dose mg/kg	Signs	Day of administration 1-7	8-14	15-21	22-28	29-35	36-42	43a)
0	No. of animals	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0
1000	No. of animals	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in female rats during the pre-mating period (Main group)

Dose mg/kg	Signs	Day of administration														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 1-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in dams during the gestation period (Main group)

Dose mg/kg	Signs	Administration																						
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22a)
0	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
100	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	3
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	2
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a): Gestation day

Table 1-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in dams during the lactation period (Main group)

Dose mg/kg	Signs	Administration 0	1	2	3	4a)	5b)
0	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
100	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
300	No. of dams	11	11	11	11	11	11
	No. of dams with abnormal findings	0	0	0	0	0	0
1000	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0

a): Lactation day
b): Day of necropsy

Table 1-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in female rats (Satellite group, administration period)

Dose mg/kg	Signs	Day of administration						
		1-7	8-14	15-21	22-28	29-35	36-42	43a)
0	No. of animals	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0
1000	No. of animals	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in male rats (Recovery period)

Dose mg/kg	Signs	Day of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Clinical signs in female rats (Recovery period)

Dose mg/kg	Signs	Day of recovery														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
0	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1000	No. of animals	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a): Day of necropsy

Table 2-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 1 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 3 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 4 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 5 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 6 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Week 1 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 1)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Posture					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12

Table 2-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 7)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Posture					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12

Table 2-11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 14)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Posture					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12

Table 2-12 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 20)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Posture					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12

Table 2-13 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Main group, Lactation day 4)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Posture					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12

Table 2-14 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 1 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-15 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 2 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-16 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 3 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-17 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 4 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-18 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 5 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-19 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Satellite group, Week 6 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-20 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 1 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-21 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: home cage observation (Week 2 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-22 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Week 1 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-23 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: home cage observation (Week 2 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-24 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 1 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-25 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	11
Some resistance/avoidance		0	0	0	1
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	12	12	9
Soft		2	0	0	3
Reactivity to handling					
Easy		11	12	12	12
Slightly awkward		1	0	0	0

Table 2-26 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 3 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	12	10
Soft		0	1	0	2
Reactivity to handling					
Easy		12	11	12	11
Slightly awkward		0	1	0	1

Table 2-27 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	11
Soft		0	0	0	1
Reactivity to handling					
Easy		12	12	12	11
Slightly awkward		0	0	0	1

Table 2-28 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	10
Soft		0	0	0	2
Reactivity to handling					
Easy		12	12	12	12

Table 2-29 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 6 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	11
Some resistance/avoidance		0	0	0	1
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	12	11	11
Soft		1	0	1	1
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-30 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 1 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-31 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-32 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 1)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Ease of removal from cage					
Easy		12	12	11	12
Fur condition					
Normal		12	12	11	12
Skin					
Normal		12	12	11	12
Secretions-Eye, Nose					
Absent		12	12	11	12
Exophthalmos					
Absent		12	12	11	12
Palpebral closure					
Normal		12	12	11	12
Mucosal membranes					
Normal		12	12	11	12
Lacrimation					
Normal		12	12	11	12
Piloerection					
Absent		12	12	11	12
Pupil size					
Normal		12	12	11	12
Salivation					
None		12	12	11	12
Abnormal respiration					
Absent		12	12	11	12
Vocalization					
None		12	12	11	12
Reactivity to handling					
Easy		12	12	11	12

Table 2-33 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 7)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Ease of removal from cage					
Easy		12	12	11	12
Fur condition					
Normal		12	12	11	12
Skin					
Normal		12	12	11	12
Secretions-Eye, Nose					
Absent		12	12	11	12
Exophthalmos					
Absent		12	12	11	12
Palpebral closure					
Normal		12	12	11	12
Mucosal membranes					
Normal		12	12	11	12
Lacrimation					
Normal		12	12	11	12
Piloerection					
Absent		12	12	11	12
Pupil size					
Normal		12	12	11	12
Salivation					
None		12	12	11	12
Abnormal respiration					
Absent		12	12	11	12
Vocalization					
None		12	12	11	12
Reactivity to handling					
Easy		12	12	11	12

Table 2-34 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 14)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Ease of removal from cage					
Easy		12	12	11	12
Fur condition					
Normal		12	12	11	12
Skin					
Normal		12	12	11	12
Secretions-Eye, Nose					
Absent		12	12	11	12
Exophthalmos					
Absent		12	12	11	12
Palpebral closure					
Normal		12	12	11	12
Mucosal membranes					
Normal		12	12	11	12
Lacrimation					
Normal		12	12	11	12
Piloerection					
Absent		12	12	11	12
Pupil size					
Normal		12	12	11	12
Salivation					
None		12	12	11	12
Abnormal respiration					
Absent		12	12	11	12
Vocalization					
None		12	12	11	12
Reactivity to handling					
Easy		12	12	11	12

Table 2-35 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 20)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Ease of removal from cage					
Easy		12	12	11	12
Fur condition					
Normal		12	12	11	12
Skin					
Normal		12	12	11	12
Secretions-Eye, Nose					
Absent		12	12	11	12
Exophthalmos					
Absent		12	12	11	12
Palpebral closure					
Normal		12	12	11	12
Mucosal membranes					
Normal		12	12	11	12
Lacrimation					
Normal		12	12	11	12
Piloerection					
Absent		12	12	11	12
Pupil size					
Normal		12	12	11	12
Salivation					
None		12	12	11	12
Abnormal respiration					
Absent		12	12	11	12
Vocalization					
None		12	12	11	12
Reactivity to handling					
Easy		12	12	11	12

Table 2-36 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Main group, Lactation day 4)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Ease of removal from cage					
Easy		12	12	11	12
Fur condition					
Normal		12	12	11	12
Skin					
Normal		12	12	11	12
Secretions-Eye, Nose					
Absent		12	12	11	12
Exophthalmos					
Absent		12	12	11	12
Palpebral closure					
Normal		12	12	11	12
Mucosal membranes					
Normal		12	12	11	12
Lacrimation					
Normal		12	12	11	12
Piloerection					
Absent		12	12	11	12
Pupil size					
Normal		12	12	11	12
Salivation					
None		12	12	11	12
Abnormal respiration					
Absent		12	12	11	12
Vocalization					
None		12	12	11	12
Reactivity to handling					
Easy		12	12	11	12

Table 2-37 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 1 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-38 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-39 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 3 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-40 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 4 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-41 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 5 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-42 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 6 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Ease of removal from cage			
Easy		10	10
Fur condition			
Normal		10	10
Skin			
Normal		10	10
Secretions-Eye, Nose			
Absent		10	10
Exophthalmos			
Absent		10	10
Palpebral closure			
Normal		10	10
Mucosal membranes			
Normal		10	10
Lacrimation			
Normal		10	10
Piloerection			
Absent		10	10
Pupil size			
Normal		10	10
Salivation			
None		10	10
Abnormal respiration			
Absent		10	10
Vocalization			
None		10	10
Reactivity to handling			
Easy		10	10

Table 2-43 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 1 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	4
Soft		0	1
Reactivity to handling			
Easy		5	5

Table 2-44 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	4
Soft		0	1
Reactivity to handling			
Easy		5	4
Slightly awkward		0	1

Table 2-45 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Week 1 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-46 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: in-the-hand observation (Week 2 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-47 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 1 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	5± 2	5± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	12	11
Small amount		1	0	0	1

No significant difference in any treated groups from control group.

Table 2-48 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	4± 2	4± 2	3± 2
Defecation count (Mean±S.D.)		0± 1	0± 0	0± 0	0± 0
Urination					
None		12	12	11	11
Small amount		0	0	1	1

No significant difference in any treated groups from control group.

Table 2-49 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 3 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	5± 2	5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	11	12
Small amount		1	1	1	0

No significant difference in any treated groups from control group.

Table 2-50 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 4 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	4± 2	4± 2	3± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	12
Small amount		0	0	1	0

No significant difference in any treated groups from control group.

Table 2-51 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 5 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	5± 2	4± 1	3± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	12	12
Small amount		1	1	0	0

No significant difference in any treated groups from control group.

Table 2-52 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 6 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	4± 2	4± 1	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	11	11
Small amount		1	1	1	1

No significant difference in any treated groups from control group.

Table 2-53 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Week 1 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		8± 2	7± 2	7± 2	7± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-54 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		8± 2	7± 2	9± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-55 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 1)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Arousal					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12
Stereotypy					
None		12	12	11	12
Gait					
Normal		12	12	11	12
Posture					
Normal		12	12	11	12
Grooming					
None		12	12	11	12
Rearing (Mean±S.D.)		6± 2	6± 2	7± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	12

No significant difference in any treated groups from control group.

Table 2-56 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 7)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Arousal					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12
Stereotypy					
None		12	12	11	12
Gait					
Normal		12	12	11	12
Posture					
Normal		12	12	11	12
Grooming					
None		12	12	11	12
Rearing (Mean±S.D.)		6± 1	6± 3	6± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	11	11	12
Small amount		0	1	0	0

No significant difference in any treated groups from control group.

Table 2-57 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 14)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Arousal					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12
Stereotypy					
None		12	12	11	12
Gait					
Normal		12	12	11	12
Posture					
Normal		12	12	11	12
Grooming					
None		12	12	11	12
Rearing (Mean±S.D.)		7± 1	6± 2	6± 2	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-58 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Gestation day 20)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Arousal					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12
Stereotypy					
None		12	12	11	12
Gait					
Normal		12	12	11	12
Posture					
Normal		12	12	11	12
Grooming					
None		12	12	11	12
Rearing (Mean±S.D.)		5± 1	6± 2	5± 1	4± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	12

No significant difference in any treated groups from control group.

Table 2-59 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Main group, Lactation day 4)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	11	12
Arousal					
Normal		12	12	11	12
Convulsion					
None		12	12	11	12
Abnormal behavior					
None		12	12	11	12
Stereotypy					
None		12	12	11	12
Gait					
Normal		12	12	11	12
Posture					
Normal		12	12	11	12
Grooming					
None		12	12	11	12
Rearing (Mean±S.D.)		7± 2	7± 2	7± 1	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-60 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		7± 3	8± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-61 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 2 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		7± 3	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-62 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 3 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		7± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-63 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 4 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 2	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-64 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 2	9± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-65 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Satellite group, Week 6 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 1	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	9
Small amount		0	1

No significant difference between treated group and control group.

Table 2-66 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 1 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		5± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-67 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in male rats: open field observation (Week 2 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		4± 2	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		4	5
Small amount		1	0

No significant difference between treated group and control group.

Table 2-68 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		7± 2	6± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-69 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Detailed clinical signs in female rats: open field observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
No/minimal location		0	1
Normal		5	4
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		7± 2	7± 4
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	4
Small amount		0	1

No significant difference between treated group and control group.

Table 2-70 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Manipulative test of male rats (Week 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		84±22	96±12	77±16	104±14

No significant difference in any treated groups from control group.

Table 2-71 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Manipulative test of female rats (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		57± 8	47±22	46±11	65±19

No significant difference in any treated groups from control group.

Table 2-72 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Manipulative test of female rats (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		62±15	57±12

No significant difference between treated group and control group.

Table 2-73 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Manipulative test of male rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		86±25	105± 7

No significant difference between treated group and control group.

Table 2-74 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Manipulative test of female rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		67±13	69±14

No significant difference between treated group and control group.

Table 2-75 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Grip strength of male rats (Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1583	923
	S.D.	224	172
100	No.	5	5
	Mean	1677	989
	S.D.	299	177
300	No.	5	5
	Mean	1306	909
	S.D.	203	156
1000	No.	5	5
	Mean	1697	1043
	S.D.	201	155

No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-76 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Grip strength of female rats (Main group, Lactation day 4)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1257	861
	S.D.	243	140
100	No.	5	5
	Mean	1264	722
	S.D.	164	158
300	No.	5	5
	Mean	1302	855
	S.D.	195	121
1000	No.	5	5
	Mean	1296	907
	S.D.	204	220

No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-77 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Grip strength of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1258	758
	S.D.	170	120
1000	No.	5	5
	Mean	1266	649
	S.D.	212	169

No.: No. of animals
No significant difference between treated group and control group.

Table 2-78 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Grip strength of male rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1779	1027
	S.D.	140	261
1000	No.	5	5
	Mean	1870	1105
	S.D.	204	133

No.: No. of animals
No significant difference between treated group and control group.

Table 2-79 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Grip strength of female rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1369	913
	S.D.	173	155
1000	No.	5	5
	Mean	1388	693
	S.D.	220	222

No.: No. of animals
No significant difference between treated group and control group.

Table 2-80 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of male rats (Week 6 of administration)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	402	406	234	92	41	62	1236
	S.D.	27	70	97	67	63	77	144
100	No.	5	5	5	5	5	5	5
	Mean	432	360	288	247	207	249	1782
	S.D.	62	42	169	146	158	214	706
300	No.	5	5	5	5	5	5	5
	Mean	406	357	292	254	172	111	1592
	S.D.	78	91	69	138	140	84	479
1000	No.	5	5	5	5	5	5	5
	Mean	418	365	146	127	62	146	1263
	S.D.	31	27	121	131	99	137	417

Unit : Count
No.: No. of animals
No significant difference in any treated groups from control group.

Table 2-81 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of female rats (Main group, Lactation day 4)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	443	314	167	130	115	80	1249
	S.D.	40	121	140	164	100	97	463
100	No.	5	5	5	5	5	5	5
	Mean	407	312	200	132	109	98	1258
	S.D.	24	72	143	160	94	87	390
300	No.	5	5	5	5	5	5	5
	Mean	423	291	130	179	106	74	1202
	S.D.	38	134	137	180	79	99	411
1000	No.	5	5	5	5	5	5	5
	Mean	386*	233	88	21	82	67	878
	S.D.	23D	104	106	29	144	139	476

Unit : Count
No.: No. of animals
* : $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 2-82 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	401	326	263	232	138	34	1394
	S.D.	18	13	72	126	134	23	297
1000	No.	5	5	5	5	5	5	5
	Mean	435	329	306	266	196	79	1610
	S.D.	48	67	78	39	112	90	338

Unit : Count
No.: No. of animals
No significant difference between treated group and control group.

Table 2-83 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	292	216	179	60	14	60	822
	S.D.	75	95	136	39	9	92	339
1000	No.	5	5	5	5	5	5	5
	Mean	337	136	171	84	50	73	852
	S.D.	31	23	145	52	57	86	312

Unit : Count
No.: No. of animals
No significant difference between treated group and control group.

Table 2-84 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	340	269	151	169	214	186	1329
	S.D.	30	43	127	134	68	131	316
1000	No.	5	5	5	5	5	5	5
	Mean	319	207	190	172	144	83	1115
	S.D.	95	155	161	103	115	89	596

Unit : Count
No.: No. of animals
No significant difference between treated group and control group.

Table 3-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of male rats (Administration period)

Dose mg/kg		Day of administration 1	8	15	22	29	36	42	Gain 1-42
	No.	12	12	12	12	12	12	12	12
0	Mean	405	433	453	468	489	513	520	115
	S.D.	16	15	17	18	19	21	21	19
	No.	12	12	12	12	12	12	12	12
100	Mean	405	435	457	478	501	528	535	131
	S.D.	12	12	11	10	11	12	11	13
	No.	12	12	12	12	12	12	12	12
300	Mean	405	435	459	480	504	528	542	137**
	S.D.	14	18	23	24	26	27	27	15D
	No.	12	12	12	12	12	12	12	12
1000	Mean	404	436	458	475	497	519	529	125
	S.D.	16	19	26	26	30	30	34	21

Unit: g
No.: No. of animals
**: $p<0.01$ (Significant difference from control group)
D: Dunnett's test

Table 3-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration 1	8	15	Gain 1-15
	No.	12	12	12	12
0	Mean	251	266	271	20
	S.D.	17	18	18	12
	No.	12	12	12	12
100	Mean	250	260	270	19
	S.D.	14	13	15	9
	No.	12	12	12	12
300	Mean	251	259	272	21
	S.D.	12	12	13	9
	No.	12	12	12	12
1000	Mean	252	261	268	16
	S.D.	15	15	18	7

Unit: g
No.: No. of animals
No significant difference in any treated groups from control group.

Table 3-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of dams during the gestation period (Main group)

Dose mg/kg		Administration 0	7	14	20a)	Gain 0-20
	No.	12	12	12	12	12
0	Mean	282	312	347	430	148
	S.D.	20	19	16	26	15
	No.	12	12	12	12	12
100	Mean	275	312	347	425	149
	S.D.	17	15	16	22	18
	No.	11	11	11	11	11
300	Mean	279	314	352	431	153
	S.D.	11	11	15	21	19
	No.	12	12	12	12	12
1000	Mean	278	311	346	434	156
	S.D.	18	19	24	26	12

Unit: g
No.: No. of dams
a): Gestation day
No significant difference in any treated groups from control group.

Table 3-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of dams during the lactation period (Main group)

Dose mg/kg		Administration 0	Administration 4a)	Gain 0-4
	No.	12	12	12
0	Mean	334	351	16
	S.D.	22	15	17
	No.	12	12	12
100	Mean	333	348	15
	S.D.	20	18	17
	No.	11	11	11
300	Mean	342	350	8
	S.D.	16	17	15
	No.	12	12	12
1000	Mean	337	346	9
	S.D.	31	20	16

Unit: g
No.: No. of dams
a): Lactation day
No significant difference in any treated groups from control group.

Table 3-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of female rats (Satellite group, administration period)

Dose mg/kg		Day of administration 1	8	15	22	29	36	42	Gain 1-42
	No.	10	10	10	10	10	10	10	10
0	Mean	248	261	274	281	288	302	303	56
	S.D.	13	16	19	18	20	22	19	11
	No.	10	10	10	10	10	10	10	10
1000	Mean	246	260	270	278	285	293	297	51
	S.D.	12	18	21	24	29	31	30	21

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 3-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14	Gain 1-14
	No.	5	5	5	5
0	Mean	516	532	537	21
	S.D.	16	20	19	5
	No.	5	5	5	5
1000	Mean	527	543	553	26
	S.D.	26	22	27	5

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 3-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of female rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14	Gain 1-14
	No.	5	5	5	5
0	Mean	319	328	325	5
	S.D.	17	18	15	12
	No.	5	5	5	5
1000	Mean	300	307	306	6
	S.D.	31	30	30	5

Unit: g
No.: No. of animals
No significant difference between treated group and control group.

Table 4-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of male rats (Administration period)

Dose mg/kg		Day of administration 1	8	15	30	36	42
	No.	12	12	12	12	12	12
0	Mean	29	30	29	28	29	26
	S.D.	2	3	3	2	3	2
	No.	12	12	12	12	12	12
100	Mean	29	30	28	30	30	28
	S.D.	1	2	3	2	2	2
	No.	12	12	12	12	12	12
300	Mean	28	30	30	29	30	29
	S.D.	2	2	3	2	2	2
	No.	12	12	12	12	12	12
1000	Mean	27	30	30	29	29	27
	S.D.	3	3	3	4	3	4

Unit: g/rat/day
No.: No. of animals
No significant difference in any treated groups from control group.

Table 4-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration 1	8	15
0	No.	12	12	12
	Mean	20	23	20
	S.D.	3	2	2
100	No.	12	12	12
	Mean	20	21	21
	S.D.	2	3	3
300	No.	12	12	12
	Mean	19	19**	20
	S.D.	3	4D	3
1000	No.	12	12	12
	Mean	20	19*	19
	S.D.	3	3D	3

Unit: g/rat/day
No.: No. of animals
*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
D: Dunnett's test

Table 4-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of dams during the gestation period (Main group)

Dose mg/kg		Administration 1	7	14	20a)
0	No.	12	12	12	12
	Mean	22	26	27	25
	S.D.	3	2	2	2
100	No.	12	12	12	12
	Mean	22	27	27	25
	S.D.	2	2	2	3
300	No.	11	11	11	11
	Mean	22	26	27	23
	S.D.	3	2	2	1
1000	No.	12	12	12	12
	Mean	22	26	27	25
	S.D.	3	3	3	2

Unit: g/rat/day
No.: No. of dams
a): Gestation day
No significant difference in any treated groups from control group.

Table 4-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of dams during the lactation period (Main group)

Dose mg/kg		Administration 2	4a)
0	No.	12	12
	Mean	27	43
	S.D.	4	4
100	No.	12	12
	Mean	25	42
	S.D.	7	7
300	No.	11	11
	Mean	22	41
	S.D.	5	6
1000	No.	12	12
	Mean	24	40
	S.D.	5	4

Unit: g/rat/day
No.: No. of dams
a): Lactation day
No significant difference in any treated groups from control group.

Table 4-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of female rats (Satellite group, administration period)

Dose mg/kg		Day of administration					
		1	8	15	30	36	42
0	No.	10	10	10	10	10	10
	Mean	18	20	23	21	21	19
	S.D.	3	4	3	3	2	4
1000	No.	10	10	10	10	10	10
	Mean	18	21	22	20	20	19
	S.D.	3	5	3	2	3	2

Unit: g/rat/day
No.: No. of animals
No significant difference between treated group and control group.

Table 4-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
	No.	5	5	5
0	Mean	29	29	28
	S.D.	1	3	2
	No.	5	5	5
1000	Mean	27	28	27
	S.D.	2	1	2

Unit: g/rat/day
No.: No. of animals
No significant difference between treated group and control group.

Table 4-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Food consumption of female rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
	No.	5	5	5
0	Mean	19	21	17
	S.D.	2	2	3
	No.	5	5	5
1000	Mean	18	20	17
	S.D.	2	4	4

Unit: g/rat/day
No.: No. of animals
No significant difference between treated group and control group.

Table 5-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	0	1	0	4	0	1	3	1	0	0	3	2	0	0	5	0	0	0	0
100	5	0	0	0	0	0	0	1	1	3	1	1	3	0	0	1	2	1	1	0	5	0	0	0	0
300	5	0	0	0	0	0	0	0	4	1	2	3	0	0	0	2	1	2	0	0	5	0	0	0	0
1000	5	0	0	0	0	0	0	0	2	3	0	2	3	0	0	2	2	1	0	0	5	0	0	0	0

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	1	4	0	0	0	5	0	0	0	5	0	0	0	0	5	0
100	5	4	1	0	0	0	4	1	0	0	5	0	0	0	0	5	0
300	5	1	4	0	0	0	5	0	0	0	5	0	0	0	0	5	0
1000	5	1	4	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	URINE SEDIMENT																																					
		RBC					WBC					SEC					SREC					Cast			CRYSTALLIZATION									
																									PS					CO				
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0
100	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0
300	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Table 5-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Water intake and urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	38	17.1	2051	1.89	5.21	2.34
		S.D.	7	5.9	485	0.26	0.79	0.35
100	5	Mean	46	23.6	1612	2.03	5.43	2.50
		S.D.	15	12.8	395	0.47	1.44	0.50
300	5	Mean	50	22.4	1793	1.62	4.98	2.22
		S.D.	21	14.8	749	0.30	0.74	0.48
1000	5	Mean	42	23.9	1620	1.82	5.22	2.34
		S.D.	21	11.2	584	0.45	1.33	0.38

No significant difference in any treated groups from control group.

Table 5-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	0	1	0	4	2	3	0	0	0	5	0	0	0	0	5	0	0	0	0
1000	5	0	0	0	1	0	1	0	2	1	2	2	1	0	0	3	2	0	0	0	5	0	0	0	0

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0
1000	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.	URINE SEDIMENT																																
																									CRYSTALLIZATION									
		RBC					WBC					SEC					SREC					Cast			PS					CO				
		-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

\- : Negative
+- : Slight
\+ : Mild
++ : Moderate
+++ : Severe

Table 5-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	33	12.3	1979	1.23	3.37	1.53
		S.D.	10	6.5	540	0.34	1.07	0.44
1000	5	Mean	29	8.8	2441	1.13	3.19	1.40
		S.D.	4	2.4	331	0.29	0.59	0.30

No significant difference between treated group and control group.

Table 5-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	0	1	1	3	2	1	2	0	0	2	1	2	0	0	5	0	0	0	0
1000	5	0	0	0	0	0	0	0	3	2	1	2	2	0	0	1	2	1	1	0	5	0	0	0	0

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	1	4	0	0	0	4	1	0	0	5	0	0	0	0	5	0
1000	5	4	1	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of male rats (Week 2 of recovery)

		URINE SEDIMENT																															
																									CRYSTALLIZATION									
		RBC					WBC					SEC					SREC					Cast			PS					CO				
Dose mg/kg	No.	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Table 5-12 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Water intake and urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	44	18.6	1909	1.77	5.52	2.31
		S.D.	6	5.4	132	0.46	1.44	0.55
1000	5	Mean	48	25.6	1668	1.97	5.46	2.37
		S.D.	31	15.1	693	0.60	1.44	0.51

No significant difference between treated group and control group.

Table 5-13 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	pH									1) Protein					2) Ketone body					3) Glucose				
		5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	-	+-	+	++	+++	-	+-	+	++	+++	-	+	++	+++	++++
0	5	0	0	0	0	0	1	0	1	3	3	2	0	0	0	4	1	0	0	0	5	0	0	0	0
1000	5	0	0	0	3	0	0	0	0	2	2	3	0	0	0	2	3	0	0	0	5	0	0	0	0

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL

Table 5-14 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.	4) Occult blood					5) Bilirubin				6) Urobilinogen				7) Color		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0
1000	5	5	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0

4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Table 5-15 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Urinalysis of female rats (Week 2 of recovery)

		URINE SEDIMENT																																				
																													CRYSTALLIZATION											
		RBC					WBC					SEC					SREC					Cast			PS					CO				
Dose mg/kg	No.	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	1	4	0	0	0	5	0	0	0	0
1000	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Table 5-16 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Water intake and urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	37	13.1	1970	1.16	3.10	1.40
		S.D.	21	9.4	683	0.19	0.67	0.34
1000	5	Mean	31	9.0	2350	0.93	2.76	1.18
		S.D.	10	4.9	666	0.17	0.53	0.26

No significant difference between treated group and control group.

Table 6-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of male rats (End of administration)

Dose mg/kg	No.		RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	5	Mean	856	15.5	43.6	50.9	18.1	35.5	2.3	104.3	17.8	25.6	295
		S.D.	21	0.3	1.1	0.9	0.3	0.6	0.4	7.6	2.3	2.4	47
100	5	Mean	906*	15.4	43.9	48.5*	17.0*	35.0	2.2	98.3	16.9	23.5	276
		S.D.	29D	0.4	1.3	1.4D	0.6D	0.2	0.3	11.6	0.9	2.0	20
300	5	Mean	876	15.3	43.7	49.9	17.5	35.0	2.1	102.1	16.9	25.6	292
		S.D.	26	0.5	1.3	1.1	0.3	0.3	0.4	13.7	1.8	4.9	24
1000	5	Mean	884	15.4	44.2	50.0	17.4	34.8	2.2	105.8	17.5	23.8	269
		S.D.	16	0.5	1.1	1.8	0.8	0.5	0.2	15.8	3.2	0.7	34

*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 6-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of male rats (End of administration)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			$\times 10^2/\mu L$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	74.2	73.1	22.1	1.5	0.3	2.6	0.5	53.9	16.6	1.0	0.3	2.0	0.4
		S.D.	22.3	5.3	4.4	0.4	0.1	0.8	0.3	16.1	6.2	0.3	0.2	1.0	0.3
100	5	Mean	85.8	70.6	23.7	1.7	0.3	3.0	0.8	60.4	20.4	1.3	0.3	2.7	0.8
		S.D.	31.3	4.9	6.2	1.1	0.2	0.7	0.8	21.6	10.0	0.5	0.2	1.4	0.9
300	5	Mean	65.3	71.2	22.9	1.9	0.3	2.9	0.7	46.3	15.1	1.2	0.2	1.9	0.5
		S.D.	17.2	4.5	4.3	0.4	0.2	0.4	0.5	11.8	5.3	0.3	0.2	0.6	0.4
1000	5	Mean	66.9	72.2	23.6	1.5	0.3	2.1	0.3	48.3	15.8	1.0	0.2	1.4	0.2
		S.D.	8.5	3.7	3.4	0.7	0.1	0.3	0.1	7.3	2.6	0.4	0.1	0.2	0.1

LUC: Large unstained cells
No significant difference in any treated groups from control group.

Table 6-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	5	Mean	788	14.4	41.8	53.2	18.3	34.5	6.3	144.8	14.0	18.1	381
		S.D.	63	1.0	2.4	1.4	0.2	0.5	2.5	29.1	0.8	1.5	79
100	5	Mean	792	14.2	41.2	52.0	17.9	34.4	5.4	146.2	14.0	17.8	290
		S.D.	31	0.5	1.8	1.3	0.4	0.7	0.9	12.7	0.7	4.5	49
300	5	Mean	775	14.0	40.4	52.2	18.1	34.6	5.6	146.9	14.5	21.1	300
		S.D.	52	0.7	2.0	2.0	0.7	0.1	1.8	23.1	0.4	2.8	41
1000	5	Mean	745	13.7	39.4	52.9	18.3	34.7	7.0	148.2	14.5	19.1	263*
		S.D.	50	0.5	1.9	1.3	0.6	0.5	1.2	18.5	1.1	1.5	63D

*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 6-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts (X10²/μL)					
			X10²/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	131.5	61.0	35.2	0.8	0.4	2.3	0.4	79.8	46.5	1.0	0.5	3.1	0.6
		S.D.	24.2	6.9	7.0	0.2	0.1	0.7	0.1	16.6	13.3	0.2	0.2	1.2	0.2
100	5	Mean	102.8	66.9	29.0	1.1	0.2*	2.4	0.4	66.8	31.6	1.1	0.2*	2.6	0.5
		S.D.	39.5	7.2	6.8	0.4	0.1D	0.7	0.2	20.8	16.6	0.7	0.2D	1.5	0.4
300	5	Mean	84.0*	70.2	24.8*	1.3	0.3	2.7	0.8	58.9	20.9*	1.1	0.2*	2.3	0.6
		S.D.	5.8D	2.8	2.9D	0.8	0.1	1.0	0.4	4.3	3.2D	0.7	0.1D	0.8	0.4
1000	5	Mean	90.1	61.6	33.5	0.9	0.3	3.0	0.8	54.5	31.2	0.8	0.2*	2.7	0.7
		S.D.	30.1	5.4	5.8	0.3	0.1	0.3	0.6	15.7	13.9	0.4	0.1D	0.8	0.5

LUC: Large unstained cells
*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 6-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	5	Mean	849	15.7	44.1	51.9	18.4	35.5	2.0	109.2	13.8	18.1	228
		S.D.	37	0.4	1.2	1.1	0.4	0.3	0.5	16.5	0.9	2.3	9
1000	5	Mean	871	15.6	43.9	50.4*	17.9*	35.5	1.8	110.6	13.8	18.5	211*
		S.D.	38	0.5	2.2	0.8T	0.3T	0.6	0.8	14.3	0.6	0.9	13T

*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 6-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			$\times 10^2/\mu L$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	49.5	76.1	19.9	1.6	0.3	1.6	0.4	38.1	9.4	0.8	0.1	0.8	0.2
		S.D.	12.0	6.1	5.6	0.4	0.1	0.5	0.3	11.8	1.6	0.2	0.1	0.1	0.2
1000	5	Mean	40.1	71.5	24.4	1.3	0.2	2.3	0.4	28.2	10.1	0.5*	0.0	1.0	0.2
		S.D.	12.7	5.3	5.1	0.3	0.1	0.7	0.2	7.0	5.2	0.1T	0.1	0.5	0.1

LUC: Large unstained cells
*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 6-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of male rats (End of recovery)

Dose mg/kg	No.		RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	5	Mean	932	16.1	46.3	49.7	17.3	34.7	2.1	95.5	15.5	22.8	268
		S.D.	48	0.2	0.6	2.0	0.9	0.5	0.1	1.8	1.5	3.1	43
1000	5	Mean	913	15.8	45.2	49.5	17.4	35.0	2.1	101.6	15.7	22.4	257
		S.D.	20	0.4	1.1	1.1	0.3	0.2	0.4	11.3	2.0	2.0	31

No significant difference between treated group and control group.

Table 6-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of male rats (End of recovery)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts (×10²/μL)					
			×10²/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	76.5	75.0	20.1	1.7	0.3	2.4	0.6	57.5	15.4	1.3	0.2	1.7	0.4
		S.D.	21.1	4.9	4.9	0.5	0.1	0.5	0.3	17.0	5.2	0.6	0.1	0.3	0.1
1000	5	Mean	74.6	73.5	21.2	2.0	0.3	2.5	0.5	55.6	15.1	1.5	0.2	1.8	0.4
		S.D.	22.7	5.5	5.6	0.8	0.0	0.5	0.4	19.7	3.6	0.8	0.1	0.4	0.3

LUC: Large unstained cells
No significant difference between treated group and control group.

Table 6-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of female rats (End of recovery)

Dose mg/kg	No.		RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	5	Mean	845	15.5	43.7	51.8	18.4	35.5	2.0	108.5	12.2	18.1	198
		S.D.	37	0.5	1.3	2.4	0.9	0.2	0.5	14.7	0.5	1.8	16
1000	5	Mean	861	15.3	42.8	49.8	17.8	35.7	2.0	112.6	12.1	18.9	180
		S.D.	29	0.4	1.0	1.3	0.4	0.3	0.3	7.4	0.1	1.0	20

No significant difference between treated group and control group.

Table 6-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Hematology of female rats (End of recovery)

Dose mg/kg	No.		WBC	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			$\times 10^2/\mu L$	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	54.3	76.1	19.6	1.6	0.2	2.0	0.4	41.2	10.7	0.9	0.1	1.1	0.2
		S.D.	8.7	7.3	7.3	0.3	0.0	0.5	0.2	7.2	4.3	0.2	0.0	0.3	0.1
1000	5	Mean	46.4	77.8	17.0	1.9	0.2	2.4	0.7	36.0	8.0	0.8	0.1	1.1	0.3
		S.D.	6.5	6.7	6.9	0.8	0.1	0.7	0.4	5.0	3.8	0.3	0.0	0.3	0.2

LUC: Large unstained cells
No significant difference between treated group and control group.

Table 7-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	5	Mean	66	29	61	1	382	8.1	48	38	78	0.1	140
		S.D.	5	4	18	0	67	2.9	11	17	9	0.0	12
100	5	Mean	69	31	52	1	367	7.2	50	52	84	0.1	146
		S.D.	6	2	12	0	42	1.1	14	14	14	0.0	11
300	5	Mean	67	29	52	1	359	8.4	50	36	83	0.1	141
		S.D.	7	2	16	0	68	4.3	6	12	3	0.0	11
1000	5	Mean	63	28	43	1	329	10.5	50	33	83	0.1	130
		S.D.	7	4	8	0	80	6.9	10	14	13	0.0	7

No significant difference in any treated groups from control group.

Table 7-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	15	0.25	144	4.3	108	9.5	5.7	5.7	3.1	1.16
		S.D.	4	0.04	1	0.2	2	0.3	0.7	0.1	0.1	0.08
100	5	Mean	15	0.24	142	4.5	106	9.5	5.9	5.7	3.1	1.17
		S.D.	3	0.04	1	0.1	1	0.3	0.5	0.3	0.1	0.07
300	5	Mean	14	0.24	143	4.4	107	9.5	5.8	5.7	3.0	1.14
		S.D.	1	0.04	1	0.2	1	0.3	0.5	0.2	0.1	0.09
1000	5	Mean	15	0.25	143	4.4	106	9.6	5.8	5.6	3.1	1.19
		S.D.	2	0.04	2	0.1	1	0.5	0.7	0.2	0.1	0.04

No significant difference in any treated groups from control group.

Table 7-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	5	Mean	80	52	33	1	277	23.9	54	87	119	0.1	122
		S.D.	16	10	6	1	84	21.6	7	25	13	0.0	11
100	5	Mean	69	41	39	1	321	14.4	55	62	111	0.1	126
		S.D.	9	12	9	0	84	8.1	8	42	12	0.0	8
300	5	Mean	78	44	42	1	238	14.5	50	52	101	0.1	113
		S.D.	18	15	11	0	65	8.7	8	26	18	0.0	9
1000	5	Mean	77	40	44	1	190	14.2	53	53	110	0.1	114
		S.D.	8	7	9	0	47	3.3	7	22	10	0.0	6

No significant difference in any treated groups from control group.

Table 7-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	14	0.24	139	4.3	104	10.2	6.8	6.0	3.4	1.26
		S.D.	2	0.04	1	0.3	3	0.2	0.6	0.4	0.2	0.04
100	5	Mean	13	0.24	141	4.3	107	10.2	6.5	5.9	3.3	1.24
		S.D.	1	0.02	2	0.3	3	0.2	0.3	0.2	0.1	0.09
300	5	Mean	16	0.24	141	4.2	108*	10.1	6.5	6.0	3.3	1.25
		S.D.	3	0.03	1	0.4	1D	0.3	0.7	0.1	0.1	0.10
1000	5	Mean	15	0.26	141	4.1	107	10.1	6.7	6.0	3.3	1.22
		S.D.	2	0.03	1	0.2	2	0.4	0.7	0.1	0.1	0.12

*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 7-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	5	Mean	61	26	42	1	205	13.6	64	21	127	0.1	134
		S.D.	6	1	6	0	86	4.9	6	10	10	0.0	10
1000	5	Mean	59	30**	41	1	176	10.9	65	20	123	0.1	136
		S.D.	7	1T	8	0	36	3.3	16	7	27	0.0	12

**: $p<0.01$ (Significant difference from control group)
T: Student's t-test

Table 7-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	16	0.26	141	4.4	109	10.0	4.4	6.3	3.6	1.35
		S.D.	2	0.01	1	0.1	1	0.3	1.0	0.3	0.2	0.06
1000	5	Mean	17	0.29	141	4.3	108	10.1	4.5	6.4	3.6	1.33
		S.D.	2	0.03	1	0.2	1	0.3	0.7	0.4	0.2	0.13

No significant difference between treated group and control group.

Table 7-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	5	Mean	65	31	48	1	329	11.2	52	55	84	0.1	142
		S.D.	10	4	6	0	65	5.6	6	32	9	0.0	13
1000	5	Mean	70	29	49	1	312	12.1	50	30	79	0.1	138
		S.D.	6	1	6	0	49	6.6	12	11	14	0.0	20

No significant difference between treated group and control group.

Table 7-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	16	0.22	142	4.4	105	9.8	5.5	5.8	3.0	1.09
		S.D.	1	0.04	1	0.2	1	0.2	0.4	0.0	0.0	0.04
1000	5	Mean	17	0.26	142	4.5	106	9.6	5.7	5.7	3.0	1.11
		S.D.	2	0.05	1	0.3	1	0.2	0.4	0.2	0.0	0.06

No significant difference between treated group and control group.

Table 7-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	5	Mean	58	26	43	1	170	16.2	77	31	139	0.1	137
		S.D.	6	5	10	0	20	5.9	19	16	32	0.0	6
1000	5	Mean	68	34	42	1	133*	14.3	73	23	130	0.1	136
		S.D.	21	15	9	0	17T	4.4	5	20	9	0.0	10

*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 7-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	5	Mean	15	0.30	141	4.2	108	10.0	3.9	6.5	3.7	1.30
		S.D.	1	0.02	2	0.4	2	0.3	0.5	0.4	0.3	0.10
1000	5	Mean	15	0.28	141	4.2	107	10.0	3.7	6.3	3.6	1.35
		S.D.	2	0.02	1	0.1	1	0.1	0.9	0.4	0.2	0.13

No significant difference between treated group and control group.

Table 8-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of male rats (End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7
		Mean	493	2.11	13.6	22.7	267	1.46
		S.D.	21	0.10	1.3	2.0	74	0.08
	100	No.	12	12	12	12	12	12
		Mean	506	2.09	13.6	23.4	334	1.46
		S.D.	12	0.08	1.5	3.4	115	0.07
	300	No.	12	12	12	12	12	12
		Mean	508	2.11	13.8	23.1	276	1.58
		S.D.	27	0.08	1.4	4.0	57	0.16
	1000	No.	7	7	7	7	7	7
		Mean	503	2.19	13.6	23.4	283	1.44
		S.D.	34	0.06	1.0	3.6	49	0.12
Relative	0	No.		7	7	7	7	7
		Mean		0.43	2.8	4.6	55	0.30
		S.D.		0.03	0.3	0.3	16	0.01
	100	No.		12	12	12	12	12
		Mean		0.41	2.7	4.6	66	0.29
		S.D.		0.02	0.3	0.7	24	0.02
	300	No.		12	12	12	12	12
		Mean		0.42	2.7	4.6	55	0.31
		S.D.		0.02	0.2	0.8	12	0.03
	1000	No.		7	7	7	7	7
		Mean		0.44	2.7	4.7	56	0.29
		S.D.		0.03	0.2	0.8	8	0.01

No significant difference in any treated groups from control group.

Table 8-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of male rats (End of administration)

	Dose mg/kg		Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7
		Mean	12.23	0.79	3.15	61	1.74	1.22
		S.D.	1.13	0.11	0.29	10	0.15	0.12
	100	No.	12	12	12	12	12	12
		Mean	12.93	0.81	3.18	72	1.86	1.37
		S.D.	0.99	0.12	0.19	12	0.23	0.26
	300	No.	12	12	12	12	12	12
		Mean	12.96	0.80	3.27	69	1.86	1.34
		S.D.	1.00	0.09	0.24	12	0.21	0.19
	1000	No.	7	7	7	7	7	7
		Mean	12.60	0.81	3.21	75	1.85	1.48
		S.D.	1.32	0.07	0.26	14	0.28	0.23
Relative	0	No.	7	7	7	7	7	7
		Mean	2.48	0.16	0.64	13	0.35	0.25
		S.D.	0.15	0.03	0.04	2	0.04	0.03
	100	No.	12	12	12	12	12	12
		Mean	2.55	0.16	0.63	14	0.37	0.27
		S.D.	0.18	0.02	0.04	2	0.04	0.05
	300	No.	12	12	12	12	12	12
		Mean	2.55	0.16	0.65	14	0.37	0.27
		S.D.	0.09	0.01	0.04	2	0.04	0.03
	1000	No.	7	7	7	7	7	7
		Mean	2.50	0.16	0.64	15	0.37	0.29
		S.D.	0.13	0.02	0.04	3	0.06	0.04

No significant difference in any treated groups from control group.

Table 8-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of male rats (End of administration)

	Dose mg/kg		Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	0	No.	7	7
		Mean	3.21	1307
		S.D.	0.29	193
	100	No.	12	12
		Mean	3.18	1314
		S.D.	0.30	94
	300	No.	12	12
		Mean	3.30	1314
		S.D.	0.24	110
	1000	No.	7	7
		Mean	3.18	1323
		S.D.	0.16	104
Relative	0	No.	7	7
		Mean	0.65	265
		S.D.	0.04	36
	100	No.	12	12
		Mean	0.63	260
		S.D.	0.06	20
	300	No.	12	12
		Mean	0.65	259
		S.D.	0.05	21
	1000	No.	7	7
		Mean	0.63	263
		S.D.	0.05	18

No significant difference in any treated groups from control group.

Table 8-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of female rats (Lactation day 5)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
		No.	12	12	12	12	12	12
	0	Mean	318	2.03	18.7	16.8	229	1.04
		S.D.	15	0.08	1.9	2.9	67	0.08
		No.	12	12	12	12	12	12
Absolute	100	Mean	313	1.96*	18.3	16.6	251	1.00
		S.D.	21	0.05D	2.4	4.5	57	0.07
		No.	11	11	11	11	11	11
	300	Mean	318	1.97	18.2	16.0	287	1.03
		S.D.	14	0.05	2.0	3.2	71	0.06
		No.	12	12	12	12	12	12
	1000	Mean	312	1.99	18.2	17.2	218	1.02
		S.D.	17	0.06	1.9	3.2	45	0.06
		No.		12	12	12	12	12
	0	Mean		0.64	5.9	5.3	72	0.33
		S.D.		0.04	0.5	0.9	20	0.02
		No.		12	12	12	12	12
Relative	100	Mean		0.63	5.9	5.3	80	0.32
		S.D.		0.04	0.8	1.3	16	0.02
		No.		11	11	11	11	11
	300	Mean		0.62	5.7	5.0	90	0.32
		S.D.		0.03	0.7	1.0	22	0.02
		No.		12	12	12	12	12
	1000	Mean		0.64	5.8	5.5	70	0.33
		S.D.		0.03	0.5	0.9	14	0.02

*: $p<0.05$ (Significant difference from control group)
D: Dunnett's test

Table 8-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of female rats (Lactation day 5)

	Dose mg/kg		Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	12	12	12	12	12	12
		Mean	10.85	0.76	2.27	82	116.3	756
		S.D.	0.96	0.13	0.18	11	15.1	118
	100	No.	12	12	12	12	12	12
		Mean	10.00*	0.67	2.15	76	102.0**	715
		S.D.	0.73D	0.07	0.16	13	10.0D	89
	300	No.	11	11	11	11	11	11
		Mean	10.22	0.68	2.22	79	108.8	799
		S.D.	0.74	0.09	0.11	9	10.3	124
	1000	No.	12	12	12	12	12	12
		Mean	10.24	0.71	2.18	81	106.7	782
		S.D.	0.62	0.09	0.17	10	7.9	76
Relative	0	No.	12	12	12	12	12	12
		Mean	3.41	0.24	0.71	26	36.5	237
		S.D.	0.23	0.04	0.04	3	4.5	37
	100	No.	12	12	12	12	12	12
		Mean	3.20	0.21	0.69	24	32.7	230
		S.D.	0.22	0.02	0.05	5	4.2	33
	300	No.	11	11	11	11	11	11
		Mean	3.21	0.22	0.70	25	34.3	251
		S.D.	0.21	0.03	0.04	3	4.0	39
	1000	No.	12	12	12	12	12	12
		Mean	3.29	0.23	0.70	26	34.2	251
		S.D.	0.23	0.03	0.05	3	2.2	28

*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
D: Dunnett's test

Table 8-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of female rats (Satellite group, End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	277	1.96	15.7	14.8	335	0.88
		S.D.	15	0.08	1.0	2.3	65	0.09
	1000	No.	5	5	5	5	5	5
		Mean	279	1.94	16.0	14.1	286	0.93
		S.D.	33	0.08	2.3	3.0	88	0.08
Relative	0	No.		5	5	5	5	5
		Mean		0.71	5.7	5.4	121	0.32
		S.D.		0.02	0.3	1.0	21	0.02
	1000	No.		5	5	5	5	5
		Mean		0.70	5.8	5.1	101	0.33
		S.D.		0.06	0.9	1.3	23	0.03

No significant difference between treated group and control group.

Table 8-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of female rats (Satellite group, End of administration)

	Dose mg/kg		Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	7.01	0.51	1.86	64	87.1	561
		S.D.	0.49	0.04	0.12	11	17.5	98
	1000	No.	5	5	5	5	5	5
		Mean	6.97	0.51	1.88	70	94.8	549
		S.D.	1.01	0.09	0.15	14	6.8	114
Relative	0	No.	5	5	5	5	5	5
		Mean	2.53	0.19	0.67	23	31.6	203
		S.D.	0.09	0.01	0.02	4	7.0	42
	1000	No.	5	5	5	5	5	5
		Mean	2.49	0.18	0.68	26	34.2	200
		S.D.	0.15	0.03	0.09	8	4.1	49

No significant difference between treated group and control group.

Table 8-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of male rats (End of recovery)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	509	2.14	13.0	21.9	256	1.49
		S.D.	17	0.07	1.1	6.9	45	0.06
	1000	No.	5	5	5	5	5	5
		Mean	524	2.18	12.6	22.4	252	1.46
		S.D.	29	0.08	1.2	3.3	47	0.14
Relative	0	No.		5	5	5	5	5
		Mean		0.42	2.6	4.3	50	0.29
		S.D.		0.03	0.2	1.3	10	0.01
	1000	No.		5	5	5	5	5
		Mean		0.42	2.4	4.3	48	0.28
		S.D.		0.03	0.2	0.5	7	0.02

No significant difference between treated group and control group.

Table 8-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of male rats (End of recovery)

	Dose mg/kg		Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	13.72	0.82	3.32	62	1.73	1.43
		S.D.	1.56	0.09	0.31	9	0.25	0.26
	1000	No.	5	5	5	5	5	5
		Mean	12.81	0.79	3.28	67	1.85	1.45
		S.D.	1.08	0.12	0.18	8	0.23	0.25
Relative	0	No.	5	5	5	5	5	5
		Mean	2.69	0.16	0.65	12	0.34	0.28
		S.D.	0.24	0.02	0.06	1	0.06	0.05
	1000	No.	5	5	5	5	5	5
		Mean	2.44	0.15	0.63	13	0.35	0.28
		S.D.	0.12	0.02	0.02	2	0.03	0.04

No significant difference between treated group and control group.

Table 8-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of male rats (End of recovery)

	Dose mg/kg		Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	0	No.	5	5
		Mean	3.25	1382
		S.D.	0.13	44
	1000	No.	5	5
		Mean	3.37	1306*
		S.D.	0.14	40T
Relative	0	No.	5	5
		Mean	0.64	272
		S.D.	0.04	15
	1000	No.	5	5
		Mean	0.65	250*
		S.D.	0.04	10T

*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 8-11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of female rats (End of recovery)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	308	1.95	17.7	15.1	285	0.95
		S.D.	14	0.05	2.3	3.0	77	0.05
	1000	No.	5	5	5	5	5	5
		Mean	289	1.97	17.4	13.1	307	0.93
		S.D.	26	0.04	3.5	1.8	67	0.06
Relative	0	No.		5	5	5	5	5
		Mean		0.63	5.7	4.9	92	0.31
		S.D.		0.02	0.6	0.8	23	0.01
	1000	No.		5	5	5	5	5
		Mean		0.69	6.0	4.5	105	0.32
		S.D.		0.06	0.8	0.6	16	0.02

No significant difference between treated group and control group.

Table 8-12 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Organ weight of female rats (End of recovery)

	Dose mg/kg		Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5	5
		Mean	7.83	0.57	1.94	65	100.0	552
		S.D.	0.90	0.07	0.13	11	23.8	124
	1000	No.	5	5	5	5	5	5
		Mean	7.03	0.49	1.95	72	81.6	584
		S.D.	0.75	0.04	0.09	18	8.9	113
Relative	0	No.	5	5	5	5	5	5
		Mean	2.54	0.19	0.63	21	32.4	180
		S.D.	0.21	0.02	0.02	3	7.2	44
	1000	No.	5	5	5	5	5	5
		Mean	2.43	0.17	0.68	24	28.4	202
		S.D.	0.08	0.02	0.05	5	4.2	32

No significant difference between treated group and control group.

Table 9-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Gross pathological findings (End of administration (D42))

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
Findings	Number:	7	12	12	7
All tissues					
Not remarkable		7	12	12	7

M : Male

Table 9-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Gross pathological findings (End of administration (D42))

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	1000
	Number:	5	5
Stomach			
Focus,dark red,glandular stomach		1	0

F : Female

Table 9-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Gross pathological findings (End of administration (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
	Number:	12	12	11	12
Stomach					
Focus,dark red,glandular stomach		1	2	2	1

F : Female

Table 9-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Gross pathological findings (End of recovery period)

Organs / Findings	Sex:	M	M	F	F
	Dose(mg/kg):	0	1000	0	1000
	Number:	5	5	5	5
Stomach					
Focus,dark red,glandular stomach		1	0	2	0

M : Male, F : Female

Table 9-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Gross pathological findings (Undelivered)

Organs / Findings	Sex:	F
	Dose(mg/kg):	300
	Number:	1
All tissues		
Not remarkable		1

F : Female

Table 10-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
	Number:	5	5	5	5
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebellum(pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Epididymis					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Cell infiltration		0	0	0	1
minimal		0	0	0	1
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	0	0	5
Not remarkable		2	0	0	2
Regeneration,tubular		3	0	0	3
minimal		3	0	0	3
Liver					
Number examined		5	0	0	5
Microgranuloma		5	0	0	5
minimal		5	0	0	5

M : Male

Table 10-2 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
	Number:	5	5	5	5
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Aggregation,foamy cell		1	0	0	0
minimal		1	0	0	0
Lymph node,mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pituitary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Prostate					
Number examined		5	0	0	5
Not remarkable		1	0	0	1
Cell infiltration		4	0	0	4
minimal		4	0	0	4
Salivary gland,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Seminal vesicle(Coagulating gland)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Skeletal muscle,femoral					
Number examined		5	0	0	5
Not remarkable		3	0	0	3
Degeneration,muscular		2	0	0	2
minimal		2	0	0	2
Spinal cord,thoracic					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spleen					
Number examined		5	0	0	5
Not remarkable		1	0	0	0
Hematopoiesis,extramedullary		4	0	0	5
minimal		4	0	0	5

M : Male

Table 10-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	100	300	1000
	Number:	5	5	5	5
Stomach					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Testis					
Number examined		5	0	0	5
Not remarkable		3	0	0	5
Atrophy,seminiferous tubular		2	0	0	0
minimal		2	0	0	0
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Trachea					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Urinary bladder					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

M : Male

Table 10-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (D42))

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	1000
	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Bone+Bone marrow,femoral			
Number examined		5	5
Not remarkable		5	5
Cerebellum(pons)			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Eye			
Number examined		5	5
Not remarkable		5	5
Heart			
Number examined		5	5
Not remarkable		5	5
Intestine,duodenum			
Number examined		5	5
Not remarkable		5	5
Intestine,jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine,ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine,cecum			
Number examined		5	5
Not remarkable		5	5
Intestine,colon			
Number examined		5	5
Not remarkable		5	5
Intestine,rectum			
Number examined		5	5
Not remarkable		5	5
Kidney			
Number examined		5	5
Not remarkable		2	4
Regeneration,tubular		1	0
minimal		1	0
Urinary cast,hyaline		1	0
minimal		1	0
Cell infiltration		1	1
minimal		1	1
Hyperplasia,transitional,focal		1	0
mild		1	0
Liver			
Number examined		5	5
Microgranuloma		5	5
minimal		5	5

F : Female

Table 10-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (D42))

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	1000
	Number:	5	5
Lung(bronchus)			
Number examined		5	5
Not remarkable		5	5
Lymph node,mesenteric			
Number examined		5	5
Not remarkable		5	5
Lymph node,submandibular			
Number examined		5	5
Not remarkable		5	5
Ovary			
Number examined		5	5
Not remarkable		5	5
Pancreas			
Number examined		5	5
Not remarkable		5	5
Parathyroid			
Number examined		5	5
Not remarkable		5	5
Pituitary			
Number examined		5	5
Not remarkable		5	5
Salivary gland,submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5
Skeletal muscle,femoral			
Number examined		5	5
Not remarkable		5	5
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		0	2
Hematopoiesis,extramedullary		5	3
minimal		5	3
Stomach			
Number examined		5	5
Not remarkable		5	5
Thymus			
Number examined		5	5
Not remarkable		5	5

F : Female

Table 10-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (D42))

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	1000
	Number:	5	5
Thyroid			
Number examined		5	5
Not remarkable		5	5
Trachea			
Number examined		5	5
Not remarkable		5	5
Urinary bladder			
Number examined		5	5
Not remarkable		5	5
Uterus			
Number examined		5	5
Not remarkable		5	5
Vagina			
Number examined		5	5
Not remarkable		5	5

F : Female

Table 10-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
	Number:	5	5	5	5
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebellum(pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Fibrosis,myocardial		0	0	0	1
minimal		0	0	0	1
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Liver					
Number examined		5	0	0	5
Not remarkable		0	0	0	2
Microgranuloma		5	0	0	3
minimal		5	0	0	3
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
	Number:	5	5	5	5
Lymph node,mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Ovary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pituitary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Salivary gland,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Skeletal muscle,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spinal cord,thoracic					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spleen					
Number examined		5	0	0	5
Hematopoiesis,extramedullary		5	0	0	5
minimal		4	0	0	5
mild		1	0	0	0
Stomach					
Number examined		5	0	0	5
Not remarkable		4	0	0	4
Erosion,glandular stomach		1	0	0	1
minimal		1	0	0	1
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Trachea					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of administration (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	100	300	1000
	Number:	5	5	5	5
Urinary bladder					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Uterus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Vagina					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (End of recovery period)

Organs / Findings	Sex:	M	M	F	F
	Dose(mg/kg):	0	1000	0	1000
	Number:	5	5	5	5
Epididymis					
Number examined		5	5	-	-
Not remarkable		5	5	-	-
Testis					
Number examined		5	5	-	-
Not remarkable		4	5	-	-
Atrophy,seminiferous tubular		1	0	-	-
minimal		1	0	-	-

M : Male, F : Female
- : Not applicable

Table 10-11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (Undelivered)

Organs / Findings	Sex:	F
	Dose(mg/kg):	300
	Number:	1
Adrenal		
Number examined		1
Not remarkable		1
Bone+Bone marrow,femoral		
Number examined		1
Not remarkable		1
Cerebellum(pons)		
Number examined		1
Not remarkable		1
Cerebrum		
Number examined		1
Not remarkable		1
Eye		
Number examined		1
Not remarkable		1
Heart		
Number examined		1
Not remarkable		1
Intestine,duodenum		
Number examined		1
Not remarkable		1
Intestine,jejunum		
Number examined		1
Not remarkable		1
Intestine,ileum(Peyer's patch)		
Number examined		1
Not remarkable		1
Intestine,cecum		
Number examined		1
Not remarkable		1
Intestine,colon		
Number examined		1
Not remarkable		1
Intestine,rectum		
Number examined		1
Not remarkable		1
Kidney		
Number examined		1
Regeneration,tubular		1
minimal		1
Liver		
Number examined		1
Microgranuloma		1
minimal		1
Lung(bronchus)		
Number examined		1
Aggregation,foamy cell		1
minimal		1

F : Female

Table 10-12 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (Undelivered)

Organs / Findings	Sex:	F
	Dose(mg/kg):	300
	Number:	1
Lymph node,mesenteric		
Number examined		1
Not remarkable		1
Lymph node,submandibular		
Number examined		1
Not remarkable		1
Ovary		
Number examined		1
Not remarkable		1
Pancreas		
Number examined		1
Not remarkable		1
Parathyroid		
Number examined		1
Not remarkable		1
Pituitary		
Number examined		1
Not remarkable		1
Salivary gland,submandibular		
Number examined		1
Not remarkable		1
Sciatic nerve		
Number examined		1
Not remarkable		1
Skeletal muscle,femoral		
Number examined		1
Degeneration,muscular		1
minimal		1
Spinal cord,thoracic		
Number examined		1
Not remarkable		1
Spleen		
Number examined		1
Hematopoiesis,extramedullary		1
minimal		1
Stomach		
Number examined		1
Not remarkable		1
Thymus		
Number examined		1
Not remarkable		1
Thyroid		
Number examined		1
Not remarkable		1
Trachea		
Number examined		1
Not remarkable		1

F : Female

Table 10-13 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Histopathological findings (Undelivered)

Organs / Findings	Sex:	F
	Dose(mg/kg):	300
	Number:	1
Urinary bladder		
Number examined		1
Not remarkable		1
Uterus		
Number examined		1
Not remarkable		1
Vagina		
Number examined		1
Degeneration,mucinous,mucosal		1
mild		1

F : Female

Table 11 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Estrous cycle in female rats during the pre-mating period

Dose mg/kg	No. of animals	Count of estrus						Mean duration of cycles Mean±S.D.
		0	1	2	3	4	Mean±S.D.	
0	12	1	0	0	1	10	3.6±1.2	4.0±0.0
100	12	0	0	0	5	7	3.6±0.5	4.2±0.3
300	12	0	0	0	8	4	3.3±0.5	4.2±0.3
1000	12	0	0	0	6	6	3.5±0.5	4.0±0.1

No significant difference in any treated groups from control group.

Table 12 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Mating and fertility of animals

	Male				Female			
Dose mg/kg	No. of males	Days until copulation Mean±S.D.	Copulation index (%) a)	Insemination index (%) b)	No. of females	Days until copulation Mean±S.D.	Copulation index (%) a)	Fertility index (%) c)
0	12	3.0±1.1	12/12(100.0)	12/12(100.0)	12	3.0±1.1	12/12(100.0)	12/12(100.0)
100	12	2.8±1.1	12/12(100.0)	12/12(100.0)	12	2.8±1.1	12/12(100.0)	12/12(100.0)
300	12	1.9±1.4	12/12(100.0)	11/12(91.7)	12	1.9±1.4	12/12(100.0)	11/12(91.7)
1000	12	2.5±1.4	12/12(100.0)	12/12(100.0)	12	2.5±1.4	12/12(100.0)	12/12(100.0)

a): (No. of copulated animals / No. of mated animals) × 100
b): (No. of males which impregnated females / No. of copulated males) × 100
c): (No. of pregnant females / No. of copulated females) × 100
No significant difference in any treated groups from control group.

Table 13 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Delivery data on dams

Dose mg/kg		No. of pregnant females	No. of females with liveborns	Delivery index % a)	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % b)	No. of still-borns (%)c)	No. of live-borns	External d) abnor-malities(%)e)	Live birth index % f)
	Total	12	12	100.0		198	193		2	176	0	
0	Mean				21.7	16.5	16.1	97.9	(1.1)	14.7	(0.0)	91.6
	S.D.				0.5	2.3	1.9	5.8	(2.5)	1.8	(0.0)	8.7
	Total	12	12	100.0		190	180		0	159	0	
100	Mean				21.8	15.8	15.0	94.8	(0.0)	13.3	(0.0)	88.4
	S.D.				0.5	1.3	1.4	5.2	(0.0)	2.3	(0.0)	13.8
	Total	11	11	100.0		181	172		0	159	0	
300	Mean				21.5	16.5	15.6	95.2	(0.0)	14.5	(0.0)	92.1
	S.D.				0.5	2.0	2.0	5.7	(0.0)	2.5	(0.0)	6.3
	Total	12	12	100.0		193	185		0	180	0	
1000	Mean				21.6	16.1	15.4	96.1	(0.0)	15.0	(0.0)	97.5
	S.D.				0.5	1.4	1.2	4.9	(0.0)	1.0	(0.0)	4.0

a): (No. of females which delivered liveborns / No. of pregnant females) × 100
b): (No. of implantation sites / No. of corpora lutea) × 100
c): (No. of stillborns / No. of liveborns and stillborns) × 100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100
f): (No. of liveborns / No. of implantation sites) × 100
No significant difference in any treated groups from control group.

Table 14 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Viability index of pups

Dose mg/kg		No. of dams	No. of live pups Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % a)
0	Total	12	176	175	
	Mean		14.7	14.6	99.5
	S.D.		1.8	1.7	1.7
100	Total	12	159	157	
	Mean		13.3	13.1	98.6
	S.D.		2.3	2.4	3.3
300	Total	11	159	155	
	Mean		14.5	14.1	98.1
	S.D.		2.5	2.1	6.4
1000	Total	12	180	171	
	Mean		15.0	14.3	94.8
	S.D.		1.0	1.8	8.1

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100
No significant difference in any treated groups from control group.

Table 15 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Sex ratio of pups

Dose mg/kg	No. of dams		Liveborns No. of males	Liveborns No. of females	Sex ratio of liveborns at birth a)	No. of dams	Postnatal day 4 No. of males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 b)
		Total	88	88			88	87	
0	12	Mean	7.3	7.3	0.50	12	7.3	7.3	0.50
		S.D.	1.9	1.8	0.12		1.9	1.9	0.12
		Total	82	77			82	75	
100	12	Mean	6.8	6.4	0.53	12	6.8	6.3	0.53
		S.D.	1.4	2.2	0.11		1.4	2.3	0.12
		Total	78	81			77	78	
300	11	Mean	7.1	7.4	0.50	11	7.0	7.1	0.50
		S.D.	2.0	2.7	0.15		2.0	2.2	0.14
		Total	101	79			96	75	
1000	12	Mean	8.4	6.6	0.56	12	8.0	6.3	0.55
		S.D.	2.0	1.5	0.12		2.4	1.1	0.11

a): No. of liveborn males / No. of liveborns
b): No. of live males on day 4 / No. of live pups on day 4
No significant difference in any treated groups from control group.

Table 16 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Body weight of pups

Dose mg/kg		Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
	No.	12	12	12	12	12	12
0	Mean	6.5	9.7	3.2	6.0	9.0	2.9
	S.D.	0.5	1.1	0.7	0.5	1.0	0.5
	No.	12	12	12	12	12	12
100	Mean	6.7	10.1	3.4	6.3	9.6	3.3
	S.D.	0.6	1.2	0.9	0.6	0.9	0.8
	No.	11	11	11	11	11	11
300	Mean	6.5	9.8	3.3	6.2	9.2	3.0
	S.D.	0.7	1.4	0.9	0.6	1.3	0.9
	No.	12	12	12	12	12	12
1000	Mean	6.4	9.4	2.9	6.1	8.6	2.6
	S.D.	0.4	0.9	0.7	0.3	1.2	1.0

Unit: g
No.: No. of dams
a): Postnatal day
No significant difference in any treated groups from control group.

Table 17 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg)	0	100	300	1000
Male				
No. of pups examined	88	82	77	96
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	87	75	78	75
No. of pups with abnormal findings	0	0	0	0

Appendix 1-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration						
	1-7	8-14	15-21	22-28	29-35	36-42	43a)
1001	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	
1009	-	-	-	-	-	-	
1010	-	-	-	-	-	-	
1011	-	-	-	-	-	-	
1012	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration						
	1-7	8-14	15-21	22-28	29-35	36-42	43a)
2001	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 300

Animal number	Day of administration						
	1-7	8-14	15-21	22-28	29-35	36-42	43a)
3001	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in male rats (Administration period)

Dose (mg/kg): 1000

Animal number	Day of administration						
	1-7	8-14	15-21	22-28	29-35	36-42	43a)
4001	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-
4003	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-
4005	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	
4009	-	-	-	-	-	-	
4010	-	-	-	-	-	-	
4011	-	-	-	-	-	-	
4012	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 0

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 100

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 300

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats during the pre-mating period (Main group)

Dose (mg/kg): 1000

Animal number	Day of administration														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
4101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 0

Dam number	Administration																						
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22a)
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 100

Dam number	Administration																						
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22a)
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 300

Dam number	Administration																						
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22a)
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3111	Non-pregnant																						
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the gestation period (Main group)

Dose (mg/kg): 1000

Dam number	Administration																						
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22a)
4101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
4112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d

a): Gestation day
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 0

Dam number	Administration					
	0	1	2	3	4a)	5b)
1101	-	-	-	-	-	-
1102	-	-	-	-	-	-
1103	-	-	-	-	-	-
1104	-	-	-	-	-	-
1105	-	-	-	-	-	-
1106	-	-	-	-	-	-
1107	-	-	-	-	-	-
1108	-	-	-	-	-	-
1109	-	-	-	-	-	-
1110	-	-	-	-	-	-
1111	-	-	-	-	-	-
1112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
-: No abnormal findings

Appendix 1-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 100

Dam number	Administration					
	0	1	2	3	4a)	5b)
2101	-	-	-	-	-	-
2102	-	-	-	-	-	-
2103	-	-	-	-	-	-
2104	-	-	-	-	-	-
2105	-	-	-	-	-	-
2106	-	-	-	-	-	-
2107	-	-	-	-	-	-
2108	-	-	-	-	-	-
2109	-	-	-	-	-	-
2110	-	-	-	-	-	-
2111	-	-	-	-	-	-
2112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
-: No abnormal findings

Appendix 1-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 300

Dam number	Administration					
	0	1	2	3	4a)	5b)
3101	-	-	-	-	-	-
3102	-	-	-	-	-	-
3103	-	-	-	-	-	-
3104	-	-	-	-	-	-
3105	-	-	-	-	-	-
3106	-	-	-	-	-	-
3107	-	-	-	-	-	-
3108	-	-	-	-	-	-
3109	-	-	-	-	-	-
3110	-	-	-	-	-	-
3111	Non-pregnant					
3112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
-: No abnormal findings

Appendix 1-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in dams during the lactation period (Main group)

Dose (mg/kg): 1000

Dam number	Administration					
	0	1	2	3	4a)	5b)
4101	-	-	-	-	-	-
4102	-	-	-	-	-	-
4103	-	-	-	-	-	-
4104	-	-	-	-	-	-
4105	-	-	-	-	-	-
4106	-	-	-	-	-	-
4107	-	-	-	-	-	-
4108	-	-	-	-	-	-
4109	-	-	-	-	-	-
4110	-	-	-	-	-	-
4111	-	-	-	-	-	-
4112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
-: No abnormal findings

Appendix 1-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration						
	1-7	8-14	15-21	22-28	29-35	36-42	43a)
1113	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	
1119	-	-	-	-	-	-	
1120	-	-	-	-	-	-	
1121	-	-	-	-	-	-	
1122	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats (Satellite group, administration period)

Dose (mg/kg): 1000

Animal number	Day of administration						
	1-7	8-14	15-21	22-28	29-35	36-42	43a)
4113	-	-	-	-	-	-	-
4114	-	-	-	-	-	-	-
4115	-	-	-	-	-	-	-
4116	-	-	-	-	-	-	-
4117	-	-	-	-	-	-	-
4118	-	-	-	-	-	-	
4119	-	-	-	-	-	-	
4120	-	-	-	-	-	-	
4121	-	-	-	-	-	-	
4122	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in male rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in male rats (Recovery period)

Dose (mg/kg): 1000

Animal number	Day of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual clinical signs in female rats (Recovery period)

Dose (mg/kg): 1000

Animal number	Day of recovery														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)
4118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 2-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 300

	Animal number (3001-3012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 300

	Animal number (3001-3012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-31

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-32

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-33

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-34

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-35

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-36

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-37

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-38

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-39

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-40

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-41

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-42

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-43

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-44

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-45

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-46

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-47

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-48

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-49

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-50

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-51

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
NP: Non-pregnant

Appendix 2-52

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-53

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 0

	Animal number (1113-1122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-54

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 1000

	Animal number (4113-4122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-55

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 0

	Animal number (1113-1122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-56

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-57

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 0

	Animal number (1113-1122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-58

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-59

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 0

	Animal number (1113-1122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-60

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 1000

	Animal number (4113-4122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-61

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 0

	Animal number (1113-1122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-62

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-63

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-64

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-65

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-66

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-67

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-68

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-69

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-70

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-71

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-72

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-73

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-74

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-75

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation (Week 1 of administration)

Dose (mg/kg) : 300

	Animal number (3001-3012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-76

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-77

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	1	0	0	0	0	0	0	0	1	0	0
Reactivity to handling n)	0	0	0	1	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-78

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-79

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 300

	Animal number (3001-3012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-80

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	1	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	1	0	0	0	0	0	0	0	1	1	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-81

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-82

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	1	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	1	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	1	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-83

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-84

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	1	0	0	0	0	0	0	0	1	0	0
Reactivity to handling n)	0	1	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-85

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-86

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-87

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 300

	Animal number (3001-3012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-88

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	1	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	1	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-89

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-90

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-91

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 300

	Animal number (3001-3012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-92

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	1	0	0	0	1	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-93

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 0

	Animal number (1001-1012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	1	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-94

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 100

	Animal number (2001-2012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-95

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	1	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	1	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-96

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)

Dose (mg/kg) : 1000

	Animal number (4001-4012)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	1	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	1	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-97

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-98

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-99

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 300

	Animal number (3101-3112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-100

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-101

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-102

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-103

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 300

	Animal number (3101-3112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-104

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-105

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-106

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-107

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-108

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-109

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-110

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-111

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-112

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-113

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-114

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-115

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-116

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-117

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-118

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-119

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-120

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-121

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 0

	Animal number (1101-1112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-122

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 100

	Animal number (2101-2112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-123

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-124

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)

Dose (mg/kg) : 1000

	Animal number (4101-4112)											
Parameter	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-125

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 0

	Animal number (1113-1122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-126

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-127

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-128

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-129

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-130

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 1000

	Animal number (4113-4122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-131

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-132

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-133

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-134

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 1000

	Animal number (4113-4122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-135

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-136

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 1000

	Animal number (4113-4122)									
Parameter	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-137

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-138

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	1	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-139

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-140

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	1	0	0
Reactivity to handling n)	0	1	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-141

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-142

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-143

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-144

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, unkempt fur, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-145

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	8	3	4	5	5	5	4	3	4	1	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-146

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	4	5	10	4	6	2	7	8	5	5
Defecation count	0	0	0	0	0	1	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-147

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	4	6	5	4	8	3	3	4	8	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-148

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	4	7	5	4	4	5	6	4	10	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-149

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	5	4	4	4	6	3	4	4	4	1	5
Defecation count	0	0	0	0	0	0	3	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-150

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	7	2	4	6	2	4	4	6	7	1	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-151

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	4	6	3	4	5	5	2	2	5	7
Defecation count	0	0	0	0	0	0	0	0	1	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-152

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	6	3	3	4	3	2	5	4	2	8	0
Defecation count	0	0	0	1	0	0	0	0	0	0	1	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-153

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	6	0	5	4	5	3	5	3	2	4	5
Defecation count	0	0	0	0	0	0	1	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-154

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	4	3	4	9	3	4	4	8	4	1	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-155

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	5	3	6	3	6	8	0	6	5	6	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-156

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	4	5	4	4	7	5	6	1	3	7	1
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-157

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	8	2	2	5	4	3	2	2	4	5	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-158

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	2	3	8	4	4	3	6	6	4	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-159

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	3	7	2	5	7	2	6	3	5	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-160

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	2	2	4	6	4	3	6	1	2	3	0
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-161

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	6	2	3	5	3	4	5	6	4	4	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-162

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	3	2	8	3	3	5	6	6	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-163

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	3	5	4	5	6	4	5	3	1	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-164

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	2	3	2	5	4	2	6	1	3	5	1
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-165

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	1	4	5	2	7	4	5	7	7	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-166

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	4	2	7	1	4	6	6	4	4	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-167

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	3	4	4	2	4	7	4	3	6	5	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-168

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	2	4	5	3	3	2	6	5	4	6	1
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-169

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	7	7	11	8	6	6	8	10	8	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-170

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	4	4	7	7	9	8	4	6	9	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-171

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	9	4	11	11	7	7	7	7	5	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-172

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	6	8	8	9	8	5	7	6	6	6	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-173

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	4	5	6	10	7	9	8	9	12	9	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-174

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	7	4	5	9	7	12	5	6	7	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-175

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	7	8	10	17	8	8	8	8	5	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-176

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	4	9	8	10	8	6	7	4	9	6	8
Defecation count	0	0	1	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-177

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	5	4	5	5	3	4	6	7	8	6	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-178

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	8	6	8	2	6	8	5	6	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-179

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	8	6	2	9	10	4	5	10	9	6		5
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-180

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	4	9	5	10	7	7	7	4	7	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-181

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	4	6	6	6	5	6	6	8	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-182

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	4	7	5	9	5	5	9	4	1	6	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-183

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	10	8	5	6	6	6	5	9	6	6		4
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-184

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	4	6	7	8	8	4	7	3	7	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-185

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	7	7	9	5	5	6	8	6	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-186

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	6	4	8	5	5	8	4	6	9	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-187

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	6	6	3	8	8	6	5	5	8	5		7
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-188

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	2	8	7	5	8	6	5	7	7	4	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-189

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	6	6	5	6	5	4	5	6	5	6	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-190

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	6	4	7	5	4	7	3	7	8	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-191

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	7	6	6	6	6	5	3	6	4	4		5
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-192

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	3	6	4	5	6	2	4	4	4	3	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-193

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	5	6	7	8	8	6	11	6	8	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-194

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	8	5	4	7	7	7	6	5	8	10
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-195

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 NP	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	9	8	6	7	7	8	7	7	6	8		5
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-196

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)

Dose (mg/kg) : 1000

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	10	3	8	6	9	8	7	6	4	7	7	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-197

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	11	5	9	4	3	11	6	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-198

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	3	6	7	6	8	15	6	7	10	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-199

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	6	6	13	5	3	11	6	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-200

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	7	7	9	11	6	7	10	0
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-201

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	4	7	6	9	10	5	11	4	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-202

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	8	10	9	9	5	5	9	0
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-203

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	8	10	9	14	11	6	9	8	8	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-204

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	9	7	6	10	6	7	6	6	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-205

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	7	8	11	11	10	8	10	6
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-206

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	11	8	9	15	12	5	7	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-207

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	7	9	7	8	9	7	7	7	8	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-208

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	13	5	7	11	8	8	8	7	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-209

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	4	5	7	3
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-210

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	1	5	5	5	3
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-211

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	1	4	5	4	5
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-212

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	3	5	4	6	5
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-213

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	5	8	6	8	9
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-214

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	11	6	7	3	5
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-215

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	11	6	7	7
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-216

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	U	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	9	5	8	0	11
Defecation count	0	0	0	1	0
Urination h)	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-217

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	54	109	70	92	94

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-218

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 100

Parameter	Animal number (2008-2012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	104	82	98	109	86

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-219

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 300

Parameter	Animal number (3008-3012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	64	83	96	84	56

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-220

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of male rats (Week 6 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	110	117	112	96	83

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-221

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 0

Parameter	Animal number (1101-1107)				
	1	2	4	5	7
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	49	55	58	71	53

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-222

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 100

Parameter	Animal number (2103-2112)				
	3	7	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	39	81	56	29	30

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-223

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 300

Parameter	Animal number (3101-3110)				
	1	4	7	8	10
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	42	40	51	35	64

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-224

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 1000

Parameter	Animal number (4104-4112)				
	4	6	9	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	49	49	64	94	71

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-225

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	60	49	61	54	87

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-226

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	73	42	64	56	52

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-227

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of male rats (Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	52	115	99	96	69

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-228

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of male rats (Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	103	106	110	110	94

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-229

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Week 2 of recovery)

Dose (mg/kg) : 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	60	62	77	54	84

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-230

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual manipulative test of female rats (Week 2 of recovery)

Dose (mg/kg) : 1000

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	79	67	86	53	60

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-231

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1008	1297	648
1009	1729	998
1010	1861	1025
1011	1440	1075
1012	1589	867
Mean	1583	923
S.D.	224	172

Appendix 2-232

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 100

Animal number	Fore limb g	Hind limb g
2008	1806	1046
2009	1146	757
2010	1876	1129
2011	1770	1160
2012	1785	852
Mean	1677	989
S.D.	299	177

Appendix 2-233

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 300

Animal number	Fore limb g	Hind limb g
3008	1620	1143
3009	1397	862
3010	1213	891
3011	1164	937
3012	1137	712
Mean	1306	909
S.D.	203	156

Appendix 2-234

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of male rats (Week 6 of administration)

Dose (mg/kg) : 1000

Animal number	Fore limb g	Hind limb g
4008	1892	1273
4009	1842	1006
4010	1738	941
4011	1389	882
4012	1624	1114
Mean	1697	1043
S.D.	201	155

Appendix 2-235

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1101	1253	886
1102	1474	1074
1104	1484	769
1105	1178	868
1107	894	707
Mean	1257	861
S.D.	243	140

Appendix 2-236

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 100

Animal number	Fore limb g	Hind limb g
2103	1083	786
2107	1458	849
2110	1362	516
2111	1313	866
2112	1106	593
Mean	1264	722
S.D.	164	158

Appendix 2-237

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 300

Animal number	Fore limb g	Hind limb g
3101	1388	1015
3104	995	940
3107	1225	714
3108	1461	818
3110	1440	786
Mean	1302	855
S.D.	195	121

Appendix 2-238

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 1000

Animal number	Fore limb g	Hind limb g
4104	1338	819
4106	1053	751
4109	1147	738
4111	1575	1267
4112	1368	959
Mean	1296	907
S.D.	204	220

Appendix 2-239

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1118	1342	688
1119	1039	735
1120	1277	822
1121	1154	927
1122	1480	619
Mean	1258	758
S.D.	170	120

Appendix 2-240

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 1000

Animal number	Fore limb g	Hind limb g
4118	1320	493
4119	1311	906
4120	1550	726
4121	1178	600
4122	972	522
Mean	1266	649
S.D.	212	169

Appendix 2-241

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of male rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1008	1883	575
1009	1534	1164
1010	1852	1236
1011	1810	1075
1012	1815	1084
Mean	1779	1027
S.D.	140	261

Appendix 2-242

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of male rats (Week 2 of recovery)

Dose (mg/kg) : 1000

Animal number	Fore limb g	Hind limb g
4008	2193	1152
4009	1865	1264
4010	1636	966
4011	1873	1174
4012	1782	968
Mean	1870	1105
S.D.	204	133

Appendix 2-243

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Fore limb g	Hind limb g
1118	1176	1090
1119	1233	983
1120	1504	891
1121	1347	931
1122	1583	669
Mean	1369	913
S.D.	173	155

Appendix 2-244

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual grip strength of female rats (Week 2 of recovery)

Dose (mg/kg) : 1000

Animal number	Fore limb g	Hind limb g
4118	1466	669
4119	1363	1027
4120	1597	775
4121	1490	471
4122	1023	525
Mean	1388	693
S.D.	220	222

Appendix 2-245

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1008	397	366	353	73	0	78	1267
1009	365	327	200	65	153	19	1129
1010	426	514	321	180	10	23	1474
1011	432	417	154	133	23	0	1159
1012	390	404	142	7	17	189	1149
Mean	402	406	234	92	41	62	1236
S.D.	27	70	97	67	63	77	144

Unit : Count

Appendix 2-246

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 100

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2008	471	402	445	354	377	399	2448
2009	495	310	27	28	21	1	882
2010	339	322	219	174	58	59	1171
2011	451	394	408	299	301	286	2139
2012	406	370	341	379	277	498	2271
Mean	432	360	288	247	207	249	1782
S.D.	62	42	169	146	158	214	706

Unit : Count

Appendix 2-247

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 300

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3008	360	264	196	79	2	134	1035
3009	454	373	343	355	207	220	1952
3010	304	278	326	147	48	2	1105
3011	504	488	244	405	300	55	1996
3012	408	384	352	283	302	144	1873
Mean	406	357	292	254	172	111	1592
S.D.	78	91	69	138	140	84	479

Unit : Count

Appendix 2-248

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of male rats (Week 6 of administration)

Dose (mg/kg) : 1000

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	384	381	65	3	1	249	1083
4009	425	361	287	315	234	326	1948
4010	467	380	269	206	1	38	1361
4011	413	319	45	78	59	6	920
4012	403	382	63	32	14	111	1005
Mean	418	365	146	127	62	146	1263
S.D.	31	27	121	131	99	137	417

Unit : Count

Appendix 2-249

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1101	420	107	30	11	44	33	645
1102	400	376	342	350	91	13	1572
1104	492	345	57	7	3	6	910
1105	480	420	120	20	201	115	1356
1107	423	320	287	261	236	235	1762
Mean	443	314	167	130	115	80	1249
S.D.	40	121	140	164	100	97	463

Unit : Count

Appendix 2-250

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 100

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2103	412	311	118	5	62	0	908
2107	404	344	358	366	219	161	1852
2110	370	230	178	232	203	181	1394
2111	414	260	328	44	28	141	1215
2112	437	414	19	12	33	7	922
Mean	407	312	200	132	109	98	1258
S.D.	24	72	143	160	94	87	390

Unit : Count

Appendix 2-251

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 300

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3101	417	194	62	300	165	145	1283
3104	447	147	14	173	135	212	1128
3107	452	427	340	412	186	3	1820
3108	439	437	197	3	15	9	1100
3110	360	250	37	5	28	0	680
Mean	423	291	130	179	106	74	1202
S.D.	38	134	137	180	79	99	411

Unit : Count

Appendix 2-252

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Main group, Lactation day 4)

Dose (mg/kg) : 1000

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4104	354	76	25	5	19	0	479
4106	380	291	207	11	28	0	917
4109	398	285	0	6	10	1	700
4111	381	181	8	12	15	18	615
4112	417	333	202	72	340	316	1680
Mean	386	233	88	21	82	67	878
S.D.	23	104	106	29	144	139	476

Unit : Count

Appendix 2-253

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1118	412	333	285	262	120	30	1442
1119	388	341	372	308	323	56	1788
1120	427	311	184	12	12	10	956
1121	390	330	214	258	218	15	1425
1122	387	315	261	319	16	59	1357
Mean	401	326	263	232	138	34	1394
S.D.	18	13	72	126	134	23	297

Unit : Count

Appendix 2-254

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg) : 1000

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118	485	400	331	266	261	190	1933
4119	447	299	362	320	156	10	1594
4120	384	228	181	237	29	30	1089
4121	386	359	371	283	324	163	1886
4122	475	357	285	222	210	1	1550
Mean	435	329	306	266	196	79	1610
S.D.	48	67	78	39	112	90	338

Unit : Count

Appendix 2-255

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of male rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1008	420	295	372	113	19	17	1236
1009	292	329	217	88	18	19	963
1010	258	123	58	27	10	29	505
1011	261	209	208	39	24	225	966
1012	230	125	39	31	1	12	438
Mean	292	216	179	60	14	60	822
S.D.	75	95	136	39	9	92	339

Unit : Count

Appendix 2-256

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of male rats (Week 2 of recovery)

Dose (mg/kg) : 1000

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	342	123	287	50	12	169	983
4009	305	153	161	28	43	2	692
4010	379	156	345	144	151	164	1339
4011	351	103	9	64	21	26	574
4012	309	146	53	133	24	5	670
Mean	337	136	171	84	50	73	852
S.D.	31	23	145	52	57	86	312

Unit : Count

Appendix 2-257

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Week 2 of recovery)

Dose (mg/kg) : 0

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1118	347	337	283	347	283	289	1886
1119	299	256	218	219	196	57	1245
1120	376	283	10	4	143	281	1097
1121	355	239	226	199	161	29	1209
1122	322	232	19	74	287	276	1210
Mean	340	269	151	169	214	186	1329
S.D.	30	43	127	134	68	131	316

Unit : Count

Appendix 2-258

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual motor activity of female rats (Week 2 of recovery)

Dose (mg/kg) : 1000

Animal number	Interval (minutes)						
	0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118	368	370	320	246	294	219	1817
4119	427	357	383	243	53	22	1485
4120	335	93	173	246	204	41	1092
4121	173	23	0	30	10	8	244
4122	294	192	76	93	157	127	939
Mean	319	207	190	172	144	83	1115
S.D.	95	155	161	103	115	89	596

Unit : Count

Appendix 3-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
1001	408	436	451	451	462	484	490	82
1002	411	422	446	450	474	506	509	98
1003	413	450	478	495	519	539	558	145
1004	392	432	452	468	487	512	520	128
1005	400	426	447	468	484	506	520	120
1006	400	424	453	477	500	529	543	143
1007	446	461	474	495	514	537	543	97
1008	416	447	469	473	504	530	530	114
1009	398	436	466	487	503	534	519	121
1010	389	422	438	452	475	493	507	118
1011	383	404	418	441	459	477	492	109
1012	408	430	443	460	484	508	508	100
Mean	405	433	453	468	489	513	520	115
S.D.	16	15	17	18	19	21	21	19

Unit: g

Appendix 3-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration							Gain
	1	8	15	22	29	36	42	1-42
2001	397	419	444	463	480	512	527	130
2002	416	441	457	472	496	524	527	111
2003	414	446	455	479	503	534	545	131
2004	412	447	464	485	505	526	535	123
2005	384	415	443	469	496	524	534	150
2006	425	455	481	497	522	549	557	132
2007	402	429	462	484	507	538	546	144
2008	411	437	449	469	494	512	525	114
2009	391	426	450	472	497	520	526	135
2010	405	445	471	490	516	537	539	134
2011	399	428	449	479	506	544	546	147
2012	400	430	458	477	491	516	518	118
Mean	405	435	457	478	501	528	535	131
S.D.	12	12	11	10	11	12	11	13

Unit: g

Appendix 3-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
3001	403	433	461	486	507	526	546	143
3002	424	468	498	518	537	561	574	150
3003	412	450	478	507	533	549	560	148
3004	416	455	490	507	533	559	566	150
3005	407	420	440	464	490	519	543	136
3006	421	455	485	501	537	566	584	163
3007	380	410	437	453	467	490	507	127
3008	398	426	439	463	495	522	533	135
3009	406	426	448	471	491	523	535	129
3010	404	425	448	478	506	529	537	133
3011	381	413	430	444	467	480	495	114
3012	402	434	458	468	485	510	518	116
Mean	405	435	459	480	504	528	542	137
S.D.	14	18	23	24	26	27	27	15

Unit: g

Appendix 3-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of male rats (Administration period)

Dose (mg/kg): 1000

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4001	387	409	416	428	440	464	483	96
4002	404	436	451	466	484	507	517	113
4003	397	433	437	463	484	491	497	100
4004	422	452	487	504	525	540	567	145
4005	429	477	515	522	551	576	593	164
4006	419	456	486	507	527	553	548	129
4007	400	435	456	475	494	512	516	116
4008	384	413	445	462	487	513	526	142
4009	413	437	455	482	519	545	565	152
4010	401	432	451	459	475	506	511	110
4011	414	437	457	478	505	522	535	121
4012	381	416	442	459	475	499	492	111
Mean	404	436	458	475	497	519	529	125
S.D.	16	19	26	26	30	30	34	21

Unit: g

Appendix 3-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	Gain 1-15
1101	242	251	259	17
1102	263	298	306	43
1103	251	258	254	3
1104	247	270	283	36
1105	231	246	254	23
1106	268	282	284	16
1107	239	249	253	14
1108	246	259	260	14
1109	268	273	277	9
1110	285	297	298	13
1111	226	251	260	34
1112	247	258	262	15
Mean	251	266	271	20
S.D.	17	18	18	12

Unit: g

Appendix 3-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 100

Animal number	Day of administration 1	8	15	Gain 1-15
2101	257	261	252	-5
2102	240	250	265	25
2103	242	248	259	17
2104	246	258	259	13
2105	252	262	278	26
2106	271	280	285	14
2107	274	280	297	23
2108	259	276	287	28
2109	252	264	275	23
2110	241	241	255	14
2111	224	243	251	27
2112	247	261	271	24
Mean	250	260	270	19
S.D.	14	13	15	9

Unit: g

Appendix 3-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	Gain 1-15
3101	257	271	280	23
3102	246	264	265	19
3103	253	254	258	5
3104	251	253	275	24
3105	265	274	289	24
3106	255	261	280	25
3107	236	260	276	40
3108	274	279	290	16
3109	243	248	271	28
3110	253	260	272	19
3111	247	250	256	9
3112	227	237	248	21
Mean	251	259	272	21
S.D.	12	12	13	9

Unit: g

Appendix 3-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats during the pre-mating period (Main group)

Dose (mg/kg): 1000

Animal number	Day of administration 1	8	15	Gain 1-15
4101	222	238	243	21
4102	274	284	287	13
4103	238	249	249	11
4104	248	250	266	18
4105	238	240	236	-2
4106	258	262	273	15
4107	242	259	259	17
4108	251	263	266	15
4109	267	276	292	25
4110	262	281	284	22
4111	259	260	275	16
4112	262	268	282	20
Mean	252	261	268	16
S.D.	15	15	18	7

Unit: g

Appendix 3-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 0

Dam number	Administration 0	7	14	20a)	Gain 0-20
1101	266	299	330	406	140
1102	312	335	361	434	122
1103	265	289	328	404	139
1104	278	324	360	438	160
1105	264	304	347	436	172
1106	305	332	365	458	153
1107	256	292	328	398	142
1108	285	300	342	427	142
1109	296	333	362	459	163
1110	314	339	369	479	165
1111	268	296	334	409	141
1112	275	296	336	412	137
Mean	282	312	347	430	148
S.D.	20	19	16	26	15

Unit: g
a): Gestation day

Appendix 3-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 100

Dam number	Administration 0	7	14	20a)	Gain 0-20
2101	261	309	346	414	153
2102	270	319	357	433	163
2103	268	310	363	453	185
2104	271	302	338	428	157
2105	286	314	346	408	122
2106	303	334	375	458	155
2107	303	338	364	422	119
2108	290	324	353	444	154
2109	276	312	344	437	161
2110	256	293	325	397	141
2111	248	288	322	387	139
2112	273	306	333	413	140
Mean	275	312	347	425	149
S.D.	17	15	16	22	18

Unit: g
a): Gestation day

Appendix 3-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 300

Dam number	Administration 0	7	14	20a)	Gain 0-20
3101	283	306	348	416	133
3102	279	310	342	403	124
3103	281	314	358	441	160
3104	271	314	344	429	158
3105	290	323	359	445	155
3106	287	310	341	415	128
3107	283	318	358	451	168
3108	292	338	388	476	184
3109	271	314	350	412	141
3110	271	315	352	426	155
3111	Non-pregnant				
3112	256	292	331	431	175
Mean	279	314	352	431	153
S.D.	11	11	15	21	19

Unit: g
a): Gestation day

Appendix 3-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the gestation period (Main group)

Dose (mg/kg): 1000

Dam number	Administration 0	7	14	20a)	Gain 0-20
4101	248	285	307	397	149
4102	294	338	374	453	159
4103	262	295	320	396	134
4104	268	308	347	436	168
4105	254	278	306	396	142
4106	283	312	350	431	148
4107	269	310	339	431	162
4108	283	308	350	437	154
4109	295	324	365	462	167
4110	304	334	380	480	176
4111	279	308	351	441	162
4112	292	329	360	442	150
Mean	278	311	346	434	156
S.D.	18	19	24	26	12

Unit: g
a): Gestation day

Appendix 3-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 0

Dam number	Administration 0	Administration 4a)	Gain 0-4
1101	321	334	13
1102	346	356	10
1103	347	350	3
1104	326	359	33
1105	335	348	13
1106	322	377	55
1107	298	329	31
1108	338	352	14
1109	362	354	-8
1110	380	375	-5
1111	320	341	21
1112	318	334	16
Mean	334	351	16
S.D.	22	15	17

Unit: g
a): Lactation day

Appendix 3-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 100

Dam number	Administration 0	Administration 4a)	Gain 0-4
2101	335	350	15
2102	313	353	40
2103	339	356	17
2104	346	340	-6
2105	338	339	1
2106	358	385	27
2107	363	360	-3
2108	342	358	16
2109	306	352	46
2110	321	335	14
2111	331	327	-4
2112	300	316	16
Mean	333	348	15
S.D.	20	18	17

Unit: g
a): Lactation day

Appendix 3-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 300

Dam number	Administration 0	Administration 4a)	Gain 0-4
3101	327	369	42
3102	325	338	13
3103	361	348	-13
3104	352	350	-2
3105	345	363	18
3106	333	335	2
3107	346	347	1
3108	370	381	11
3109	344	359	15
3110	348	342	-6
3111	Non-pregnant		
3112	314	319	5
Mean	342	350	8
S.D.	16	17	15

Unit: g
a): Lactation day

Appendix 3-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of dams during the lactation period (Main group)

Dose (mg/kg): 1000

Dam number	Administration 0	Administration 4a)	Gain 0-4
4101	289	316	27
4102	376	379	3
4103	318	330	12
4104	333	340	7
4105	282	313	31
4106	349	351	2
4107	359	341	-18
4108	352	343	-9
4109	367	370	3
4110	368	365	-3
4111	312	348	36
4112	333	352	19
Mean	337	346	9
S.D.	31	20	16

Unit: g
a): Lactation day

Appendix 3-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
1113	236	238	245	256	268	272	282	46
1114	250	252	271	280	284	308	306	56
1115	231	242	249	252	254	268	272	41
1116	240	261	279	292	295	307	319	79
1117	239	255	255	269	270	282	293	54
1118	270	292	305	315	314	329	330	60
1119	260	270	279	288	304	314	315	55
1120	240	262	281	278	302	323	306	66
1121	246	269	281	289	283	297	288	42
1122	265	268	290	287	310	324	323	58
Mean	248	261	274	281	288	302	303	56
S.D.	13	16	19	18	20	22	19	11

Unit: g

Appendix 3-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats (Satellite group, administration period)

Dose (mg/kg): 1000

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4113	248	253	270	281	293	291	303	55
4114	236	255	271	276	272	286	295	59
4115	263	284	298	305	322	338	339	76
4116	225	227	235	236	227	236	241	16
4117	244	269	276	290	291	306	311	67
4118	247	262	265	264	277	285	280	33
4119	266	281	289	310	319	322	318	52
4120	239	241	251	259	268	264	278	39
4121	253	276	296	301	312	326	333	80
4122	238	250	246	256	269	272	271	33
Mean	246	260	270	278	285	293	297	51
S.D.	12	18	21	24	29	31	30	21

Unit: g

Appendix 3-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of male rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14	Gain 1-14
1008	532	553	558	26
1009	532	553	555	23
1010	508	523	531	23
1011	494	511	515	21
1012	513	518	526	13
Mean	516	532	537	21
S.D.	16	20	19	5

Unit: g

Appendix 3-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of male rats (Recovery period)

Dose (mg/kg): 1000

Animal number	Day of recovery 1	8	14	Gain 1-14
4008	528	540	547	19
4009	562	571	593	31
4010	513	537	544	31
4011	538	556	561	23
4012	493	511	519	26
Mean	527	543	553	26
S.D.	26	22	27	5

Unit: g

Appendix 3-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14	Gain 1-14
1118	340	345	343	3
1119	315	335	336	21
1120	318	330	323	5
1121	295	297	305	10
1122	328	334	316	-12
Mean	319	328	325	5
S.D.	17	18	15	12

Unit: g

Appendix 3-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of female rats (Recovery period)

Dose (mg/kg): 1000

Animal number	Day of recovery 1	8	14	Gain 1-14
4118	292	288	299	7
4119	327	328	339	12
4120	278	289	282	4
4121	336	349	335	-1
4122	266	282	275	9
Mean	300	307	306	6
S.D.	31	30	30	5

Unit: g

Appendix 4-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 0

Animal number	Day of administration					
	1	8	15	30	36	42
1001	25	30	27	26	27	27
1002	29	25	29	27	29	26
1003	28	30	32	25	29	28
1004	30	33	30	28	29	26
1005	29	29	25	31	27	24
1006	26	31	31	26	27	28
1007	30	30	29	28	29	27
1008	32	33	30	28	34	26
1009	33	33	34	31	37	23
1010	29	33	31	29	28	28
1011	25	27	26	27	26	26
1012	28	28	27	29	28	27
Mean	29	30	29	28	29	26
S.D.	2	3	3	2	3	2

Unit: g/rat/day

Appendix 4-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 100

Animal number	Day of administration					
	1	8	15	30	36	42
2001	27	28	26	31	31	30
2002	28	30	28	30	27	28
2003	30	31	27	30	28	30
2004	27	31	27	30	26	28
2005	28	26	28	30	30	29
2006	29	30	31	32	30	28
2007	28	30	32	33	29	29
2008	32	31	26	26	29	30
2009	30	31	32	28	31	28
2010	28	29	30	30	29	24
2011	28	27	23	32	33	29
2012	29	30	29	29	33	26
Mean	29	30	28	30	30	28
S.D.	1	2	3	2	2	2

Unit: g/rat/day

Appendix 4-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 300

Animal number	Day of administration					
	1	8	15	30	36	42
3001	28	30	30	29	29	30
3002	27	34	32	29	34	31
3003	27	29	31	27	30	26
3004	33	33	35	32	31	31
3005	26	27	26	31	29	30
3006	32	31	34	32	32	32
3007	27	29	31	28	26	30
3008	29	32	28	28	29	30
3009	30	29	26	30	33	25
3010	28	31	29	30	30	27
3011	26	31	28	30	26	28
3012	28	29	30	27	28	25
Mean	28	30	30	29	30	29
S.D.	2	2	3	2	2	2

Unit: g/rat/day

Appendix 4-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of male rats (Administration period)

Dose (mg/kg): 1000

Animal number	Day of administration					
	1	8	15	30	36	42
4001	25	27	26	24	25	26
4002	29	30	27	28	29	25
4003	28	35	29	27	31	28
4004	34	33	34	26	30	32
4005	29	34	36	38	31	34
4006	28	31	34	30	31	27
4007	27	29	29	30	25	29
4008	24	26	28	31	28	24
4009	29	28	30	29	32	28
4010	26	28	27	27	31	21
4011	25	28	28	26	26	26
4012	25	27	31	31	28	25
Mean	27	30	30	29	29	27
S.D.	3	3	3	4	3	4

Unit: g/rat/day

Appendix 4-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 0

Animal number	Day of administration		
	1	8	15
1101	18	19	22
1102	21	25	24
1103	20	21	16
1104	15	22	23
1105	17	23	21
1106	23	23	18
1107	18	22	20
1108	19	23	18
1109	22	24	18
1110	25	27	20
1111	15	22	21
1112	21	23	19
Mean	20	23	20
S.D.	3	2	2

Unit: g/rat/day

Appendix 4-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 100

Animal number	Day of administration		
	1	8	15
2101	22	20	13
2102	20	23	23
2103	20	18	22
2104	19	23	17
2105	21	22	22
2106	23	24	18
2107	22	20	23
2108	21	23	24
2109	20	20	20
2110	18	15	21
2111	16	22	20
2112	19	18	24
Mean	20	21	21
S.D.	2	3	3

Unit: g/rat/day

Appendix 4-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 300

Animal number	Day of administration		
	1	8	15
3101	18	19	20
3102	20	22	18
3103	21	20	14
3104	22	13	23
3105	19	23	21
3106	20	19	24
3107	15	26	23
3108	24	17	22
3109	19	15	22
3110	19	15	19
3111	20	17	17
3112	14	20	22
Mean	19	19	20
S.D.	3	4	3

Unit: g/rat/day

Appendix 4-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats during the pre-mating period (Main group)

Dose (mg/kg): 1000

Animal number	Day of administration		
	1	8	15
4101	13	20	18
4102	22	19	20
4103	20	19	15
4104	18	14	20
4105	22	21	15
4106	20	19	22
4107	19	21	18
4108	20	24	15
4109	23	21	22
4110	20	22	19
4111	23	14	20
4112	21	18	23
Mean	20	19	19
S.D.	3	3	3

Unit: g/rat/day

Appendix 4-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 0

Dam number	Administration			
	1	7	14	20a)
1101	24	27	24	24
1102	25	26	24	23
1103	15	25	26	25
1104	23	25	28	24
1105	23	26	32	27
1106	24	27	29	22
1107	20	25	28	26
1108	19	22	25	23
1109	21	31	26	25
1110	25	25	30	30
1111	21	24	28	27
1112	21	24	26	22
Mean	22	26	27	25
S.D.	3	2	2	2

Unit: g/rat/day
a): Gestation day

Appendix 4-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 100

Dam number	Administration 1	7	14	20a)
2101	20	29	28	25
2102	22	27	31	26
2103	21	31	31	31
2104	22	26	26	28
2105	22	26	24	23
2106	26	29	29	27
2107	22	26	24	23
2108	21	29	27	23
2109	21	26	27	24
2110	23	23	24	23
2111	23	24	26	22
2112	24	29	27	26
Mean	22	27	27	25
S.D.	2	2	2	3

Unit: g/rat/day
a): Gestation day

Appendix 4-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 300

Dam number	Administration			
	1	7	14	20a)
3101	21	24	28	22
3102	17	26	27	24
3103	19	29	30	24
3104	26	26	27	24
3105	20	25	27	23
3106	21	24	25	22
3107	29	28	29	23
3108	24	28	32	27
3109	22	27	25	22
3110	24	25	26	23
3111	Non-pregnant			
3112	22	27	25	23
Mean	22	26	27	23
S.D.	3	2	2	1

Unit: g/rat/day
a): Gestation day

Appendix 4-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the gestation period (Main group)

Dose (mg/kg): 1000

Dam number	Administration 1	7	14	20a)
4101	21	26	24	26
4102	22	28	29	24
4103	17	23	25	24
4104	24	25	28	25
4105	19	22	22	27
4106	23	24	25	24
4107	14	31	28	29
4108	22	27	27	23
4109	26	26	30	27
4110	24	29	32	26
4111	23	19	28	25
4112	25	28	27	22
Mean	22	26	27	25
S.D.	3	3	3	2

Unit: g/rat/day
a): Gestation day

Appendix 4-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 0

Dam number	Administration 2	4a)
1101	34	46
1102	23	40
1103	27	38
1104	32	44
1105	25	45
1106	36	53
1107	30	38
1108	24	45
1109	24	40
1110	24	47
1111	26	41
1112	24	44
Mean	27	43
S.D.	4	4

Unit: g/rat/day
a): Lactation day

Appendix 4-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 100

Dam number	Administration 2	4a)
2101	32	40
2102	37	50
2103	32	40
2104	20	38
2105	20	37
2106	23	38
2107	20	36
2108	28	41
2109	34	61
2110	25	44
2111	18	38
2112	15	38
Mean	25	42
S.D.	7	7

Unit: g/rat/day
a): Lactation day

Appendix 4-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 300

Dam number	Administration 2	4a)
3101	31	42
3102	27	36
3103	16	32
3104	25	46
3105	24	46
3106	21	35
3107	22	40
3108	22	48
3109	24	47
3110	16	34
3111	Non-pregnant	
3112	16	44
Mean	22	41
S.D.	5	6

Unit: g/rat/day
a): Lactation day

Appendix 4-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of dams during the lactation period (Main group)

Dose (mg/kg): 1000

Dam number	Administration	
	2	4a)
4101	27	41
4102	28	40
4103	19	38
4104	22	40
4105	29	40
4106	23	42
4107	14	29
4108	22	36
4109	24	43
4110	20	43
4111	31	43
4112	26	47
Mean	24	40
S.D.	5	4

Unit: g/rat/day
a): Lactation day

Appendix 4-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats (Satellite group, administration period)

Dose (mg/kg): 0

Animal number	Day of administration					
	1	8	15	30	36	42
1113	17	13	20	22	16	22
1114	21	17	23	28	24	22
1115	16	19	20	16	19	15
1116	17	23	25	21	21	24
1117	17	22	19	19	20	22
1118	19	24	25	22	21	20
1119	21	24	20	22	21	18
1120	13	24	25	19	24	13
1121	16	23	23	19	21	16
1122	20	15	25	20	22	20
Mean	18	20	23	21	21	19
S.D.	3	4	3	3	2	4

Unit: g/rat/day

Appendix 4-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats (Satellite group, administration period)

Dose (mg/kg): 1000

Animal number	Day of administration					
	1	8	15	30	36	42
4113	18	15	23	22	16	18
4114	15	23	24	22	21	21
4115	22	27	27	21	24	19
4116	13	15	19	17	18	18
4117	15	23	22	20	21	19
4118	20	25	22	18	22	17
4119	20	23	18	20	21	15
4120	18	14	18	21	13	19
4121	19	24	25	23	24	21
4122	20	24	18	19	20	19
Mean	18	21	22	20	20	19
S.D.	3	5	3	2	3	2

Unit: g/rat/day

Appendix 4-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of male rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery		
	1	8	14
1008	28	28	29
1009	31	33	29
1010	29	30	30
1011	29	27	25
1012	28	27	25
Mean	29	29	28
S.D.	1	3	2

Unit: g/rat/day

Appendix 4-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of male rats (Recovery period)

Dose (mg/kg): 1000

Animal number	Day of recovery		
	1	8	14
4008	26	26	27
4009	29	29	30
4010	24	28	27
4011	30	27	25
4012	26	29	25
Mean	27	28	27
S.D.	2	1	2

Unit: g/rat/day

Appendix 4-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats (Recovery period)

Dose (mg/kg): 0

Animal number	Day of recovery		
	1	8	14
1118	22	23	20
1119	18	22	20
1120	17	20	17
1121	19	17	18
1122	19	21	12
Mean	19	21	17
S.D.	2	2	3

Unit: g/rat/day

Appendix 4-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual food consumption of female rats (Recovery period)

Dose (mg/kg): 1000

Animal number	Day of recovery		
	1	8	14
4118	20	16	22
4119	17	16	19
4120	18	19	15
4121	21	25	16
4122	15	23	13
Mean	18	20	17
S.D.	2	4	4

Unit: g/rat/day

Appendix 5-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1008	>=9.0	+-	+-	-	+-	-	+-	Y
1009	>=9.0	+	+-	-	+-	-	+-	Y
1010	>=9.0	+	+	-	-	-	+-	Y
1011	8.0	++	+	-	+-	-	+-	Y
1012	>=9.0	+	+-	-	+-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	+-	-
1010	-	-	+-	-	-	+-	-
1011	-	-	+-	-	-	+-	-
1012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	47	24.4	1480	2.00	5.68	2.34
1009	33	19.2	1910	2.04	5.75	2.84
1010	35	13.7	2160	1.53	4.81	2.08
1011	31	9.1	2800	1.73	3.99	1.95
1012	43	19.3	1904	2.16	5.81	2.47
Mean	38	17.1	2051	1.89	5.21	2.34
S.D.	7	5.9	485	0.26	0.79	0.35

Appendix 5-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 100

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
2008	8.5	+	+-	-	-	-	+-	Y
2009	>=9.0	+	+	-	-	+	+-	Y
2010	>=9.0	+-	+-	-	-	-	+-	Y
2011	8.0	-	-	-	+-	-	+-	Y
2012	>=9.0	+	++	-	-	-	+-	Y

1) - : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2) - : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3) - : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4) - : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5) - : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6) +- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7) LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 100

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
2008	-	-	+-	-	-	+-	-
2009	-	-	+-	-	-	+-	-
2010	-	-	+-	-	-	+-	-
2011	-	-	+-	-	-	+-	-
2012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 100

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
2008	37	20.0	2048	2.16	6.67	2.92
2009	39	12.8	1664	1.33	3.35	1.74
2010	44	18.8	1768	1.84	5.20	2.26
2011	73	45.8	974	2.56	6.92	2.93
2012	37	20.4	1604	2.28	5.03	2.65
Mean	46	23.6	1612	2.03	5.43	2.50
S.D.	15	12.8	395	0.47	1.44	0.50

Appendix 5-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 300

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
3008	8.5	-	-	-	+-	-	+-	Y
3009	>=9.0	+-	+	-	+-	-	+-	Y
3010	8.5	+-	+-	-	+-	-	+-	Y
3011	8.5	-	-	-	+-	-	+-	Y
3012	8.5	+-	+	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 300

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
3008	-	-	+-	-	-	+-	-
3009	-	-	+-	-	-	+-	-
3010	-	-	+-	-	-	+-	-
3011	-	-	+-	-	-	+-	-
3012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 300

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
3008	83	43.1	842	1.81	5.94	2.67
3009	38	12.0	2224	1.34	4.35	1.85
3010	43	10.3	2558	1.44	4.18	1.73
3011	58	33.2	1150	2.06	5.48	2.79
3012	30	13.6	2190	1.47	4.93	2.04
Mean	50	22.4	1793	1.62	4.98	2.22
S.D.	21	14.8	749	0.30	0.74	0.48

Appendix 5-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 1000

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4008	>=9.0	+	+-	-	-	-	+-	Y
4009	8.5	+-	-	-	+-	-	+-	Y
4010	8.5	+-	-	-	+-	-	+-	Y
4011	>=9.0	+	+-	-	+-	-	+-	Y
4012	>=9.0	+	+	-	+-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 1000

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+-	-
4009	-	-	+-	-	-	+-	-
4010	-	-	+-	-	-	+-	-
4011	-	-	+-	-	-	+-	-
4012	-	-	+-	-	-	-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of male rats (Week 6 of administration)

Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	43	18.5	1912	1.44	5.72	2.37
4009	58	31.4	1066	1.70	5.02	2.20
4010	56	36.7	1210	2.57	6.81	2.94
4011	47	24.7	1416	1.83	5.36	2.32
4012	6	8.0	2494	1.55	3.17	1.89
Mean	42	23.9	1620	1.82	5.22	2.34
S.D.	21	11.2	584	0.45	1.33	0.38

Appendix 5-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1118	8.0	-	-	-	-	-	+-	Y
1119	>=9.0	+-	-	-	-	-	+-	Y
1120	>=9.0	-	-	-	-	-	+-	Y
1121	>=9.0	+-	-	-	-	-	+-	Y
1122	>=9.0	+-	-	-	-	-	+-	Y

1) - : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2) - : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3) - : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4) - : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5) - : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6) +- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7) LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	-	-
1119	-	-	+-	-	-	+-	-
1120	-	-	+-	-	-	+-	-
1121	-	-	+-	-	-	-	-
1122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	42	18.3	1364	1.54	3.47	1.83
1119	26	6.3	2290	0.77	2.32	1.10
1120	45	20.3	1586	1.58	5.09	2.11
1121	27	9.0	1946	1.08	2.66	1.12
1122	24	7.6	2710	1.20	3.33	1.50
Mean	33	12.3	1979	1.23	3.37	1.53
S.D.	10	6.5	540	0.34	1.07	0.44

Appendix 5-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 1000

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118	8.5	+-	-	-	-	-	+-	Y
4119	>=9.0	-	-	-	-	-	+-	Y
4120	6.5	+-	+-	-	-	-	+-	Y
4121	8.5	-	-	-	-	-	+-	Y
4122	7.5	+	+-	-	-	-	+-	Y

1) - : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2) - : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3) - : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4) - : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5) - : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6) +- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7) LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 1000

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	+-	-
4119	-	-	+-	-	-	+-	-
4120	-	-	+-	-	-	-	-
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	28	8.3	2302	1.13	2.97	1.33
4119	30	8.6	2152	1.05	2.73	1.15
4120	27	7.0	2880	1.06	3.07	1.29
4121	35	12.8	2168	1.61	4.22	1.92
4122	25	7.1	2702	0.81	2.97	1.29
Mean	29	8.8	2441	1.13	3.19	1.40
S.D.	4	2.4	331	0.29	0.59	0.30

Appendix 5-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1008	>=9.0	-	-	-	+-	-	+-	Y
1009	>=9.0	+-	+-	-	+-	-	+-	Y
1010	8.5	+	+	-	-	+	+-	Y
1011	>=9.0	+	+	-	+-	-	+-	Y
1012	8.0	-	-	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	-	-
1010	-	-	+-	-	-	+-	-
1011	-	-	+-	-	-	+-	-
1012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	50	22.2	1912	1.91	6.83	2.80
1009	49	23.6	1686	1.94	6.22	2.60
1010	36	13.9	1956	1.36	4.26	1.81
1011	38	11.8	1962	1.27	3.70	1.63
1012	45	21.6	2030	2.38	6.61	2.72
Mean	44	18.6	1909	1.77	5.52	2.31
S.D.	6	5.4	132	0.46	1.44	0.55

Appendix 5-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 1000

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4008	>=9.0	+	+	-	-	-	+-	Y
4009	8.5	+-	+-	-	+-	-	+-	Y
4010	8.5	-	-	-	-	-	+-	Y
4011	>=9.0	+-	+-	-	-	-	+-	Y
4012	8.5	+	++	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 1000

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+-	-
4009	-	-	+-	-	-	+-	-
4010	-	-	+-	-	-	-	-
4011	-	-	+-	-	-	+-	-
4012	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of male rats (Week 2 of recovery)

Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	40	15.7	1914	1.35	4.62	2.07
4009	84	38.1	868	2.06	4.94	2.21
4010	69	45.5	1114	2.64	8.02	3.09
4011	43	16.5	1836	1.35	4.74	1.82
4012	3	12.1	2608	2.44	4.98	2.66
Mean	48	25.6	1668	1.97	5.46	2.37
S.D.	31	15.1	693	0.60	1.44	0.51

Appendix 5-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1118	8.5	-	-	-	-	-	+-	Y
1119	>=9.0	-	-	-	-	-	+-	Y
1120	>=9.0	-	-	-	-	-	+-	Y
1121	7.5	+-	+-	-	-	-	+-	Y
1122	>=9.0	+-	-	-	-	-	+-	Y

1)	- : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2)	- : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3)	- : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4)	- : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5)	- : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6)	+- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7)	LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	+-	-
1119	-	-	+-	-	-	+-	-
1120	-	-	+-	-	-	-	-
1121	-	-	+-	-	-	+-	-
1122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	73	29.7	956	1.37	4.15	1.96
1119	28	9.4	2236	1.18	3.00	1.33
1120	27	11.1	1984	1.24	3.23	1.38
1121	36	9.0	1836	0.85	2.36	1.06
1122	20	6.5	2836	1.16	2.76	1.26
Mean	37	13.1	1970	1.16	3.10	1.40
S.D.	21	9.4	683	0.19	0.67	0.34

Appendix 5-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 1000

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118	6.5	+-	+-	-	-	-	+-	Y
4119	6.5	-	+-	-	-	-	+-	Y
4120	>=9.0	+-	-	-	-	-	+-	Y
4121	>=9.0	-	-	-	-	-	+-	Y
4122	6.5	+-	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 1000

	URINE SEDIMENT						
						CRYSTALLIZATION	
Animal number	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	-	-
4119	-	-	+-	-	-	-	-
4120	-	-	+-	-	-	+-	-
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	+-	-

SEC : Squamous Epithelial Cell
SREC : Small Round Epithelial Cell
PS : Phosphate Salts
CO : Calcium Oxalate

- : Negative
+- : Slight
+ : Mild
++ : Moderate
+++ : Severe

Appendix 5-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual water intake and urinalysis of female rats (Week 2 of recovery)

Dose (mg/kg): 1000

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	28	7.2	2572	0.73	2.73	1.04
4119	34	9.2	1970	0.92	2.65	1.23
4120	23	6.7	2750	0.99	2.72	1.22
4121	47	17.3	1396	1.18	3.60	1.56
4122	23	4.8	3064	0.84	2.12	0.86
Mean	31	9.0	2350	0.93	2.76	1.18
S.D.	10	4.9	666	0.17	0.53	0.26

Appendix 6-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of male rats (End of administration)

Dose mg/kg	Animal number	RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	1001	883	15.6	45.1	51.0	17.7	34.7	2.8	114.2	18.5	27.4	375
	1002	850	15.7	44.2	52.0	18.4	35.4	2.3	96.5	14.8	24.0	251
	1003	873	15.6	43.2	49.5	17.9	36.2	2.4	109.3	19.5	28.7	285
	1004	831	14.9	42.3	50.8	17.9	35.2	1.7	104.2	16.1	24.5	286
	1005	845	15.6	43.3	51.2	18.4	36.0	2.2	97.4	20.2	23.2	280
	Mean	856	15.5	43.6	50.9	18.1	35.5	2.3	104.3	17.8	25.6	295
	S.D.	21	0.3	1.1	0.9	0.3	0.6	0.4	7.6	2.3	2.4	47
100	2001	935	15.6	44.7	47.8	16.7	34.9	1.9	83.8	16.0	25.1	268
	2002	917	16.0	45.7	49.8	17.4	34.9	2.3	104.3	17.8	22.3	255
	2003	863	15.2	43.4	50.3	17.7	35.1	2.5	88.7	17.8	26.2	280
	2004	923	15.1	43.4	47.0	16.3	34.7	1.8	103.2	16.7	22.2	269
	2005	891	15.0	42.5	47.7	16.8	35.2	2.3	111.6	16.0	21.9	307
	Mean	906	15.4	43.9	48.5	17.0	35.0	2.2	98.3	16.9	23.5	276
	S.D.	29	0.4	1.3	1.4	0.6	0.2	0.3	11.6	0.9	2.0	20
300	3001	898	15.7	44.3	49.3	17.5	35.4	2.6	101.3	17.4	28.5	277
	3002	877	15.7	45.4	51.7	17.9	34.6	2.2	91.9	18.3	31.3	334
	3003	880	15.2	43.3	49.2	17.2	35.0	2.0	108.7	13.7	18.5	283
	3004	893	15.4	43.8	49.1	17.3	35.2	1.5	87.1	17.7	26.4	274
	3005	832	14.6	41.9	50.4	17.6	34.8	2.3	121.4	17.2	23.2	293
	Mean	876	15.3	43.7	49.9	17.5	35.0	2.1	102.1	16.9	25.6	292
	S.D.	26	0.5	1.3	1.1	0.3	0.3	0.4	13.7	1.8	4.9	24
1000	4001	904	14.7	43.2	47.8	16.3	34.0	2.1	86.0	15.2	24.7	220
	4002	871	15.2	43.1	49.5	17.5	35.3	2.2	126.1	15.2	23.0	276
	4003	899	15.4	43.9	48.8	17.1	35.0	2.2	112.3	19.3	24.5	278
	4004	878	15.9	45.4	51.7	18.1	35.1	2.5	94.1	15.4	23.4	260
	4005	869	15.7	45.2	52.0	18.1	34.8	2.0	110.4	22.3	23.6	313
	Mean	884	15.4	44.2	50.0	17.4	34.8	2.2	105.8	17.5	23.8	269
	S.D.	16	0.5	1.1	1.8	0.8	0.5	0.2	15.8	3.2	0.7	34

Appendix 6-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of male rats (End of administration)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu L$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1001	82.1	67.1	27.8	1.2	0.3	3.2	0.4	55.1	22.8	1.0	0.3	2.6	0.3
	1002	44.9	79.8	16.7	1.4	0.2	1.6	0.2	35.8	7.5	0.6	0.1	0.7	0.1
	1003	77.5	68.6	25.0	1.6	0.5	3.5	0.8	53.2	19.4	1.2	0.4	2.7	0.6
	1004	62.3	74.3	21.3	2.1	0.2	1.9	0.2	46.3	13.2	1.3	0.1	1.2	0.1
	1005	104.4	75.9	19.5	1.0	0.4	2.6	0.7	79.3	20.3	1.0	0.4	2.7	0.7
	Mean	74.2	73.1	22.1	1.5	0.3	2.6	0.5	53.9	16.6	1.0	0.3	2.0	0.4
	S.D.	22.3	5.3	4.4	0.4	0.1	0.8	0.3	16.1	6.2	0.3	0.2	1.0	0.3
100	2001	126.7	65.8	29.2	0.8	0.5	3.3	0.5	83.3	37.0	1.0	0.6	4.2	0.6
	2002	49.0	73.3	20.1	3.4	0.3	2.8	0.3	35.9	9.8	1.6	0.1	1.4	0.1
	2003	84.6	73.6	21.6	0.8	0.3	2.9	0.8	62.3	18.2	0.7	0.3	2.5	0.7
	2004	105.2	75.4	16.4	1.8	0.5	3.8	2.1	79.3	17.3	1.9	0.5	4.0	2.3
	2005	63.3	64.8	31.1	1.7	0.1	2.0	0.2	41.0	19.7	1.1	0.1	1.3	0.1
	Mean	85.8	70.6	23.7	1.7	0.3	3.0	0.8	60.4	20.4	1.3	0.3	2.7	0.8
	S.D.	31.3	4.9	6.2	1.1	0.2	0.7	0.8	21.6	10.0	0.5	0.2	1.4	0.9
300	3001	90.9	70.5	23.2	1.7	0.6	2.9	1.2	64.1	21.1	1.5	0.5	2.6	1.1
	3002	65.2	63.9	30.3	2.4	0.3	2.7	0.3	41.7	19.7	1.6	0.2	1.7	0.2
	3003	44.8	73.5	20.4	2.2	0.3	2.8	0.8	32.9	9.1	1.0	0.2	1.3	0.3
	3004	69.8	72.5	20.8	1.7	0.3	3.5	1.2	50.6	14.5	1.2	0.2	2.4	0.9
	3005	55.6	75.7	19.8	1.5	0.2	2.6	0.2	42.1	11.0	0.8	0.1	1.4	0.1
	Mean	65.3	71.2	22.9	1.9	0.3	2.9	0.7	46.3	15.1	1.2	0.2	1.9	0.5
	S.D.	17.2	4.5	4.3	0.4	0.2	0.4	0.5	11.8	5.3	0.3	0.2	0.6	0.4
1000	4001	62.7	77.4	18.6	1.2	0.2	2.0	0.5	48.5	11.7	0.8	0.1	1.3	0.3
	4002	81.9	74.0	22.7	0.7	0.4	2.0	0.3	60.6	18.6	0.5	0.3	1.6	0.3
	4003	65.3	71.7	23.6	2.1	0.4	2.0	0.3	46.8	15.4	1.4	0.2	1.3	0.2
	4004	63.0	70.0	25.5	2.3	0.2	1.7	0.3	44.1	16.1	1.5	0.1	1.1	0.2
	4005	61.5	67.9	27.6	1.4	0.2	2.6	0.3	41.7	17.0	0.8	0.2	1.6	0.2
	Mean	66.9	72.2	23.6	1.5	0.3	2.1	0.3	48.3	15.8	1.0	0.2	1.4	0.2
	S.D.	8.5	3.7	3.4	0.7	0.1	0.3	0.1	7.3	2.6	0.4	0.1	0.2	0.1

LUC: Large unstained cells

Appendix 6-3 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of female rats (Lactation day 5)

Dose mg/kg	Animal number	RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	1101	855	15.4	44.0	51.5	18.0	34.9	4.0	113.3	13.9	18.5	284
	1102	802	14.8	42.9	53.4	18.5	34.6	6.6	144.6	13.2	18.6	367
	1104	791	14.5	42.0	53.1	18.3	34.5	4.9	129.0	15.1	19.7	395
	1105	684	12.7	37.8	55.3	18.6	33.7	10.4	191.1	14.6	18.2	501
	1107	806	14.8	42.4	52.6	18.3	34.9	5.5	146.0	13.4	15.6	356
	Mean	788	14.4	41.8	53.2	18.3	34.5	6.3	144.8	14.0	18.1	381
	S.D.	63	1.0	2.4	1.4	0.2	0.5	2.5	29.1	0.8	1.5	79
100	2103	831	14.9	44.1	53.0	17.9	33.8	6.2	130.1	13.2	13.8	245
	2107	812	14.5	40.8	50.2	17.8	35.5	4.8	164.7	14.2	23.6	291
	2110	762	13.6	39.3	51.6	17.8	34.5	5.8	150.2	14.7	16.6	289
	2111	761	14.1	40.7	53.5	18.5	34.6	4.0	141.7	14.6	21.5	254
	2112	794	13.9	41.1	51.8	17.5	33.7	6.0	144.5	13.5	13.6	369
	Mean	792	14.2	41.2	52.0	17.9	34.4	5.4	146.2	14.0	17.8	290
	S.D.	31	0.5	1.8	1.3	0.4	0.7	0.9	12.7	0.7	4.5	49
300	3101	826	14.5	41.8	50.7	17.6	34.6	3.8	111.3	14.2	21.6	359
	3104	699	12.9	37.4	53.5	18.5	34.6	6.9	150.7	14.1	18.8	290
	3107	810	14.7	42.3	52.2	18.2	34.8	4.5	140.0	14.9	18.4	249
	3108	746	14.1	40.9	54.8	18.9	34.4	8.1	161.4	14.8	21.2	316
	3110	794	13.7	39.5	49.8	17.2	34.5	4.5	171.1	14.4	25.4	288
	3111a)	816Z	14.6Z	41.1Z	50.4Z	17.9Z	35.5Z	2.6Z	106.3Z	13.7Z	16.8Z	243Z
	Mean	775	14.0	40.4	52.2	18.1	34.6	5.6	146.9	14.5	21.1	300
	S.D.	52	0.7	2.0	2.0	0.7	0.1	1.8	23.1	0.4	2.8	41
1000	4104	793	13.9	40.3	50.8	17.5	34.6	6.2	167.8	14.5	18.1	212
	4106	725	13.6	38.4	53.0	18.7	35.3	6.8	165.3	14.3	19.9	206
	4109	790	14.3	41.8	52.9	18.1	34.3	6.4	148.0	16.1	20.1	364
	4111	743	13.6	39.7	53.4	18.3	34.2	6.4	127.1	13.1	17.0	265
	4112	673	12.9	36.7	54.5	19.1	35.1	9.2	132.7	14.6	20.3	270
	Mean	745	13.7	39.4	52.9	18.3	34.7	7.0	148.2	14.5	19.1	263
	S.D.	50	0.5	1.9	1.3	0.6	0.5	1.2	18.5	1.1	1.5	63

a) : Non-pregnant
Z : Data was excluded from statistical analysis.

Appendix 6-4 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of female rats (Lactation day 5)

Dose mg/kg	Animal number	WBC	Differential leukocyte counts (%)						Differential leukocyte counts (X10²/μL)					
		X10²/μL	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1101	146.1	55.8	39.9	0.5	0.4	3.1	0.3	81.5	58.3	0.8	0.6	4.5	0.4
	1102	161.1	67.1	28.8	0.8	0.5	2.4	0.5	108.1	46.4	1.2	0.7	3.8	0.8
	1104	101.1	67.3	29.5	0.8	0.3	1.6	0.6	68.0	29.8	0.8	0.3	1.6	0.6
	1105	135.3	51.8	44.9	0.8	0.3	1.7	0.5	70.0	60.8	1.1	0.4	2.3	0.7
	1107	113.7	62.9	32.8	0.9	0.3	2.8	0.3	71.5	37.3	1.1	0.4	3.2	0.3
	Mean	131.5	61.0	35.2	0.8	0.4	2.3	0.4	79.8	46.5	1.0	0.5	3.1	0.6
	S.D.	24.2	6.9	7.0	0.2	0.1	0.7	0.1	16.6	13.3	0.2	0.2	1.2	0.2
100	2103	138.0	62.6	31.6	1.7	0.3	3.4	0.5	86.4	43.6	2.3	0.4	4.7	0.7
	2107	83.5	67.0	29.9	1.1	0.1	1.6	0.2	55.9	24.9	1.0	0.1	1.4	0.2
	2110	89.6	64.6	31.4	0.8	0.2	2.8	0.2	57.9	28.2	0.7	0.2	2.5	0.2
	2111	54.2	79.1	17.3	1.1	0.2	1.9	0.4	42.9	9.4	0.6	0.1	1.0	0.2
	2112	148.6	61.1	34.9	0.7	0.2	2.2	0.8	90.8	51.9	1.1	0.4	3.3	1.1
	Mean	102.8	66.9	29.0	1.1	0.2	2.4	0.4	66.8	31.6	1.1	0.2	2.6	0.5
	S.D.	39.5	7.2	6.8	0.4	0.1	0.7	0.2	20.8	16.6	0.7	0.2	1.5	0.4
300	3101	89.3	73.5	21.2	2.1	0.2	1.7	1.4	65.6	19.0	1.9	0.2	1.5	1.2
	3104	84.1	69.2	27.6	0.5	0.2	1.9	0.5	58.2	23.2	0.5	0.2	1.6	0.4
	3107	89.8	67.4	27.8	0.8	0.3	3.2	0.5	60.5	25.0	0.7	0.3	2.9	0.4
	3108	76.0	72.8	22.7	0.7	0.3	2.5	1.1	55.4	17.2	0.5	0.2	1.9	0.8
	3110	80.9	68.1	24.8	2.2	0.3	4.2	0.4	55.0	20.1	1.8	0.3	3.4	0.3
	3111a)	67.3Z	84.9Z	10.5Z	1.8Z	0.3Z	2.1Z	0.5Z	57.2Z	7.0Z	1.2Z	0.2Z	1.4Z	0.3Z
	Mean	84.0	70.2	24.8	1.3	0.3	2.7	0.8	58.9	20.9	1.1	0.2	2.3	0.6
	S.D.	5.8	2.8	2.9	0.8	0.1	1.0	0.4	4.3	3.2	0.7	0.1	0.8	0.4
1000	4104	64.4	59.5	34.6	0.9	0.3	3.4	1.3	38.3	22.3	0.6	0.2	2.2	0.9
	4106	51.6	70.4	24.9	0.8	0.3	3.1	0.5	36.4	12.9	0.4	0.1	1.6	0.3
	4109	103.0	63.0	30.7	1.4	0.4	2.9	1.5	64.9	31.6	1.5	0.4	3.0	1.6
	4111	116.7	57.2	38.6	0.8	0.2	3.0	0.4	66.7	45.0	0.9	0.2	3.5	0.4
	4112	114.7	57.9	38.5	0.5	0.2	2.6	0.3	66.4	44.2	0.6	0.2	3.0	0.4
	Mean	90.1	61.6	33.5	0.9	0.3	3.0	0.8	54.5	31.2	0.8	0.2	2.7	0.7
	S.D.	30.1	5.4	5.8	0.3	0.1	0.3	0.6	15.7	13.9	0.4	0.1	0.8	0.5

LUC: Large unstained cells
a) : Non-pregnant
Z : Data was excluded from statistical analysis.

Appendix 6-5 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	1113	788	15.1	42.2	53.6	19.2	35.8	2.7	84.2	12.8	14.3	234
	1114	864	15.8	45.1	52.2	18.3	35.1	1.8	111.7	15.1	19.6	213
	1115	851	15.7	44.0	51.6	18.4	35.6	1.6	112.9	13.3	17.6	231
	1116	889	16.2	45.2	50.8	18.2	35.8	1.6	107.3	13.6	19.6	233
	1117	855	15.5	43.9	51.3	18.1	35.2	2.4	130.1	14.1	19.6	231
	Mean	849	15.7	44.1	51.9	18.4	35.5	2.0	109.2	13.8	18.1	228
	S.D.	37	0.4	1.2	1.1	0.4	0.3	0.5	16.5	0.9	2.3	9
1000	4113	887	16.1	45.4	51.2	18.1	35.4	3.2	116.8	13.9	19.7	219
	4114	846	15.3	42.6	50.4	18.0	35.8	1.2	114.9	13.5	17.5	188
	4115	877	15.8	45.0	51.3	18.0	35.1	1.5	90.0	13.0	19.1	221
	4116	921	16.0	45.9	49.8	17.3	34.8	1.5	103.6	14.5	18.5	215
	4117	823	14.8	40.7	49.5	17.9	36.3	1.4	127.6	14.3	17.7	212
	Mean	871	15.6	43.9	50.4	17.9	35.5	1.8	110.6	13.8	18.5	211
	S.D.	38	0.5	2.2	0.8	0.3	0.6	0.8	14.3	0.6	0.9	13

Appendix 6-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu L$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1113	42.9	70.1	26.1	1.6	0.2	1.7	0.2	30.0	11.2	0.7	0.1	0.7	0.1
	1114	35.1	71.4	23.9	2.1	0.2	2.3	0.2	25.1	8.4	0.7	0.1	0.8	0.1
	1115	55.9	84.5	12.9	1.0	0.2	1.1	0.3	47.2	7.2	0.6	0.1	0.6	0.2
	1116	66.3	80.3	15.6	1.7	0.5	1.3	0.7	53.2	10.3	1.1	0.3	0.9	0.4
	1117	47.3	74.3	21.1	1.8	0.3	1.8	0.8	35.1	10.0	0.9	0.1	0.9	0.4
	Mean	49.5	76.1	19.9	1.6	0.3	1.6	0.4	38.1	9.4	0.8	0.1	0.8	0.2
	S.D.	12.0	6.1	5.6	0.4	0.1	0.5	0.3	11.8	1.6	0.2	0.1	0.1	0.2
1000	4113	60.0	64.6	31.2	1.2	0.2	2.3	0.6	38.7	18.7	0.7	0.1	1.4	0.4
	4114	37.6	71.5	24.3	1.0	0.1	2.7	0.5	26.9	9.1	0.4	0.0	1.0	0.2
	4115	43.5	70.1	25.0	1.4	0.2	3.2	0.2	30.5	10.9	0.6	0.1	1.4	0.1
	4116	31.8	79.4	16.7	1.2	0.1	2.0	0.5	25.3	5.3	0.4	0.0	0.6	0.2
	4117	27.5	71.7	24.6	1.7	0.2	1.5	0.4	19.7	6.7	0.5	0.0	0.4	0.1
	Mean	40.1	71.5	24.4	1.3	0.2	2.3	0.4	28.2	10.1	0.5	0.0	1.0	0.2
	S.D.	12.7	5.3	5.1	0.3	0.1	0.7	0.2	7.0	5.2	0.1	0.1	0.5	0.1

LUC: Large unstained cells

Appendix 6-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of male rats (End of recovery)

Dose mg/kg	Animal number	RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	1008	971	15.9	46.5	47.9	16.4	34.2	2.0	96.7	14.3	20.0	227
	1009	862	16.0	45.2	52.4	18.6	35.4	2.2	93.0	15.2	27.8	235
	1010	973	16.4	46.9	48.3	16.9	34.9	2.0	96.0	17.5	21.3	264
	1011	902	16.0	46.3	51.3	17.7	34.5	2.2	97.4	13.9	23.5	282
	1012	951	16.0	46.4	48.8	16.9	34.6	2.1	94.4	16.6	21.3	334
	Mean	932	16.1	46.3	49.7	17.3	34.7	2.1	95.5	15.5	22.8	268
	S.D.	48	0.2	0.6	2.0	0.9	0.5	0.1	1.8	1.5	3.1	43
1000	4008	939	16.1	45.8	48.8	17.2	35.2	1.5	107.3	18.8	21.8	247
	4009	905	15.3	43.7	48.3	17.0	35.1	2.1	86.0	15.5	22.4	210
	4010	893	16.0	45.6	51.1	17.9	35.1	2.4	110.8	14.8	22.2	266
	4011	930	16.2	46.4	49.9	17.4	34.8	2.4	93.3	13.5	20.1	267
	4012	899	15.5	44.5	49.5	17.3	34.8	2.0	110.7	15.9	25.6	293
	Mean	913	15.8	45.2	49.5	17.4	35.0	2.1	101.6	15.7	22.4	257
	S.D.	20	0.4	1.1	1.1	0.3	0.2	0.4	11.3	2.0	2.0	31

Appendix 6-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of male rats (End of recovery)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu L$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1008	51.2	80.1	14.8	1.0	0.1	3.0	1.0	41.0	7.6	0.5	0.1	1.5	0.5
	1009	84.1	73.7	21.5	1.5	0.3	2.5	0.5	62.0	18.1	1.2	0.3	2.1	0.4
	1010	87.1	70.5	24.8	2.4	0.3	1.7	0.3	61.4	21.6	2.1	0.3	1.5	0.3
	1011	101.8	80.2	15.1	1.7	0.4	2.1	0.5	81.6	15.4	1.8	0.4	2.1	0.5
	1012	58.4	70.6	24.5	1.8	0.2	2.5	0.5	41.3	14.3	1.0	0.1	1.5	0.3
	Mean	76.5	75.0	20.1	1.7	0.3	2.4	0.6	57.5	15.4	1.3	0.2	1.7	0.4
	S.D.	21.1	4.9	4.9	0.5	0.1	0.5	0.3	17.0	5.2	0.6	0.1	0.3	0.1
1000	4008	81.1	79.6	14.3	2.0	0.3	2.5	1.1	64.6	11.6	1.7	0.3	2.1	0.9
	4009	84.2	74.3	19.3	3.2	0.3	2.4	0.5	62.6	16.2	2.7	0.2	2.1	0.5
	4010	63.4	66.8	27.9	1.8	0.3	3.0	0.2	42.3	17.7	1.2	0.2	1.9	0.2
	4011	102.0	77.6	18.6	1.2	0.4	1.8	0.4	79.1	19.0	1.2	0.4	1.8	0.4
	4012	42.3	69.0	26.0	1.6	0.3	2.9	0.2	29.2	11.0	0.7	0.1	1.2	0.1
	Mean	74.6	73.5	21.2	2.0	0.3	2.5	0.5	55.6	15.1	1.5	0.2	1.8	0.4
	S.D.	22.7	5.5	5.6	0.8	0.0	0.5	0.4	19.7	3.6	0.8	0.1	0.4	0.3

LUC: Large unstained cells

Appendix 6-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of female rats (End of recovery)

Dose mg/kg	Animal number	RBC $\times 10^4/\mu L$	Hb g/dL	Ht %	MCV fL	MCH pg	MCHC g/dL	Reticu-locyte %	Plate-let $\times 10^4/\mu L$	PT s	APTT s	Fibri-nogen mg/dL
0	1118	795	15.3	43.0	54.1	19.2	35.4	2.4	119.2	11.5	19.8	182
	1119	841	14.9	42.2	50.2	17.7	35.3	2.5	119.9	12.0	17.8	192
	1120	840	16.2	45.7	54.4	19.3	35.4	1.4	85.5	12.9	19.9	186
	1121	847	15.6	43.6	51.4	18.4	35.9	2.4	102.1	11.9	17.4	221
	1122	900	15.5	43.9	48.8	17.3	35.4	1.5	115.9	12.5	15.7	207
	Mean	845	15.5	43.7	51.8	18.4	35.5	2.0	108.5	12.2	18.1	198
	S.D.	37	0.5	1.3	2.4	0.9	0.2	0.5	14.7	0.5	1.8	16
1000	4118	821	14.7	41.5	50.5	18.0	35.5	2.3	123.4	11.9	19.5	161
	4119	867	15.4	42.6	49.2	17.8	36.2	2.4	103.9	12.2	18.7	197
	4120	846	15.6	43.8	51.8	18.4	35.6	1.9	116.1	12.2	17.6	157
	4121	873	15.1	42.5	48.7	17.3	35.5	1.9	109.7	12.1	20.3	192
	4122	897	15.6	43.8	48.8	17.4	35.6	1.6	109.9	12.0	18.3	195
	Mean	861	15.3	42.8	49.8	17.8	35.7	2.0	112.6	12.1	18.9	180
	S.D.	29	0.4	1.0	1.3	0.4	0.3	0.3	7.4	0.1	1.0	20

Appendix 6-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual hematology of female rats (End of recovery)

Dose mg/kg	Animal number	WBC $\times 10^2/\mu L$	Differential leukocyte counts (%)						Differential leukocyte counts ($\times 10^2/\mu L$)					
			Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	1118	57.7	73.2	22.1	1.3	0.3	2.7	0.4	42.2	12.7	0.7	0.2	1.5	0.3
	1119	67.3	78.4	17.5	1.7	0.2	1.9	0.4	52.7	11.8	1.1	0.1	1.3	0.2
	1120	44.7	79.7	15.9	1.6	0.2	2.4	0.2	35.7	7.1	0.7	0.1	1.1	0.1
	1121	53.2	65.0	30.8	1.5	0.2	1.6	0.8	34.6	16.4	0.8	0.1	0.9	0.4
	1122	48.7	84.0	11.8	2.1	0.2	1.5	0.3	41.0	5.7	1.0	0.1	0.7	0.2
	Mean	54.3	76.1	19.6	1.6	0.2	2.0	0.4	41.2	10.7	0.9	0.1	1.1	0.2
	S.D.	8.7	7.3	7.3	0.3	0.0	0.5	0.2	7.2	4.3	0.2	0.0	0.3	0.1
1000	4118	57.1	74.0	21.5	1.0	0.3	2.1	1.0	42.2	12.3	0.6	0.2	1.2	0.6
	4119	42.2	82.4	10.5	2.2	0.2	3.5	1.2	34.8	4.4	0.9	0.1	1.5	0.5
	4120	46.3	86.4	9.4	1.1	0.2	2.3	0.5	40.0	4.4	0.5	0.1	1.1	0.2
	4121	40.2	76.8	18.3	2.8	0.2	1.6	0.3	30.8	7.4	1.1	0.1	0.6	0.1
	4122	46.1	69.5	25.2	2.3	0.3	2.4	0.3	32.0	11.6	1.1	0.1	1.1	0.1
	Mean	46.4	77.8	17.0	1.9	0.2	2.4	0.7	36.0	8.0	0.8	0.1	1.1	0.3
	S.D.	6.5	6.7	6.9	0.8	0.1	0.7	0.4	5.0	3.8	0.3	0.0	0.3	0.2

LUC: Large unstained cells

Appendix 7-1 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of male rats (End of administration)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	1001	63	27	60	1	322	5.0	55	31	85	0.1	122
	1002	75	29	89	1	400	9.2	42	16	68	0.1	136
	1003	62	34	63	1	454	12.1	38	46	69	0.1	147
	1004	64	25	47	1	301	5.5	63	35	87	0.1	140
	1005	65	32	44	1	432	8.8	40	60	80	0.1	155
	Mean	66	29	61	1	382	8.1	48	38	78	0.1	140
	S.D.	5	4	18	0	67	2.9	11	17	9	0.0	12
100	2001	69	34	37	1	336	6.7	71	51	105	0.1	137
	2002	59	29	54	1	314	5.6	49	62	86	0.1	148
	2003	70	31	66	1	375	7.5	38	70	79	0.1	153
	2004	74	31	60	1	410	8.5	38	36	67	0.0	133
	2005	72	31	44	1	402	7.8	53	40	83	0.1	158
	Mean	69	31	52	1	367	7.2	50	52	84	0.1	146
	S.D.	6	2	12	0	42	1.1	14	14	14	0.0	11
300	3001	62	30	41	1	342	7.4	44	53	82	0.1	143
	3002	60	31	40	1	283	5.2	52	19	81	0.1	144
	3003	78	30	80	1	321	14.7	58	33	87	0.1	132
	3004	68	25	48	1	458	4.0	52	36	83	0.1	156
	3005	66	28	51	1	390	10.7	44	38	80	0.1	129
	Mean	67	29	52	1	359	8.4	50	36	83	0.1	141
	S.D.	7	2	16	0	68	4.3	6	12	3	0.0	11
1000	4001	59	25	32	1	462	7.5	33	19	61	0.1	136
	4002	56	27	39	1	310	6.8	51	30	88	0.1	135
	4003	71	34	48	1	254	6.4	53	43	86	0.1	134
	4004	70	29	54	1	286	9.1	54	22	86	0.1	127
	4005	60	26	43	1	332	22.6	57	51	95	0.1	120
	Mean	63	28	43	1	329	10.5	50	33	83	0.1	130
	S.D.	7	4	8	0	80	6.9	10	14	13	0.0	7

Appendix 7-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of male rats (End of administration)

Dose mg/kg	Animal number	BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1001	12	0.30	144	4.1	109	9.2	5.7	5.6	3.0	1.15
	1002	11	0.22	146	4.1	111	9.7	4.8	5.7	3.2	1.28
	1003	15	0.25	143	4.3	106	9.6	5.4	5.8	3.0	1.07
	1004	20	0.25	142	4.4	106	9.2	5.8	5.6	3.0	1.15
	1005	16	0.21	144	4.4	106	9.8	6.6	5.8	3.1	1.15
	Mean	15	0.25	144	4.3	108	9.5	5.7	5.7	3.1	1.16
	S.D.	4	0.04	1	0.2	2	0.3	0.7	0.1	0.1	0.08
100	2001	13	0.25	142	4.4	106	9.3	5.6	5.6	3.1	1.24
	2002	14	0.21	142	4.4	107	9.2	5.8	5.2	2.9	1.26
	2003	14	0.26	144	4.4	106	9.7	5.6	5.8	3.1	1.15
	2004	21	0.30	142	4.6	104	9.5	6.7	5.9	3.1	1.11
	2005	14	0.19	142	4.7	106	10.0	5.9	5.9	3.1	1.11
	Mean	15	0.24	142	4.5	106	9.5	5.9	5.7	3.1	1.17
	S.D.	3	0.04	1	0.1	1	0.3	0.5	0.3	0.1	0.07
300	3001	13	0.23	142	4.3	106	9.0	5.0	5.6	3.0	1.15
	3002	16	0.30	143	4.5	106	9.5	5.9	6.0	3.0	1.00
	3003	14	0.24	144	4.7	106	9.8	6.4	5.7	3.1	1.19
	3004	15	0.24	144	4.3	108	9.7	5.8	5.6	3.1	1.24
	3005	14	0.20	144	4.2	108	9.6	5.7	5.7	3.0	1.11
	Mean	14	0.24	143	4.4	107	9.5	5.8	5.7	3.0	1.14
	S.D.	1	0.04	1	0.2	1	0.3	0.5	0.2	0.1	0.09
1000	4001	18	0.29	139	4.3	106	9.4	5.3	5.5	3.0	1.20
	4002	14	0.29	143	4.4	106	9.4	5.3	5.8	3.1	1.15
	4003	13	0.21	143	4.3	107	9.3	5.7	5.4	3.0	1.25
	4004	15	0.25	144	4.3	106	9.6	5.7	5.6	3.0	1.15
	4005	15	0.21	144	4.5	105	10.5	6.9	5.9	3.2	1.19
	Mean	15	0.25	143	4.4	106	9.6	5.8	5.6	3.1	1.19
	S.D.	2	0.04	2	0.1	1	0.5	0.7	0.2	0.1	0.04

Appendix 7-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of female rats (Lactation day 5)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	1101	97	49	43	2	399	9.5	50	65	113	0.1	118
	1102	68	61	34	1	182	12.5	45	116	100	0.1	115
	1104	95	51	33	1	254	61.9	56	101	126	0.1	114
	1105	78	62	26	1	231	18.4	57	97	123	0.1	124
	1107	60	38	30	2	319	17.0	64	56	132	0.1	140
	Mean	80	52	33	1	277	23.9	54	87	119	0.1	122
	S.D.	16	10	6	1	84	21.6	7	25	13	0.0	11
100	2103	82	59	47	1	397	28.0	51	124	126	0.1	127
	2107	63	30	37	1	328	6.3	44	29	93	0.1	119
	2110	76	41	33	1	409	13.2	53	49	106	0.1	125
	2111	61	30	27	1	218	11.9	64	25	117	0.1	120
	2112	65	43	49	2	255	12.8	62	84	112	0.1	139
	Mean	69	41	39	1	321	14.4	55	62	111	0.1	126
	S.D.	9	12	9	0	84	8.1	8	42	12	0.0	8
300	3101	110	69	31	2	240	18.9	43	52	89	0.1	114
	3104	74	44	58	1	192	26.6	63	86	130	0.1	120
	3107	70	34	50	1	348	6.6	51	68	101	0.1	123
	3108	65	42	39	1	186	14.5	51	27	102	0.1	103
	3110	73	30	34	1	223	6.0	42	25	84	0.0	105
	3111a)	48Z	28Z	40Z	2Z	389Z	8.1Z	75Z	99Z	130Z	0.1Z	172Z
	Mean	78	44	42	1	238	14.5	50	52	101	0.1	113
	S.D.	18	15	11	0	65	8.7	8	26	18	0.0	9
1000	4104	78	36	51	1	153	11.8	52	79	109	0.1	107
	4106	68	31	44	1	146	17.1	53	28	110	0.1	117
	4109	89	44	55	1	170	16.0	48	41	99	0.1	107
	4111	72	43	38	1	236	9.6	46	73	108	0.1	119
	4112	80	48	33	1	245	16.7	64	43	126	0.1	119
	Mean	77	40	44	1	190	14.2	53	53	110	0.1	114
	S.D.	8	7	9	0	47	3.3	7	22	10	0.0	6

a) : Non-pregnant
Z : Data was excluded from statistical analysis.

Appendix 7-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of female rats (Lactation day 5)

Dose mg/kg	Animal number	BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1101	11	0.20	140	4.0	105	10.1	7.5	6.3	3.5	1.25
	1102	16	0.29	138	4.5	100	10.1	6.8	5.9	3.2	1.19
	1104	15	0.27	139	4.5	108	10.0	6.3	5.5	3.1	1.29
	1105	13	0.20	140	4.7	103	10.6	7.2	6.1	3.4	1.26
	1107	17	0.25	140	3.9	103	10.1	6.0	6.4	3.6	1.29
	Mean	14	0.24	139	4.3	104	10.2	6.8	6.0	3.4	1.26
	S.D.	2	0.04	1	0.3	3	0.2	0.6	0.4	0.2	0.04
100	2103	14	0.22	140	4.2	108	10.2	6.3	5.9	3.4	1.36
	2107	12	0.24	141	3.9	108	10.4	6.7	6.2	3.3	1.14
	2110	12	0.22	143	4.1	108	9.9	6.5	5.7	3.2	1.28
	2111	15	0.26	142	4.6	110	10.4	7.0	6.1	3.3	1.18
	2112	13	0.24	139	4.5	103	10.1	6.2	5.8	3.2	1.23
	Mean	13	0.24	141	4.3	107	10.2	6.5	5.9	3.3	1.24
	S.D.	1	0.02	2	0.3	3	0.2	0.3	0.2	0.1	0.09
300	3101	18	0.23	141	4.5	108	10.2	7.0	6.0	3.4	1.31
	3104	15	0.21	141	4.2	106	10.5	7.2	6.1	3.5	1.35
	3107	12	0.24	140	3.7	107	9.8	5.4	6.1	3.2	1.10
	3108	15	0.24	143	4.7	109	10.1	6.4	5.9	3.3	1.27
	3110	18	0.28	140	4.0	109	10.1	6.7	5.8	3.2	1.23
	3111a)	24Z	0.27Z	140Z	4.1Z	105Z	10.1Z	5.3Z	6.0Z	3.3Z	1.22Z
	Mean	16	0.24	141	4.2	108	10.1	6.5	6.0	3.3	1.25
	S.D.	3	0.03	1	0.4	1	0.3	0.7	0.1	0.1	0.10
1000	4104	15	0.28	141	3.9	106	10.0	6.6	5.9	3.3	1.27
	4106	16	0.23	141	4.4	109	9.8	6.0	6.0	3.5	1.40
	4109	18	0.31	141	4.1	106	9.7	6.1	6.0	3.2	1.14
	4111	13	0.23	142	3.9	108	10.5	7.0	6.2	3.3	1.14
	4112	13	0.25	139	4.1	105	10.6	7.8	6.0	3.2	1.14
	Mean	15	0.26	141	4.1	107	10.1	6.7	6.0	3.3	1.22
	S.D.	2	0.03	1	0.2	2	0.4	0.7	0.1	0.1	0.12

a) : Non-pregnant
Z : Data was excluded from statistical analysis.

Appendix 7-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
	1113	62	25	40	1	294	8.8	59	26	118	0.1	129
	1114	56	24	35	1	149	12.5	59	35	128	0.1	151
0	1115	55	26	50	1	305	18.0	61	14	118	0.1	129
	1116	69	26	46	1	148	19.3	70	12	129	0.1	133
	1117	63	27	41	1	131	9.2	71	16	141	0.1	126
	Mean	61	26	42	1	205	13.6	64	21	127	0.1	134
	S.D.	6	1	6	0	86	4.9	6	10	10	0.0	10
	4113	59	28	37	1	222	14.1	63	18	113	0.1	148
	4114	67	30	35	1	172	9.8	64	20	119	0.1	128
1000	4115	51	30	54	1	139	9.3	84	32	160	0.1	138
	4116	64	31	44	1	201	6.8	41	12	86	0.1	119
	4117	53	31	37	2	144	14.6	75	20	135	0.1	146
	Mean	59	30	41	1	176	10.9	65	20	123	0.1	136
	S.D.	7	1	8	0	36	3.3	16	7	27	0.0	12

Appendix 7-6 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	Animal number	BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1113	15	0.27	140	4.3	107	9.8	4.4	6.2	3.6	1.38
	1114	15	0.25	141	4.5	109	10.2	2.8	6.6	3.7	1.28
	1115	16	0.27	141	4.6	109	10.0	4.1	6.6	3.9	1.44
	1116	20	0.26	142	4.4	108	9.6	5.1	5.8	3.3	1.32
	1117	14	0.27	141	4.3	110	10.2	5.4	6.5	3.7	1.32
	Mean	16	0.26	141	4.4	109	10.0	4.4	6.3	3.6	1.35
	S.D.	2	0.01	1	0.1	1	0.3	1.0	0.3	0.2	0.06
1000	4113	19	0.32	140	4.1	106	9.8	3.5	6.3	3.4	1.17
	4114	15	0.32	141	4.2	107	9.9	3.9	5.9	3.5	1.46
	4115	15	0.25	142	4.2	107	10.5	4.9	6.8	4.0	1.43
	4116	18	0.29	141	4.5	109	9.9	5.2	6.1	3.5	1.35
	4117	19	0.29	141	4.4	109	10.3	4.8	6.7	3.7	1.23
	Mean	17	0.29	141	4.3	108	10.1	4.5	6.4	3.6	1.33
	S.D.	2	0.03	1	0.2	1	0.3	0.7	0.4	0.2	0.13

Appendix 7-7 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of male rats (End of recovery)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
	1008	49	26	43	1	234	6.8	53	100	95	0.1	139
	1009	69	31	50	1	290	8.8	55	58	88	0.1	140
0	1010	64	29	58	1	373	6.5	44	66	76	0.1	164
	1011	73	36	47	1	385	14.9	58	37	89	0.1	127
	1012	70	31	44	1	361	19.1	48	16	73	0.1	141
	Mean	65	31	48	1	329	11.2	52	55	84	0.1	142
	S.D.	10	4	6	0	65	5.6	6	32	9	0.0	13
	4008	78	30	50	0	290	6.8	40	41	70	0.1	133
	4009	69	30	47	1	326	5.5	38	35	65	0.1	153
1000	4010	62	29	43	1	313	10.5	67	36	100	0.1	159
	4011	70	28	58	1	250	21.1	58	25	85	0.1	137
	4012	73	28	48	1	383	16.7	49	13	73	0.1	108
	Mean	70	29	49	1	312	12.1	50	30	79	0.1	138
	S.D.	6	1	6	0	49	6.6	12	11	14	0.0	20

Appendix 7-8 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of male rats (End of recovery)

Dose mg/kg	Animal number	BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1008	14	0.21	142	4.2	105	10.1	5.1	5.8	3.0	1.07
	1009	16	0.26	143	4.7	104	9.7	5.9	5.7	3.0	1.11
	1010	16	0.20	141	4.2	105	9.6	5.2	5.8	3.0	1.07
	1011	18	0.27	141	4.6	106	9.7	6.0	5.8	3.0	1.07
	1012	16	0.18	142	4.5	107	9.8	5.5	5.8	3.1	1.15
	Mean	16	0.22	142	4.4	105	9.8	5.5	5.8	3.0	1.09
	S.D.	1	0.04	1	0.2	1	0.2	0.4	0.0	0.0	0.04
1000	4008	18	0.23	142	4.8	105	9.5	6.2	5.8	3.0	1.07
	4009	15	0.28	141	4.5	106	9.4	5.2	5.5	3.0	1.20
	4010	14	0.19	143	4.2	107	9.8	5.6	5.6	3.0	1.15
	4011	18	0.29	143	4.3	105	9.7	5.9	5.8	3.0	1.07
	4012	18	0.30	143	4.7	107	9.5	5.7	6.0	3.1	1.07
	Mean	17	0.26	142	4.5	106	9.6	5.7	5.7	3.0	1.11
	S.D.	2	0.05	1	0.3	1	0.2	0.4	0.2	0.0	0.06

Appendix 7-9 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of female rats (End of recovery)

Dose mg/kg	Animal number	AST (GOT) IU/L	ALT (GPT) IU/L	LDH IU/L	γ-GTP IU/L	ALP IU/L	TBA μmol/L	T.cho mg/dL	TG mg/dL	PL mg/dL	T.bili-rubin mg/dL	Glucose mg/dL
0	1118	54	23	50	1	196	21.2	103	58	186	0.1	132
	1119	55	27	43	1	155	12.4	77	31	137	0.1	144
	1120	58	21	51	1	148	13.8	54	23	102	0.1	144
	1121	69	33	46	1	169	23.6	86	23	151	0.1	132
	1122	56	24	26	1	184	10.0	67	18	118	0.1	135
	Mean	58	26	43	1	170	16.2	77	31	139	0.1	137
	S.D.	6	5	10	0	20	5.9	19	16	32	0.0	6
1000	4118	58	24	35	1	135	11.9	64	18	124	0.1	128
	4119	46	20	42	1	133	18.7	76	58	146	0.1	141
	4120	73	40	46	1	111	13.3	72	13	126	0.1	141
	4121	61	28	33	1	130	8.7	78	12	128	0.1	148
	4122	101	58	55	1	158	18.9	74	14	125	0.1	123
	Mean	68	34	42	1	133	14.3	73	23	130	0.1	136
	S.D.	21	15	9	0	17	4.4	5	20	9	0.0	10

Appendix 7-10 A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual blood chemistry of female rats (End of recovery)

Dose mg/kg	Animal number	BUN mg/dL	Crea-tinine mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	Albumin g/dL	A/G
0	1118	13	0.29	140	3.8	106	10.4	3.4	6.8	4.0	1.43
	1119	17	0.29	140	4.3	106	9.7	4.4	6.2	3.6	1.38
	1120	15	0.31	142	4.4	108	10.0	4.2	6.3	3.5	1.25
	1121	15	0.30	144	3.8	110	10.3	3.4	7.1	3.9	1.22
	1122	16	0.33	141	4.8	109	9.7	4.0	6.2	3.4	1.21
	Mean	15	0.30	141	4.2	108	10.0	3.9	6.5	3.7	1.30
	S.D.	1	0.02	2	0.4	2	0.3	0.5	0.4	0.3	0.10
1000	4118	17	0.27	142	4.0	108	10.1	2.4	6.6	3.9	1.44
	4119	16	0.29	141	4.4	107	10.0	3.7	6.6	3.7	1.28
	4120	15	0.31	141	4.2	106	9.9	4.3	5.8	3.5	1.52
	4121	13	0.27	141	4.2	108	10.1	3.3	6.5	3.7	1.32
	4122	16	0.25	142	4.2	107	10.0	4.7	6.1	3.3	1.18
	Mean	15	0.28	141	4.2	107	10.0	3.7	6.3	3.6	1.35
	S.D.	2	0.02	1	0.1	1	0.1	0.9	0.4	0.2	0.13

Appendix 8-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
	1001	457	2.11	14.4	11.3	9.4	20.7	305	1.32
	1002	477	2.13	12.6	10.8	10.2	21.0	285	1.44
	1003	513	2.19	15.1	12.4	12.5	24.9	220	1.53
	1004	499	1.92	11.9	11.1	9.1	20.2	372	1.41
Absolute	1005	488	2.02	15.4	11.7	11.8	23.5	196	1.49
	1006	514	2.17	12.7	11.7	11.9	23.6	323	1.57
	1007	506	2.20	13.3	13.1	11.6	24.7	170	1.47
	Mean	493	2.11	13.6	11.7	10.9	22.7	267	1.46
	S.D.	21	0.10	1.3	0.8	1.3	2.0	74	0.08
	1001		0.46	3.2	2.5	2.1	4.5	67	0.29
	1002		0.45	2.6	2.3	2.1	4.4	60	0.30
	1003		0.43	2.9	2.4	2.4	4.9	43	0.30
	1004		0.38	2.4	2.2	1.8	4.0	75	0.28
Relative	1005		0.41	3.2	2.4	2.4	4.8	40	0.31
	1006		0.42	2.5	2.3	2.3	4.6	63	0.31
	1007		0.43	2.6	2.6	2.3	4.9	34	0.29
	Mean		0.43	2.8	2.4	2.2	4.6	55	0.30
	S.D.		0.03	0.3	0.1	0.2	0.3	16	0.01

Appendix 8-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	1001	11.29	0.87	1.41	1.41	2.82	26	30	56
	1002	10.62	0.77	1.46	1.48	2.94	30	35	65
	1003	13.59	0.73	1.57	1.67	3.24	28	31	59
	1004	12.14	0.76	1.44	1.46	2.90	27	28	55
Absolute	1005	12.24	0.98	1.58	1.60	3.18	39	44	83
	1006	13.72	0.76	1.89	1.76	3.65	25	30	55
	1007	12.01	0.65	1.66	1.63	3.29	27	27	54
	Mean	12.23	0.79	1.57	1.57	3.15	29	32	61
	S.D.	1.13	0.11	0.17	0.13	0.29	5	6	10
	1001	2.47	0.19	0.31	0.31	0.62	6	7	12
	1002	2.23	0.16	0.31	0.31	0.62	6	7	14
	1003	2.65	0.14	0.31	0.33	0.63	5	6	12
	1004	2.43	0.15	0.29	0.29	0.58	5	6	11
Relative	1005	2.51	0.20	0.32	0.33	0.65	8	9	17
	1006	2.67	0.15	0.37	0.34	0.71	5	6	11
	1007	2.37	0.13	0.33	0.32	0.65	5	5	11
	Mean	2.48	0.16	0.32	0.32	0.64	6	7	13
	S.D.	0.15	0.03	0.03	0.02	0.04	1	1	2

Appendix 8-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 0

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	1001	1.82	1.05	1.45	1.45	2.90	534	508	1042
	1002	1.86	1.22	1.39	1.40	2.79	599	568	1167
	1003	1.74	1.18	1.54	1.66	3.20	685	740	1425
	1004	1.57	1.22	1.61	1.63	3.24	652	656	1308
	1005	1.67	1.45	1.62	1.63	3.25	850	783	1633
	1006	1.96	1.23	1.73	1.70	3.43	615	590	1205
	1007	1.56	1.18	1.86	1.79	3.65	695	676	1371
	Mean	1.74	1.22	1.60	1.61	3.21	661	646	1307
	S.D.	0.15	0.12	0.16	0.14	0.29	100	97	193
Relative	1001	0.40	0.23	0.32	0.32	0.63	117	111	228
	1002	0.39	0.26	0.29	0.29	0.58	126	119	245
	1003	0.34	0.23	0.30	0.32	0.62	134	144	278
	1004	0.31	0.24	0.32	0.33	0.65	131	131	262
	1005	0.34	0.30	0.33	0.33	0.67	174	160	335
	1006	0.38	0.24	0.34	0.33	0.67	120	115	234
	1007	0.31	0.23	0.37	0.35	0.72	137	134	271
	Mean	0.35	0.25	0.32	0.32	0.65	134	131	265
	S.D.	0.04	0.03	0.03	0.02	0.04	19	17	36

Appendix 8-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	2001	495	1.97	11.2	10.6	8.5	19.1	512	1.51
	2002	504	1.99	14.6	12.9	13.0	25.9	262	1.43
	2003	519	2.11	15.7	12.2	11.9	24.1	204	1.50
	2004	506	2.09	11.7	9.7	10.5	20.2	389	1.54
	2005	508	2.03	14.2	12.4	13.7	26.1	372	1.31
	2006	524	2.17	13.1	12.6	13.6	26.2	235	1.46
	2007	516	2.10	13.1	9.0	8.4	17.4	323	1.38
	2008	494	2.17	12.2	10.7	10.3	21.0	273	1.40
	2009	498	2.08	15.3	12.5	11.6	24.1	306	1.45
	2010	508	2.26	14.2	11.0	12.1	23.1	220	1.50
	2011	520	2.08	15.1	11.4	13.3	24.7	326	1.57
	2012	483	2.07	12.4	14.3	15.0	29.3	581	1.49
	Mean	506	2.09	13.6	11.6	11.8	23.4	334	1.46
	S.D.	12	0.08	1.5	1.5	2.1	3.4	115	0.07
Relative	2001		0.40	2.3	2.1	1.7	3.9	103	0.31
	2002		0.39	2.9	2.6	2.6	5.1	52	0.28
	2003		0.41	3.0	2.4	2.3	4.6	39	0.29
	2004		0.41	2.3	1.9	2.1	4.0	77	0.30
	2005		0.40	2.8	2.4	2.7	5.1	73	0.26
	2006		0.41	2.5	2.4	2.6	5.0	45	0.28
	2007		0.41	2.5	1.7	1.6	3.4	63	0.27
	2008		0.44	2.5	2.2	2.1	4.3	55	0.28
	2009		0.42	3.1	2.5	2.3	4.8	61	0.29
	2010		0.44	2.8	2.2	2.4	4.5	43	0.30
	2011		0.40	2.9	2.2	2.6	4.8	63	0.30
	2012		0.43	2.6	3.0	3.1	6.1	120	0.31
	Mean		0.41	2.7	2.3	2.3	4.6	66	0.29
	S.D.		0.02	0.3	0.3	0.4	0.7	24	0.02

Appendix 8-5

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 100

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	2001	11.97	0.82	1.50	1.47	2.97	34	36	70
	2002	12.61	0.71	1.63	1.62	3.25	29	33	62
	2003	13.26	0.96	1.59	1.57	3.16	34	34	68
	2004	13.16	0.82	1.38	1.37	2.75	32	31	63
	2005	13.38	0.77	1.57	1.58	3.15	30	29	59
	2006	11.69	0.82	1.60	1.68	3.28	33	35	68
	2007	12.53	1.05	1.60	1.72	3.32	39	45	84
	2008	13.14	0.73	1.66	1.61	3.27	32	35	67
	2009	12.77	0.66	1.65	1.68	3.33	32	33	65
	2010	12.63	0.92	1.53	1.52	3.05	46	52	98
	2011	15.62	0.78	1.65	1.60	3.25	45	42	87
	2012	12.40	0.70	1.72	1.71	3.43	35	38	73
	Mean	12.93	0.81	1.59	1.59	3.18	35	37	72
	S.D.	0.99	0.12	0.09	0.10	0.19	5	7	12
Relative	2001	2.42	0.17	0.30	0.30	0.60	7	7	14
	2002	2.50	0.14	0.32	0.32	0.64	6	7	12
	2003	2.55	0.18	0.31	0.30	0.61	7	7	13
	2004	2.60	0.16	0.27	0.27	0.54	6	6	12
	2005	2.63	0.15	0.31	0.31	0.62	6	6	12
	2006	2.23	0.16	0.31	0.32	0.63	6	7	13
	2007	2.43	0.20	0.31	0.33	0.64	8	9	16
	2008	2.66	0.15	0.34	0.33	0.66	6	7	14
	2009	2.56	0.13	0.33	0.34	0.67	6	7	13
	2010	2.49	0.18	0.30	0.30	0.60	9	10	19
	2011	3.00	0.15	0.32	0.31	0.63	9	8	17
	2012	2.57	0.14	0.36	0.35	0.71	7	8	15
	Mean	2.55	0.16	0.32	0.32	0.63	7	7	14
	S.D.	0.18	0.02	0.02	0.02	0.04	1	1	2

Appendix 8-6

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 100

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	2001	1.62	1.11	1.34	1.35	2.69	632	563	1195
	2002	1.67	1.20	1.70	1.70	3.40	684	704	1388
	2003	1.96	1.49	1.66	1.62	3.28	716	702	1418
	2004	2.11	1.27	1.51	1.53	3.04	644	697	1341
	2005	1.91	1.74	1.45	1.51	2.96	660	706	1366
	2006	1.70	1.15	1.83	1.90	3.73	609	637	1246
	2007	2.07	1.24	1.46	1.41	2.87	579	580	1159
	2008	1.54	1.12	1.77	1.75	3.52	594	575	1169
	2009	1.60	1.11	1.75	1.68	3.43	703	678	1381
	2010	2.19	1.74	1.58	1.53	3.11	699	660	1359
	2011	2.10	1.75	1.50	1.50	3.00	653	701	1354
	2012	1.79	1.51	1.50	1.60	3.10	673	717	1390
	Mean	1.86	1.37	1.59	1.59	3.18	654	660	1314
	S.D.	0.23	0.26	0.15	0.15	0.30	44	57	94
Relative	2001	0.33	0.22	0.27	0.27	0.54	128	114	241
	2002	0.33	0.24	0.34	0.34	0.67	136	140	275
	2003	0.38	0.29	0.32	0.31	0.63	138	135	273
	2004	0.42	0.25	0.30	0.30	0.60	127	138	265
	2005	0.38	0.34	0.29	0.30	0.58	130	139	269
	2006	0.32	0.22	0.35	0.36	0.71	116	122	238
	2007	0.40	0.24	0.28	0.27	0.56	112	112	225
	2008	0.31	0.23	0.36	0.35	0.71	120	116	237
	2009	0.32	0.22	0.35	0.34	0.69	141	136	277
	2010	0.43	0.34	0.31	0.30	0.61	138	130	268
	2011	0.40	0.34	0.29	0.29	0.58	126	135	260
	2012	0.37	0.31	0.31	0.33	0.64	139	148	288
	Mean	0.37	0.27	0.31	0.31	0.63	129	130	260
	S.D.	0.04	0.05	0.03	0.03	0.06	10	12	20

Appendix 8-7

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	3001	510	2.07	13.6	12.1	10.0	22.1	218	1.94
	3002	541	2.07	15.2	11.3	11.7	23.0	224	1.50
	3003	530	2.14	16.9	9.1	10.0	19.1	278	1.58
	3004	535	2.22	13.9	11.1	10.4	21.5	267	1.70
	3005	504	1.99	13.6	12.9	10.3	23.2	230	1.68
	3006	548	2.29	14.8	15.5	16.1	31.6	355	1.63
	3007	474	2.05	12.3	15.1	13.6	28.7	337	1.40
	3008	495	2.14	12.9	9.1	11.9	21.0	295	1.43
	3009	502	2.05	14.3	13.8	12.3	26.1	265	1.64
	3010	510	2.12	13.4	11.7	8.2	19.9	324	1.52
	3011	460	2.08	13.1	9.5	8.6	18.1	177	1.36
	3012	481	2.15	11.8	11.1	12.1	23.2	346	1.55
	Mean	508	2.11	13.8	11.9	11.3	23.1	276	1.58
	S.D.	27	0.08	1.4	2.2	2.2	4.0	57	0.16
Relative	3001		0.41	2.7	2.4	2.0	4.3	43	0.38
	3002		0.38	2.8	2.1	2.2	4.3	41	0.28
	3003		0.40	3.2	1.7	1.9	3.6	52	0.30
	3004		0.41	2.6	2.1	1.9	4.0	50	0.32
	3005		0.39	2.7	2.6	2.0	4.6	46	0.33
	3006		0.42	2.7	2.8	2.9	5.8	65	0.30
	3007		0.43	2.6	3.2	2.9	6.1	71	0.30
	3008		0.43	2.6	1.8	2.4	4.2	60	0.29
	3009		0.41	2.8	2.7	2.5	5.2	53	0.33
	3010		0.42	2.6	2.3	1.6	3.9	64	0.30
	3011		0.45	2.8	2.1	1.9	3.9	38	0.30
	3012		0.45	2.5	2.3	2.5	4.8	72	0.32
	Mean		0.42	2.7	2.3	2.2	4.6	55	0.31
	S.D.		0.02	0.2	0.4	0.4	0.8	12	0.03

Appendix 8-8

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 300

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	3001	12.83	0.86	1.63	1.67	3.30	27	30	57
	3002	13.75	0.85	1.60	1.56	3.16	43	47	90
	3003	13.29	1.00	1.55	1.68	3.23	44	46	90
	3004	13.86	0.81	1.71	1.75	3.46	34	31	65
	3005	12.90	0.80	1.81	1.75	3.56	36	35	71
	3006	14.51	0.88	1.90	1.85	3.75	28	28	56
	3007	12.05	0.69	1.61	1.55	3.16	25	30	55
Absolute	3008	13.28	0.85	1.50	1.46	2.96	39	38	77
	3009	12.67	0.80	1.75	1.74	3.49	33	36	69
	3010	13.67	0.75	1.52	1.56	3.08	30	33	63
	3011	11.04	0.67	1.54	1.62	3.16	34	38	72
	3012	11.63	0.69	1.46	1.52	2.98	31	33	64
	Mean	12.96	0.80	1.63	1.64	3.27	34	35	69
	S.D.	1.00	0.09	0.13	0.12	0.24	6	6	12
	3001	2.52	0.17	0.32	0.33	0.65	5	6	11
	3002	2.54	0.16	0.30	0.29	0.58	8	9	17
	3003	2.51	0.19	0.29	0.32	0.61	8	9	17
	3004	2.59	0.15	0.32	0.33	0.65	6	6	12
	3005	2.56	0.16	0.36	0.35	0.71	7	7	14
	3006	2.65	0.16	0.35	0.34	0.68	5	5	10
	3007	2.54	0.15	0.34	0.33	0.67	5	6	12
Relative	3008	2.68	0.17	0.30	0.29	0.60	8	8	16
	3009	2.52	0.16	0.35	0.35	0.70	7	7	14
	3010	2.68	0.15	0.30	0.31	0.60	6	6	12
	3011	2.40	0.15	0.33	0.35	0.69	7	8	16
	3012	2.42	0.14	0.30	0.32	0.62	6	7	13
	Mean	2.55	0.16	0.32	0.33	0.65	7	7	14
	S.D.	0.09	0.01	0.02	0.02	0.04	1	1	2

Appendix 8-9

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 300

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	3001	1.88	1.56	1.67	1.68	3.35	744	768	1512
	3002	1.82	1.48	1.47	1.54	3.01	626	609	1235
	3003	2.01	1.62	1.56	1.56	3.12	632	661	1293
	3004	1.78	1.26	1.57	1.61	3.18	672	640	1312
	3005	2.22	1.37	1.62	1.63	3.25	613	586	1199
	3006	1.87	1.38	1.88	1.89	3.77	702	696	1398
	3007	1.43	1.10	1.57	1.58	3.15	603	611	1214
	3008	1.75	1.14	1.82	1.86	3.68	758	685	1443
	3009	1.86	1.37	1.66	1.68	3.34	655	617	1272
	3010	2.03	1.56	1.58	1.61	3.19	718	734	1452
	3011	2.00	1.22	1.54	1.56	3.10	613	601	1214
	3012	1.61	1.07	1.72	1.77	3.49	610	609	1219
	Mean	1.86	1.34	1.64	1.66	3.30	662	651	1314
	S.D.	0.21	0.19	0.12	0.12	0.24	56	58	110
Relative	3001	0.37	0.31	0.33	0.33	0.66	146	151	296
	3002	0.34	0.27	0.27	0.28	0.56	116	113	228
	3003	0.38	0.31	0.29	0.29	0.59	119	125	244
	3004	0.33	0.24	0.29	0.30	0.59	126	120	245
	3005	0.44	0.27	0.32	0.32	0.64	122	116	238
	3006	0.34	0.25	0.34	0.34	0.69	128	127	255
	3007	0.30	0.23	0.33	0.33	0.66	127	129	256
	3008	0.35	0.23	0.37	0.38	0.74	153	138	292
	3009	0.37	0.27	0.33	0.33	0.67	130	123	253
	3010	0.40	0.31	0.31	0.32	0.63	141	144	285
	3011	0.43	0.27	0.33	0.34	0.67	133	131	264
	3012	0.33	0.22	0.36	0.37	0.73	127	127	253
	Mean	0.37	0.27	0.32	0.33	0.65	131	129	259
	S.D.	0.04	0.03	0.03	0.03	0.05	11	11	21

Appendix 8-10

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
	4001	461	2.11	14.3	11.6	10.6	22.2	237	1.33
	4002	493	2.20	12.6	10.2	11.0	21.2	352	1.30
	4003	473	2.13	12.1	11.8	10.2	22.0	226	1.39
	4004	526	2.24	14.1	11.7	10.4	22.1	285	1.46
Absolute	4005	560	2.13	13.6	11.4	8.2	19.6	327	1.66
	4006	522	2.27	14.1	15.4	14.5	29.9	311	1.47
	4007	488	2.23	14.7	13.0	14.0	27.0	244	1.46
	Mean	503	2.19	13.6	12.2	11.3	23.4	283	1.44
	S.D.	34	0.06	1.0	1.6	2.2	3.6	49	0.12
	4001		0.46	3.1	2.5	2.3	4.8	51	0.29
	4002		0.45	2.6	2.1	2.2	4.3	71	0.26
	4003		0.45	2.6	2.5	2.2	4.7	48	0.29
	4004		0.43	2.7	2.2	2.0	4.2	54	0.28
Relative	4005		0.38	2.4	2.0	1.5	3.5	58	0.30
	4006		0.43	2.7	3.0	2.8	5.7	60	0.28
	4007		0.46	3.0	2.7	2.9	5.5	50	0.30
	Mean		0.44	2.7	2.4	2.3	4.7	56	0.29
	S.D.		0.03	0.2	0.4	0.5	0.8	8	0.01

Appendix 8-11

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 1000

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4001	11.87	0.85	1.43	1.42	2.85	31	35	66
	4002	11.35	0.74	1.52	1.68	3.20	36	36	72
	4003	11.91	0.83	1.61	1.59	3.20	34	37	71
	4004	13.79	0.93	1.51	1.58	3.09	43	43	86
	4005	15.01	0.80	1.77	1.92	3.69	25	31	56
	4006	12.46	0.75	1.58	1.56	3.14	48	52	100
	4007	11.84	0.74	1.62	1.70	3.32	34	41	75
	Mean	12.60	0.81	1.58	1.64	3.21	36	39	75
	S.D.	1.32	0.07	0.11	0.16	0.26	8	7	14
Relative	4001	2.57	0.18	0.31	0.31	0.62	7	8	14
	4002	2.30	0.15	0.31	0.34	0.65	7	7	15
	4003	2.52	0.18	0.34	0.34	0.68	7	8	15
	4004	2.62	0.18	0.29	0.30	0.59	8	8	16
	4005	2.68	0.14	0.32	0.34	0.66	4	6	10
	4006	2.39	0.14	0.30	0.30	0.60	9	10	19
	4007	2.43	0.15	0.33	0.35	0.68	7	8	15
	Mean	2.50	0.16	0.31	0.33	0.64	7	8	15
	S.D.	0.13	0.02	0.02	0.02	0.04	2	1	3

Appendix 8-12

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of administration)

Dose (mg/kg): 1000

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4001	1.80	1.37	1.65	1.73	3.38	595	601	1196
	4002	1.69	1.26	1.61	1.59	3.20	649	627	1276
	4003	2.16	1.28	1.53	1.57	3.10	623	586	1209
	4004	2.16	1.73	1.62	1.61	3.23	711	703	1414
	4005	1.44	1.30	1.70	1.67	3.37	647	657	1304
	4006	2.05	1.83	1.53	1.53	3.06	737	720	1457
	4007	1.65	1.57	1.49	1.46	2.95	713	694	1407
	Mean	1.85	1.48	1.59	1.59	3.18	668	655	1323
	S.D.	0.28	0.23	0.08	0.09	0.16	53	52	104
Relative	4001	0.39	0.30	0.36	0.38	0.73	129	130	259
	4002	0.34	0.26	0.33	0.32	0.65	132	127	259
	4003	0.46	0.27	0.32	0.33	0.66	132	124	256
	4004	0.41	0.33	0.31	0.31	0.61	135	134	269
	4005	0.26	0.23	0.30	0.30	0.60	116	117	233
	4006	0.39	0.35	0.29	0.29	0.59	141	138	279
	4007	0.34	0.32	0.31	0.30	0.60	146	142	288
	Mean	0.37	0.29	0.32	0.32	0.63	133	130	263
	S.D.	0.06	0.04	0.02	0.03	0.05	10	9	18

Appendix 8-13

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	1101	298	1.99	16.5	5.9	6.7	12.6	171	0.90
	1102	328	2.01	18.5	6.8	6.4	13.2	218	1.09
	1103	322	1.90	18.3	6.8	7.8	14.6	370	1.08
	1104	322	2.10	18.3	8.8	7.6	16.4	218	0.97
	1105	302	2.06	18.1	10.3	9.6	19.9	192	1.12
	1106	333	2.05	21.3	10.7	6.7	17.4	286	1.14
	1107	291	2.07	19.3	8.1	7.7	15.8	179	0.92
	1108	336	2.01	18.5	7.7	9.4	17.1	176	1.03
	1109	325	2.10	22.1	8.1	9.3	17.4	251	1.11
	1110	335	2.16	19.8	12.7	10.7	23.4	134	1.08
	1111	316	1.96	18.3	9.0	8.7	17.7	304	0.94
	1112	313	1.93	15.1	7.5	8.8	16.3	245	1.09
	Mean	318	2.03	18.7	8.5	8.3	16.8	229	1.04
	S.D.	15	0.08	1.9	1.9	1.3	2.9	67	0.08
Relative	1101		0.67	5.5	2.0	2.2	4.2	57	0.30
	1102		0.61	5.6	2.1	2.0	4.0	66	0.33
	1103		0.59	5.7	2.1	2.4	4.5	115	0.34
	1104		0.65	5.7	2.7	2.4	5.1	68	0.30
	1105		0.68	6.0	3.4	3.2	6.6	64	0.37
	1106		0.62	6.4	3.2	2.0	5.2	86	0.34
	1107		0.71	6.6	2.8	2.6	5.4	62	0.32
	1108		0.60	5.5	2.3	2.8	5.1	52	0.31
	1109		0.65	6.8	2.5	2.9	5.4	77	0.34
	1110		0.64	5.9	3.8	3.2	7.0	40	0.32
	1111		0.62	5.8	2.8	2.8	5.6	96	0.30
	1112		0.62	4.8	2.4	2.8	5.2	78	0.35
	Mean		0.64	5.9	2.7	2.6	5.3	72	0.33
	S.D.		0.04	0.5	0.6	0.4	0.9	20	0.02

Appendix 8-14

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	1101	9.83	0.71	1.05	1.03	2.08	38	44	82
	1102	10.39	0.66	1.08	1.04	2.12	37	42	79
	1103	10.18	0.75	1.18	1.16	2.34	35	40	75
	1104	9.43	0.67	1.01	1.05	2.06	37	46	83
	1105	10.29	0.82	1.19	1.07	2.26	37	41	78
	1106	12.31	1.07	1.19	1.26	2.45	42	45	87
	1107	10.47	0.59	1.03	1.01	2.04	36	42	78
Absolute	1108	12.12	0.77	1.28	1.25	2.53	37	42	79
	1109	11.23	0.69	1.18	1.17	2.35	33	39	72
	1110	12.25	0.95	1.23	1.18	2.41	58	58	116
	1111	11.03	0.75	1.25	1.26	2.51	36	39	75
	1112	10.72	0.73	1.08	1.06	2.14	39	42	81
	Mean	10.85	0.76	1.15	1.13	2.27	39	43	82
	S.D.	0.96	0.13	0.09	0.10	0.18	6	5	11
	1101	3.30	0.24	0.35	0.35	0.70	13	15	28
	1102	3.17	0.20	0.33	0.32	0.65	11	13	24
	1103	3.16	0.23	0.37	0.36	0.73	11	12	23
	1104	2.93	0.21	0.31	0.33	0.64	11	14	26
	1105	3.41	0.27	0.39	0.35	0.75	12	14	26
	1106	3.70	0.32	0.36	0.38	0.74	13	14	26
	1107	3.60	0.20	0.35	0.35	0.70	12	14	27
Relative	1108	3.61	0.23	0.38	0.37	0.75	11	13	24
	1109	3.46	0.21	0.36	0.36	0.72	10	12	22
	1110	3.66	0.28	0.37	0.35	0.72	17	17	35
	1111	3.49	0.24	0.40	0.40	0.79	11	12	24
	1112	3.42	0.23	0.35	0.34	0.68	12	13	26
	Mean	3.41	0.24	0.36	0.36	0.71	12	14	26
	S.D.	0.23	0.04	0.02	0.02	0.04	2	1	3

Appendix 8-15

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 0

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1101	50.5	38.3	88.8	545
	1102	67.9	66.8	134.7	718
	1103	60.8	58.8	119.6	747
	1104	54.0	65.2	119.2	670
	1105	67.5	72.6	140.1	920
	1106	53.3	70.0	123.3	745
	1107	44.2	48.8	93.0	749
	1108	53.8	51.2	105.0	689
	1109	61.6	61.4	123.0	931
	1110	59.3	60.9	120.2	909
	1111	57.4	52.7	110.1	801
	1112	63.1	55.2	118.3	642
	Mean	57.8	58.5	116.3	756
	S.D.	7.0	9.8	15.1	118
Relative	1101	16.9	12.9	29.8	183
	1102	20.7	20.4	41.1	219
	1103	18.9	18.3	37.1	232
	1104	16.8	20.2	37.0	208
	1105	22.4	24.0	46.4	305
	1106	16.0	21.0	37.0	224
	1107	15.2	16.8	32.0	257
	1108	16.0	15.2	31.3	205
	1109	19.0	18.9	37.8	286
	1110	17.7	18.2	35.9	271
	1111	18.2	16.7	34.8	253
	1112	20.2	17.6	37.8	205
	Mean	18.2	18.4	36.5	237
	S.D.	2.2	2.9	4.5	37

Appendix 8-16

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
	2101	323	1.94	17.4	10.2	11.0	21.2	300	1.14
	2102	297	1.95	18.0	8.5	6.1	14.6	251	1.01
	2103	319	1.93	19.8	6.8	5.8	12.6	273	1.04
	2104	317	1.90	15.7	7.7	5.9	13.6	272	0.94
	2105	306	2.00	21.6	7.6	8.6	16.2	260	0.98
	2106	359	1.96	20.5	9.8	8.0	17.8	292	1.06
	2107	335	2.04	14.5	14.7	13.2	27.9	291	0.96
Absolute	2108	319	2.02	22.7	7.0	7.5	14.5	296	1.06
	2109	310	2.00	18.2	6.6	6.0	12.6	144	1.00
	2110	299	1.94	17.4	10.8	8.8	19.6	252	0.94
	2111	295	1.89	17.9	7.6	7.7	15.3	254	1.02
	2112	280	1.94	16.3	6.8	6.8	13.6	125	0.86
	Mean	313	1.96	18.3	8.7	8.0	16.6	251	1.00
	S.D.	21	0.05	2.4	2.4	2.2	4.5	57	0.07
	2101		0.60	5.4	3.2	3.4	6.6	93	0.35
	2102		0.66	6.1	2.9	2.1	4.9	85	0.34
	2103		0.61	6.2	2.1	1.8	3.9	86	0.33
	2104		0.60	5.0	2.4	1.9	4.3	86	0.30
	2105		0.65	7.1	2.5	2.8	5.3	85	0.32
	2106		0.55	5.7	2.7	2.2	5.0	81	0.30
	2107		0.61	4.3	4.4	3.9	8.3	87	0.29
Relative	2108		0.63	7.1	2.2	2.4	4.5	93	0.33
	2109		0.65	5.9	2.1	1.9	4.1	46	0.32
	2110		0.65	5.8	3.6	2.9	6.6	84	0.31
	2111		0.64	6.1	2.6	2.6	5.2	86	0.35
	2112		0.69	5.8	2.4	2.4	4.9	45	0.31
	Mean		0.63	5.9	2.8	2.5	5.3	80	0.32
	S.D.		0.04	0.8	0.7	0.6	1.3	16	0.02

Appendix 8-17

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 100

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	2101	10.84	0.75	1.20	1.10	2.30	37	43	80
	2102	9.94	0.60	1.19	1.16	2.35	49	58	107
	2103	10.33	0.65	1.07	1.01	2.08	30	31	61
	2104	9.34	0.68	1.15	1.12	2.27	30	34	64
	2105	9.36	0.76	1.07	1.11	2.18	39	43	82
	2106	10.97	0.70	1.21	1.13	2.34	35	38	73
	2107	9.62	0.62	1.01	1.05	2.06	32	36	68
Absolute	2108	10.25	0.70	1.05	1.07	2.12	34	39	73
	2109	11.19	0.73	1.13	1.02	2.15	42	47	89
	2110	9.58	0.64	1.07	1.10	2.17	35	37	72
	2111	8.86	0.53	1.00	1.05	2.05	37	40	77
	2112	9.69	0.65	0.89	0.89	1.78	30	34	64
	Mean	10.00	0.67	1.09	1.07	2.15	36	40	76
	S.D.	0.73	0.07	0.09	0.07	0.16	6	7	13
	2101	3.36	0.23	0.37	0.34	0.71	11	13	25
	2102	3.35	0.20	0.40	0.39	0.79	16	20	36
	2103	3.24	0.20	0.34	0.32	0.65	9	10	19
	2104	2.95	0.21	0.36	0.35	0.72	9	11	20
	2105	3.06	0.25	0.35	0.36	0.71	13	14	27
	2106	3.06	0.19	0.34	0.31	0.65	10	11	20
	2107	2.87	0.19	0.30	0.31	0.61	10	11	20
Relative	2108	3.21	0.22	0.33	0.34	0.66	11	12	23
	2109	3.61	0.24	0.36	0.33	0.69	14	15	29
	2110	3.20	0.21	0.36	0.37	0.73	12	12	24
	2111	3.00	0.18	0.34	0.36	0.69	13	14	26
	2112	3.46	0.23	0.32	0.32	0.64	11	12	23
	Mean	3.20	0.21	0.35	0.34	0.69	12	13	24
	S.D.	0.22	0.02	0.03	0.03	0.05	2	3	5

Appendix 8-18

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 100

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	2101	47.5	53.8	101.3	701
	2102	65.6	52.4	118.0	691
	2103	54.0	45.5	99.5	712
	2104	47.0	47.2	94.2	789
	2105	53.5	51.9	105.4	905
	2106	51.6	49.1	100.7	591
	2107	39.2	43.1	82.3	714
	2108	52.3	59.7	112.0	721
	2109	57.4	58.6	116.0	764
	2110	50.2	44.3	94.5	573
	2111	50.5	47.2	97.7	768
	2112	50.9	51.0	101.9	655
	Mean	51.6	50.3	102.0	715
	S.D.	6.3	5.3	10.0	89
Relative	2101	14.7	16.7	31.4	217
	2102	22.1	17.6	39.7	233
	2103	16.9	14.3	31.2	223
	2104	14.8	14.9	29.7	249
	2105	17.5	17.0	34.4	296
	2106	14.4	13.7	28.1	165
	2107	11.7	12.9	24.6	213
	2108	16.4	18.7	35.1	226
	2109	18.5	18.9	37.4	246
	2110	16.8	14.8	31.6	192
	2111	17.1	16.0	33.1	260
	2112	18.2	18.2	36.4	234
	Mean	16.6	16.1	32.7	230
	S.D.	2.6	2.0	4.2	33

Appendix 8-19

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	3101	315	2.00	15.5	6.1	4.0	10.1	353	1.02
	3102	319	1.95	17.1	4.3	7.7	12.0	267	1.05
	3103	322	1.97	16.6	8.5	7.9	16.4	308	1.07
	3104	325	1.89	22.5	10.2	5.8	16.0	237	1.05
	3105	347	2.01	18.4	9.0	9.8	18.8	156	0.93
	3106	318	1.98	17.7	7.9	8.9	16.8	285	1.04
	3107	314	1.95	20.1	8.0	7.5	15.5	363	1.06
	3108	326	2.05	17.4	7.1	6.9	14.0	370	1.15
	3109	319	1.93	17.4	9.0	11.7	20.7	344	0.97
	3110	309	1.91	17.2	11.3	8.4	19.7	285	0.99
	3111a)	328Z	1.98Z	17.7Z	13.2Z	9.4Z	22.6Z	391Z	1.03Z
	3112	288	2.03	20.4	8.4	7.8	16.2	188	1.00
	Mean	318	1.97	18.2	8.2	7.9	16.0	287	1.03
	S.D.	14	0.05	2.0	1.9	2.0	3.2	71	0.06
Relative	3101		0.63	4.9	1.9	1.3	3.2	112	0.32
	3102		0.61	5.4	1.3	2.4	3.8	84	0.33
	3103		0.61	5.2	2.6	2.5	5.1	96	0.33
	3104		0.58	6.9	3.1	1.8	4.9	73	0.32
	3105		0.58	5.3	2.6	2.8	5.4	45	0.27
	3106		0.62	5.6	2.5	2.8	5.3	90	0.33
	3107		0.62	6.4	2.5	2.4	4.9	116	0.34
	3108		0.63	5.3	2.2	2.1	4.3	113	0.35
	3109		0.61	5.5	2.8	3.7	6.5	108	0.30
	3110		0.62	5.6	3.7	2.7	6.4	92	0.32
	3111a)		0.60Z	5.4Z	4.0Z	2.9Z	6.9Z	119Z	0.31Z
	3112		0.70	7.1	2.9	2.7	5.6	65	0.35
	Mean		0.62	5.7	2.6	2.5	5.0	90	0.32
	S.D.		0.03	0.7	0.6	0.6	1.0	22	0.02

a): Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-20

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 300

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	3101	9.14	0.59	1.17	1.10	2.27	41	47	88
	3102	10.14	0.79	1.15	1.18	2.33	37	41	78
	3103	10.86	0.71	1.09	1.06	2.15	40	43	83
	3104	10.62	0.66	1.16	1.22	2.38	37	40	77
	3105	11.41	0.58	1.10	1.08	2.18	38	41	79
	3106	10.76	0.72	1.11	1.11	2.22	36	36	72
	3107	10.46	0.60	1.04	1.06	2.10	41	42	83
	3108	8.95	0.80	1.09	1.12	2.21	35	36	71
	3109	10.44	0.79	1.16	1.23	2.39	44	48	92
	3110	9.77	0.67	1.03	1.04	2.07	28	33	61
	3111a)	11.69Z	0.70Z	1.24Z	1.18Z	2.42Z	31Z	31Z	62Z
	3112	9.90	0.59	1.11	1.03	2.14	40	42	82
	Mean	10.22	0.68	1.11	1.11	2.22	38	41	79
	S.D.	0.74	0.09	0.05	0.07	0.11	4	5	9
Relative	3101	2.90	0.19	0.37	0.35	0.72	13	15	28
	3102	3.18	0.25	0.36	0.37	0.73	12	13	24
	3103	3.37	0.22	0.34	0.33	0.67	12	13	26
	3104	3.27	0.20	0.36	0.38	0.73	11	12	24
	3105	3.29	0.17	0.32	0.31	0.63	11	12	23
	3106	3.38	0.23	0.35	0.35	0.70	11	11	23
	3107	3.33	0.19	0.33	0.34	0.67	13	13	26
	3108	2.75	0.25	0.33	0.34	0.68	11	11	22
	3109	3.27	0.25	0.36	0.39	0.75	14	15	29
	3110	3.16	0.22	0.33	0.34	0.67	9	11	20
	3111a)	3.56Z	0.21Z	0.38Z	0.36Z	0.74Z	9Z	9Z	19Z
	3112	3.44	0.20	0.39	0.36	0.74	14	15	28
	Mean	3.21	0.22	0.35	0.35	0.70	12	13	25
	S.D.	0.21	0.03	0.02	0.02	0.04	2	2	3

a): Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-21

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 300

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	3101	53.2	45.8	99.0	620
	3102	61.8	54.6	116.4	776
	3103	56.4	49.4	105.8	749
	3104	62.8	44.3	107.1	720
	3105	54.3	45.2	99.5	763
	3106	57.0	41.8	98.8	885
	3107	65.9	68.0	133.9	875
	3108	54.4	51.1	105.5	1106
	3109	49.0	62.3	111.3	770
	3110	50.6	53.6	104.2	740
	3111a)	45.3Z	37.8Z	83.1Z	496Z
	3112	55.4	59.6	115.0	790
	Mean	56.4	52.3	108.8	799
	S.D.	5.2	8.3	10.3	124
Relative	3101	16.9	14.5	31.4	197
	3102	19.4	17.1	36.5	243
	3103	17.5	15.3	32.9	233
	3104	19.3	13.6	33.0	222
	3105	15.6	13.0	28.7	220
	3106	17.9	13.1	31.1	278
	3107	21.0	21.7	42.6	279
	3108	16.7	15.7	32.4	339
	3109	15.4	19.5	34.9	241
	3110	16.4	17.3	33.7	239
	3111a)	13.8Z	11.5Z	25.3Z	151Z
	3112	19.2	20.7	39.9	274
	Mean	17.8	16.5	34.3	251
	S.D.	1.8	3.0	4.0	39

a): Non-pregnant
Z: Data was excluded from statistical analysis.

Appendix 8-22

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
	4101	286	1.89	15.9	9.2	7.7	16.9	233	0.94
	4102	342	2.04	20.4	6.9	7.0	13.9	257	1.06
	4103	303	1.93	16.3	8.2	8.4	16.6	145	0.99
	4104	294	2.00	20.0	6.7	8.1	14.8	196	1.04
	4105	293	1.99	17.0	5.8	7.5	13.3	163	0.94
	4106	305	2.00	17.5	8.4	7.1	15.5	284	1.09
	4107	315	2.00	17.9	8.5	9.7	18.2	223	0.96
Absolute	4108	314	1.99	20.4	9.5	9.1	18.6	244	1.00
	4109	331	1.93	17.2	8.3	8.5	16.8	221	0.99
	4110	332	2.09	21.0	9.6	15.3	24.9	238	1.12
	4111	315	2.05	18.8	11.7	9.2	20.9	259	1.04
	4112	318	1.98	15.9	8.6	7.7	16.3	148	1.05
	Mean	312	1.99	18.2	8.5	8.8	17.2	218	1.02
	S.D.	17	0.06	1.9	1.5	2.2	3.2	45	0.06
	4101		0.66	5.6	3.2	2.7	5.9	81	0.33
	4102		0.60	6.0	2.0	2.0	4.1	75	0.31
	4103		0.64	5.4	2.7	2.8	5.5	48	0.33
	4104		0.68	6.8	2.3	2.8	5.0	67	0.35
	4105		0.68	5.8	2.0	2.6	4.5	56	0.32
	4106		0.66	5.7	2.8	2.3	5.1	93	0.36
	4107		0.63	5.7	2.7	3.1	5.8	71	0.30
Relative	4108		0.63	6.5	3.0	2.9	5.9	78	0.32
	4109		0.58	5.2	2.5	2.6	5.1	67	0.30
	4110		0.63	6.3	2.9	4.6	7.5	72	0.34
	4111		0.65	6.0	3.7	2.9	6.6	82	0.33
	4112		0.62	5.0	2.7	2.4	5.1	47	0.33
	Mean		0.64	5.8	2.7	2.8	5.5	70	0.33
	S.D.		0.03	0.5	0.5	0.6	0.9	14	0.02

Appendix 8-23

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 1000

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4101	10.61	0.63	1.13	1.07	2.20	35	40	75
	4102	10.60	0.67	1.27	1.28	2.55	42	42	84
	4103	10.04	0.72	0.98	0.96	1.94	35	36	71
	4104	9.47	0.54	0.96	0.97	1.93	39	40	79
	4105	10.01	0.70	1.11	1.07	2.18	40	38	78
	4106	9.45	0.71	1.08	1.05	2.13	35	35	70
	4107	9.66	0.65	1.07	1.04	2.11	36	37	73
	4108	11.23	0.82	1.16	1.14	2.30	47	50	97
	4109	9.70	0.79	1.05	1.05	2.10	38	40	78
	4110	11.14	0.89	1.20	1.19	2.39	43	46	89
	4111	10.74	0.66	1.09	1.13	2.22	48	52	100
	4112	10.20	0.74	1.04	1.07	2.11	39	42	81
	Mean	10.24	0.71	1.10	1.09	2.18	40	42	81
	S.D.	0.62	0.09	0.09	0.09	0.17	4	5	10
Relative	4101	3.71	0.22	0.40	0.37	0.77	12	14	26
	4102	3.10	0.20	0.37	0.37	0.75	12	12	25
	4103	3.31	0.24	0.32	0.32	0.64	12	12	23
	4104	3.22	0.18	0.33	0.33	0.66	13	14	27
	4105	3.42	0.24	0.38	0.37	0.74	14	13	27
	4106	3.10	0.23	0.35	0.34	0.70	11	11	23
	4107	3.07	0.21	0.34	0.33	0.67	11	12	23
	4108	3.58	0.26	0.37	0.36	0.73	15	16	31
	4109	2.93	0.24	0.32	0.32	0.63	11	12	24
	4110	3.36	0.27	0.36	0.36	0.72	13	14	27
	4111	3.41	0.21	0.35	0.36	0.70	15	17	32
	4112	3.21	0.23	0.33	0.34	0.66	12	13	25
	Mean	3.29	0.23	0.35	0.35	0.70	13	13	26
	S.D.	0.23	0.03	0.03	0.02	0.05	1	2	3

Appendix 8-24

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Lactation day 5)

Dose (mg/kg): 1000

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4101	51.3	50.7	102.0	713
	4102	71.0	47.5	118.5	754
	4103	49.0	48.4	97.4	802
	4104	57.5	54.3	111.8	925
	4105	42.9	57.6	100.5	687
	4106	52.1	45.1	97.2	774
	4107	50.9	46.1	97.0	900
	4108	50.9	62.2	113.1	739
	4109	53.0	52.2	105.2	800
	4110	60.7	54.3	115.0	793
	4111	61.4	54.3	115.7	679
	4112	46.7	60.0	106.7	812
	Mean	54.0	52.7	106.7	782
	S.D.	7.6	5.4	7.9	76
Relative	4101	17.9	17.7	35.7	249
	4102	20.8	13.9	34.6	220
	4103	16.2	16.0	32.1	265
	4104	19.6	18.5	38.0	315
	4105	14.6	19.7	34.3	234
	4106	17.1	14.8	31.9	254
	4107	16.2	14.6	30.8	286
	4108	16.2	19.8	36.0	235
	4109	16.0	15.8	31.8	242
	4110	18.3	16.4	34.6	239
	4111	19.5	17.2	36.7	216
	4112	14.7	18.9	33.6	255
	Mean	17.3	16.9	34.2	251
	S.D.	2.0	2.0	2.2	28

Appendix 8-25

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	1113	270	1.91	15.7	8.9	9.5	18.4	375	0.81
	1114	288	2.04	15.7	7.8	5.7	13.5	261	0.97
	1115	259	1.90	14.1	9.0	6.8	15.8	312	0.76
	1116	297	2.04	15.9	6.8	5.9	12.7	424	0.97
	1117	273	1.89	17.0	6.7	6.7	13.4	301	0.87
	Mean	277	1.96	15.7	7.8	6.9	14.8	335	0.88
	S.D.	15	0.08	1.0	1.1	1.5	2.3	65	0.09
Relative	1113		0.71	5.8	3.3	3.5	6.8	139	0.30
	1114		0.71	5.5	2.7	2.0	4.7	91	0.34
	1115		0.73	5.4	3.5	2.6	6.1	120	0.29
	1116		0.69	5.4	2.3	2.0	4.3	143	0.33
	1117		0.69	6.2	2.5	2.5	4.9	110	0.32
	Mean		0.71	5.7	2.9	2.5	5.4	121	0.32
	S.D.		0.02	0.3	0.5	0.6	1.0	21	0.02

Appendix 8-26

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	1113	6.75	0.45	0.90	0.97	1.87	37	41	78
	1114	7.72	0.55	0.92	0.96	1.88	31	33	64
	1115	6.43	0.53	0.85	0.84	1.69	24	26	50
Absolute	1116	7.24	0.52	1.01	1.01	2.02	34	36	70
	1117	6.91	0.52	0.97	0.88	1.85	29	30	59
	Mean	7.01	0.51	0.93	0.93	1.86	31	33	64
	S.D.	0.49	0.04	0.06	0.07	0.12	5	6	11
	1113	2.50	0.17	0.33	0.36	0.69	14	15	29
	1114	2.68	0.19	0.32	0.33	0.65	11	11	22
	1115	2.48	0.20	0.33	0.32	0.65	9	10	19
Relative	1116	2.44	0.18	0.34	0.34	0.68	11	12	24
	1117	2.53	0.19	0.36	0.32	0.68	11	11	22
	Mean	2.53	0.19	0.34	0.33	0.67	11	12	23
	S.D.	0.09	0.01	0.02	0.02	0.02	2	2	4

Appendix 8-27

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 0

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1113	54.6	50.0	104.6	699
	1114	43.6	41.8	85.4	432
	1115	40.5	33.8	74.3	598
	1116	30.5	35.7	66.2	556
	1117	47.0	58.0	105.0	520
	Mean	43.2	43.9	87.1	561
	S.D.	8.8	10.1	17.5	98
Relative	1113	20.2	18.5	38.7	259
	1114	15.1	14.5	29.7	150
	1115	15.6	13.1	28.7	231
	1116	10.3	12.0	22.3	187
	1117	17.2	21.2	38.5	190
	Mean	15.7	15.9	31.6	203
	S.D.	3.6	3.9	7.0	42

Appendix 8-28

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	4113	278	1.91	18.4	5.6	5.0	10.6	316	0.94
	4114	276	1.94	16.9	10.3	8.1	18.4	256	0.83
	4115	319	1.99	13.4	7.8	7.5	15.3	359	1.02
	4116	229	1.82	13.7	7.8	6.4	14.2	146	0.87
	4117	295	2.04	17.7	5.9	6.1	12.0	352	0.98
	Mean	279	1.94	16.0	7.5	6.6	14.1	286	0.93
	S.D.	33	0.08	2.3	1.9	1.2	3.0	88	0.08
Relative	4113		0.69	6.6	2.0	1.8	3.8	114	0.34
	4114		0.70	6.1	3.7	2.9	6.7	93	0.30
	4115		0.62	4.2	2.4	2.4	4.8	113	0.32
	4116		0.79	6.0	3.4	2.8	6.2	64	0.38
	4117		0.69	6.0	2.0	2.1	4.1	119	0.33
	Mean		0.70	5.8	2.7	2.4	5.1	101	0.33
	S.D.		0.06	0.9	0.8	0.5	1.3	23	0.03

Appendix 8-29

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 1000

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4113	6.64	0.65	0.85	0.90	1.75	41	42	83
	4114	6.36	0.45	0.85	0.86	1.71	31	32	63
	4115	8.16	0.50	1.03	1.01	2.04	22	28	50
	4116	5.81	0.41	0.98	0.93	1.91	41	42	83
	4117	7.87	0.55	1.04	0.97	2.01	34	37	71
	Mean	6.97	0.51	0.95	0.93	1.88	34	36	70
	S.D.	1.01	0.09	0.09	0.06	0.15	8	6	14
Relative	4113	2.39	0.23	0.31	0.32	0.63	15	15	30
	4114	2.30	0.16	0.31	0.31	0.62	11	12	23
	4115	2.56	0.16	0.32	0.32	0.64	7	9	16
	4116	2.54	0.18	0.43	0.41	0.83	18	18	36
	4117	2.67	0.19	0.35	0.33	0.68	12	13	24
	Mean	2.49	0.18	0.34	0.34	0.68	13	13	26
	S.D.	0.15	0.03	0.05	0.04	0.09	4	3	8

Appendix 8-30

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (Satellite group, End of administration)

Dose (mg/kg): 1000

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4113	48.7	51.7	100.4	729
	4114	45.3	39.0	84.3	580
	4115	41.2	56.1	97.3	426
	4116	43.0	49.0	92.0	504
	4117	50.0	50.0	100.0	508
	Mean	45.6	49.2	94.8	549
	S.D.	3.7	6.3	6.8	114
Relative	4113	17.5	18.6	36.1	262
	4114	16.4	14.1	30.5	210
	4115	12.9	17.6	30.5	134
	4116	18.8	21.4	40.2	220
	4117	16.9	16.9	33.9	172
	Mean	16.5	17.7	34.2	200
	S.D.	2.2	2.7	4.1	49

Appendix 8-31

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
	1008	527	2.07	12.9	16.0	13.1	29.1	208	1.54
	1009	526	2.10	14.7	8.3	6.7	15.0	285	1.58
	1010	502	2.24	12.4	9.4	12.7	22.1	250	1.44
Absolute	1011	489	2.10	13.1	6.6	8.4	15.0	317	1.46
	1012	503	2.19	11.9	16.2	12.3	28.5	221	1.44
	Mean	509	2.14	13.0	11.3	10.6	21.9	256	1.49
	S.D.	17	0.07	1.1	4.5	2.9	6.9	45	0.06
	1008		0.39	2.4	3.0	2.5	5.5	39	0.29
	1009		0.40	2.8	1.6	1.3	2.9	54	0.30
	1010		0.45	2.5	1.9	2.5	4.4	50	0.29
Relative	1011		0.43	2.7	1.3	1.7	3.1	65	0.30
	1012		0.44	2.4	3.2	2.4	5.7	44	0.29
	Mean		0.42	2.6	2.2	2.1	4.3	50	0.29
	S.D.		0.03	0.2	0.9	0.5	1.3	10	0.01

Appendix 8-32

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	1008	15.32	0.71	1.72	1.85	3.57	31	35	66
	1009	14.50	0.96	1.49	1.63	3.12	38	38	76
	1010	14.66	0.82	1.78	1.80	3.58	25	28	53
Absolute	1011	11.78	0.77	1.46	1.42	2.88	29	31	60
	1012	12.35	0.83	1.75	1.72	3.47	26	30	56
	Mean	13.72	0.82	1.64	1.68	3.32	30	32	62
	S.D.	1.56	0.09	0.15	0.17	0.31	5	4	9
	1008	2.91	0.13	0.33	0.35	0.68	6	7	13
	1009	2.76	0.18	0.28	0.31	0.59	7	7	14
	1010	2.92	0.16	0.35	0.36	0.71	5	6	11
Relative	1011	2.41	0.16	0.30	0.29	0.59	6	6	12
	1012	2.46	0.17	0.35	0.34	0.69	5	6	11
	Mean	2.69	0.16	0.32	0.33	0.65	6	6	12
	S.D.	0.24	0.02	0.03	0.03	0.06	1	1	1

Appendix 8-33

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
	1008	1.53	1.03	1.59	1.61	3.20	697	673	1370
	1009	1.76	1.44	1.58	1.52	3.10	676	674	1350
	1010	1.42	1.46	1.70	1.74	3.44	680	657	1337
Absolute	1011	2.01	1.46	1.55	1.62	3.17	710	697	1407
	1012	1.91	1.75	1.67	1.65	3.32	760	684	1444
	Mean	1.73	1.43	1.62	1.63	3.25	705	677	1382
	S.D.	0.25	0.26	0.06	0.08	0.13	34	15	44
	1008	0.29	0.20	0.30	0.31	0.61	132	128	260
	1009	0.33	0.27	0.30	0.29	0.59	129	128	257
	1010	0.28	0.29	0.34	0.35	0.69	135	131	266
Relative	1011	0.41	0.30	0.32	0.33	0.65	145	143	288
	1012	0.38	0.35	0.33	0.33	0.66	151	136	287
	Mean	0.34	0.28	0.32	0.32	0.64	138	133	272
	S.D.	0.06	0.05	0.02	0.02	0.04	9	6	15

Appendix 8-34

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	4008	513	2.19	13.2	10.9	9.3	20.2	224	1.36
	4009	570	2.24	13.6	13.8	11.0	24.8	278	1.57
	4010	519	2.06	10.6	11.8	8.7	20.5	269	1.39
	4011	527	2.16	13.4	12.8	14.2	27.0	303	1.64
	4012	491	2.25	12.3	10.5	8.9	19.4	186	1.34
	Mean	524	2.18	12.6	12.0	10.4	22.4	252	1.46
	S.D.	29	0.08	1.2	1.4	2.3	3.3	47	0.14
Relative	4008		0.43	2.6	2.1	1.8	3.9	44	0.27
	4009		0.39	2.4	2.4	1.9	4.4	49	0.28
	4010		0.40	2.0	2.3	1.7	3.9	52	0.27
	4011		0.41	2.5	2.4	2.7	5.1	57	0.31
	4012		0.46	2.5	2.1	1.8	4.0	38	0.27
	Mean		0.42	2.4	2.3	2.0	4.3	48	0.28
	S.D.		0.03	0.2	0.2	0.4	0.5	7	0.02

Appendix 8-35

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 1000

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
Absolute	4008	12.70	0.68	1.69	1.65	3.34	37	40	77
	4009	13.86	0.88	1.69	1.82	3.51	32	35	67
	4010	12.69	0.79	1.55	1.76	3.31	27	31	58
	4011	13.67	0.94	1.54	1.66	3.20	34	39	73
	4012	11.14	0.65	1.53	1.49	3.02	30	31	61
	Mean	12.81	0.79	1.60	1.68	3.28	32	35	67
	S.D.	1.08	0.12	0.08	0.13	0.18	4	4	8
Relative	4008	2.48	0.13	0.33	0.32	0.65	7	8	15
	4009	2.43	0.15	0.30	0.32	0.62	6	6	12
	4010	2.45	0.15	0.30	0.34	0.64	5	6	11
	4011	2.59	0.18	0.29	0.31	0.61	6	7	14
	4012	2.27	0.13	0.31	0.30	0.62	6	6	12
	Mean	2.44	0.15	0.31	0.32	0.63	6	7	13
	S.D.	0.12	0.02	0.02	0.01	0.02	1	1	2

Appendix 8-36

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of male rats (End of recovery)

Dose (mg/kg): 1000

	Animal number	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)
Absolute	4008	1.75	1.71	1.75	1.72	3.47	680	648	1328
	4009	2.12	1.55	1.64	1.71	3.35	670	690	1360
	4010	1.89	1.33	1.62	1.62	3.24	647	609	1256
	4011	1.98	1.56	1.80	1.76	3.56	644	663	1307
	4012	1.51	1.08	1.63	1.62	3.25	633	648	1281
	Mean	1.85	1.45	1.69	1.69	3.37	655	652	1306
	S.D.	0.23	0.25	0.08	0.06	0.14	19	29	40
Relative	4008	0.34	0.33	0.34	0.34	0.68	133	126	259
	4009	0.37	0.27	0.29	0.30	0.59	118	121	239
	4010	0.36	0.26	0.31	0.31	0.62	125	117	242
	4011	0.38	0.30	0.34	0.33	0.68	122	126	248
	4012	0.31	0.22	0.33	0.33	0.66	129	132	261
	Mean	0.35	0.28	0.32	0.32	0.65	125	124	250
	S.D.	0.03	0.04	0.02	0.02	0.04	6	6	10

Appendix 8-37

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	1118	321	1.98	21.2	10.1	8.6	18.7	335	1.00
	1119	316	1.91	15.6	8.6	7.8	16.4	275	0.96
	1120	306	1.99	17.2	6.9	6.2	13.1	204	0.94
	1121	285	1.87	15.8	6.2	4.9	11.1	222	0.86
	1122	310	1.98	18.5	7.5	8.6	16.1	387	0.97
	Mean	308	1.95	17.7	7.9	7.2	15.1	285	0.95
	S.D.	14	0.05	2.3	1.5	1.6	3.0	77	0.05
Relative	1118		0.62	6.6	3.1	2.7	5.8	104	0.31
	1119		0.60	4.9	2.7	2.5	5.2	87	0.30
	1120		0.65	5.6	2.3	2.0	4.3	67	0.31
	1121		0.66	5.5	2.2	1.7	3.9	78	0.30
	1122		0.64	6.0	2.4	2.8	5.2	125	0.31
	Mean		0.63	5.7	2.5	2.3	4.9	92	0.31
	S.D.		0.02	0.6	0.4	0.5	0.8	23	0.01

Appendix 8-38

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	1118	8.98	0.50	0.94	1.01	1.95	32	34	66
	1119	8.62	0.62	1.08	0.95	2.03	26	28	54
	1120	7.12	0.53	0.98	0.99	1.97	38	40	78
Absolute	1121	7.14	0.52	0.88	0.85	1.73	28	27	55
	1122	7.27	0.67	1.03	1.01	2.04	34	40	74
	Mean	7.83	0.57	0.98	0.96	1.94	32	34	65
	S.D.	0.90	0.07	0.08	0.07	0.13	5	6	11
	1118	2.80	0.16	0.29	0.31	0.61	10	11	21
	1119	2.73	0.20	0.34	0.30	0.64	8	9	17
	1120	2.33	0.17	0.32	0.32	0.64	12	13	25
Relative	1121	2.51	0.18	0.31	0.30	0.61	10	9	19
	1122	2.35	0.22	0.33	0.33	0.66	11	13	24
	Mean	2.54	0.19	0.32	0.31	0.63	10	11	21
	S.D.	0.21	0.02	0.02	0.01	0.02	1	2	3

Appendix 8-39

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 0

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1118	46.7	44.1	90.8	689
	1119	51.3	56.5	107.8	524
	1120	49.4	37.0	86.4	415
	1121	37.4	39.9	77.3	673
	1122	63.2	74.5	137.7	457
	Mean	49.6	50.4	100.0	552
	S.D.	9.3	15.4	23.8	124
Relative	1118	14.5	13.7	28.3	215
	1119	16.2	17.9	34.1	166
	1120	16.1	12.1	28.2	136
	1121	13.1	14.0	27.1	236
	1122	20.4	24.0	44.4	147
	Mean	16.1	16.3	32.4	180
	S.D.	2.7	4.8	7.2	44

Appendix 8-40

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 1000

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)
Absolute	4118	280	2.02	18.2	8.0	6.5	14.5	265	0.94
	4119	316	1.94	19.5	4.8	6.7	11.5	406	0.92
	4120	270	1.93	15.0	5.5	7.7	13.2	304	0.86
	4121	317	1.99	21.5	7.7	7.4	15.1	331	1.03
	4122	263	1.99	12.9	6.1	4.9	11.0	230	0.89
	Mean	289	1.97	17.4	6.4	6.6	13.1	307	0.93
	S.D.	26	0.04	3.5	1.4	1.1	1.8	67	0.06
Relative	4118		0.72	6.5	2.9	2.3	5.2	95	0.34
	4119		0.61	6.2	1.5	2.1	3.6	128	0.29
	4120		0.71	5.6	2.0	2.9	4.9	113	0.32
	4121		0.63	6.8	2.4	2.3	4.8	104	0.32
	4122		0.76	4.9	2.3	1.9	4.2	87	0.34
	Mean		0.69	6.0	2.2	2.3	4.5	105	0.32
	S.D.		0.06	0.8	0.5	0.4	0.6	16	0.02

Appendix 8-41

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 1000

	Animal number	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)
	4118	6.76	0.55	0.95	0.90	1.85	35	36	71
	4119	7.54	0.48	0.97	0.96	1.93	30	33	63
	4120	6.28	0.47	0.96	0.95	1.91	31	31	62
Absolute	4121	8.07	0.51	1.04	1.04	2.08	50	53	103
	4122	6.52	0.46	1.02	0.96	1.98	29	30	59
	Mean	7.03	0.49	0.99	0.96	1.95	35	37	72
	S.D.	0.75	0.04	0.04	0.05	0.09	9	9	18
	4118	2.41	0.20	0.34	0.32	0.66	13	13	25
	4119	2.39	0.15	0.31	0.30	0.61	9	10	20
	4120	2.33	0.17	0.36	0.35	0.71	11	11	23
Relative	4121	2.55	0.16	0.33	0.33	0.66	16	17	32
	4122	2.48	0.17	0.39	0.37	0.75	11	11	22
	Mean	2.43	0.17	0.35	0.33	0.68	12	12	24
	S.D.	0.08	0.02	0.03	0.03	0.05	3	3	5

Appendix 8-42

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual organ weight of female rats (End of recovery)

Dose (mg/kg): 1000

	Animal number	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4118	47.3	42.8	90.1	700
	4119	44.7	44.1	88.8	596
	4120	38.2	37.4	75.6	453
	4121	35.6	33.7	69.3	686
	4122	42.4	41.8	84.2	486
	Mean	41.6	40.0	81.6	584
	S.D.	4.8	4.3	8.9	113
Relative	4118	16.9	15.3	32.2	250
	4119	14.1	14.0	28.1	189
	4120	14.1	13.9	28.0	168
	4121	11.2	10.6	21.9	216
	4122	16.1	15.9	32.0	185
	Mean	14.5	13.9	28.4	202
	S.D.	2.2	2.1	4.2	32

Appendix 9-1(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch) Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus Trachea, Thyroid, Urinary bladder

Appendix 9-2(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal
Testis	Atrophy,seminiferous tubular: minimal, bilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-3(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Testis	Atrophy,seminiferous tubular: minimal, bilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-4(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,foamy cell: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-5(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Prostate, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-6(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-7(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-8(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-9(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1mm
Other tissues	Not remarkable

Histopathology:

Testis	Atrophy,seminiferous tubular: minimal, unilateral

Following tissues : Not remarkable

Epididymis

Appendix 9-10(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-11(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1011 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-12(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1012 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-13(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2001 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-14(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2002 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-15(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2003 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-16(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2004 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-17(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2005 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-18(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2006 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-19(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2007 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-20(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2008 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-21(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2009 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-22(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2010 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-23(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2011 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-24(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2012 Male 100 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-25(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3001 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-26(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3002 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-27(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3003 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-28(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3004 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-29(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3005 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-30(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3006 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-31(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3007 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-32(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3008 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-33(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3009 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-34(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3010 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-35(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3011 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-36(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3012 Male 300 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-37(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4001 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-38(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4002 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-39(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4003 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-40(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4004 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration: minimal, mononuclear
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Prostate, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-41(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4005 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, lymphocytic ventral
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-42(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4006 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-43(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4007 Male 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-44(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4008 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-45(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4009 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-46(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4010 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-47(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4011 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-48(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4012 Male 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Epididymis, Testis

Appendix 9-49(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-50(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-51(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-52(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 44 End of administration (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-53(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-54(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-55(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-56(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-57(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-58(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-59(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-60(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-61(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1113 Female 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-62(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1114 Female 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-63(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1115 Female 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Urinary cast,hyaline: minimal Cell infiltration: minimal, lymphocytic interstitial
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-64(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1116 Female 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Hyperplasia,transitional,focal: mild
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-65(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1117 Female 0 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-66(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1118 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x2mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-67(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1119 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-68(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1120 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-69(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1121 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x2mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-70(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 1122 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-71(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2101 Female 100 mg/kg Day 46 End of administration (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 2 present 5x2mm, 4x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-72(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2102 Female 100 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-73(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2103 Female 100 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-74(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2104 Female 100 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-75(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2105 Female 100 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-76(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2106 Female 100 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-77(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2107 Female 100 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-78(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2108 Female 100 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-79(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2109 Female 100 mg/kg Day 45 End of administration (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 2 present 2x1mm, 1x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-80(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2110 Female 100 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-81(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2111 Female 100 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-82(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 2112 Female 100 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-83(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3101 Female 300 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-84(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3102 Female 300 mg/kg Day 47 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-85(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3103 Female 300 mg/kg Day 45 End of administration (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 4x2mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-86(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3104 Female 300 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-87(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3105 Female 300 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-88(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3106 Female 300 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-89(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3107 Female 300 mg/kg Day 42 End of administration (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-90(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3108 Female 300 mg/kg Day 42 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-91(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3109 Female 300 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-92(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3110 Female 300 mg/kg Day 42 End of administration (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-93(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3111 Female 300 mg/kg Day 41 Undelivered

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,foamy cell: minimal
Spleen	Hematopoiesis,extramedullary: minimal
Skeletal muscle,femoral	Degeneration,muscular: minimal
Vagina	Degeneration,mucinous,mucosal: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus

Appendix 9-94(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 3112 Female 300 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-95(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4101 Female 1000 mg/kg Day 44 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-96(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4102 Female 1000 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-97(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4103 Female 1000 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-98(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4104 Female 1000 mg/kg Day 42 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-99(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4105 Female 1000 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-100(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4106 Female 1000 mg/kg Day 42 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-101(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4107 Female 1000 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-102(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4108 Female 1000 mg/kg Day 45 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-103(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4109 Female 1000 mg/kg Day 42 End of administration (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal
Stomach	Erosion,glandular stomach: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-104(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4110 Female 1000 mg/kg Day 46 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-105(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4111 Female 1000 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Fibrosis,myocardial: minimal
Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-106(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4112 Female 1000 mg/kg Day 43 End of administration (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-107(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4113 Female 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-108(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4114 Female 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-109(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4115 Female 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-110(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4116 Female 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Cell infiltration: minimal, lymphocytic interstitial
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-111(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4117 Female 1000 mg/kg Day 43 End of administration (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-112(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4118 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-113(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4119 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-114(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4120 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-115(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4121 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-116(1/1) A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administration in rats

Individual gross and histopathological findings

Animal No. 4122 Female 1000 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 10-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 0

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
1101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
1102	M	D	D	D	D	D	D	D	D	D	D	D	D	D	D	0	-
1103	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
1104	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
1106	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
1107	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1108	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
1109	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
1110	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
1111	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
1112	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
Mean																3.6	4.0
S.D.																1.2	0.0

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 10-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 100

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
2101	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
2102	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
2103	D	P	E	E	M	D	P	E	E	M	D	P	E	M	D	3	5.0
2104	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
2105	M	D	P	E	M	D	P	E	E	M	D	P	E	E	M	3	4.5
2106	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
2107	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
2108	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
2109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
2110	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
2111	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
2112	M	D	P	E	M	D	D	P	E	M	D	P	E	M	D	3	4.5
Mean																3.6	4.2
S.D.																0.5	0.3

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 10-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 300

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
3101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
3102	M	D	P	E	E	M	D	P	E	E	M	D	P	E	E	3	5.0
3103	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
3104	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
3105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0
3106	M	D	P	E	M	D	P	E	M	D	D	P	E	M	D	3	4.5
3107	E	M	D	P	E	E	M	D	P	E	E	M	D	D	P	3	4.5
3108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
3109	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
3110	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
3111	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
3112	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
Mean																3.3	4.2
S.D.																0.5	0.3

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 10-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual estrous cycle in female rats during the pre-mating period

Dose (mg/kg): 1000

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles
4101	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0
4102	M	D	P	E	M	D	P	E	E	M	D	P	E	E	M	3	4.5
4103	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4104	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4105	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4106	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4107	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4108	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4109	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4110	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0
4111	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
4112	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0
Mean																3.5	4.0
S.D.																0.5	0.1

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling

Appendix 11-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual mating and fertility of animals

Dose (mg/kg): 0

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
1001	1101	C	1	P
1002	1102	C	2	P
1003	1103	C	4	P
1004	1104	C	2	P
1005	1105	C	3	P
1006	1106	C	4	P
1007	1107	C	2	P
1008	1108	C	4	P
1009	1109	C	4	P
1010	1110	C	4	P
1011	1111	C	2	P
1012	1112	C	4	P

C: Copulated P: Pregnant

Appendix 11-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual mating and fertility of animals

Dose (mg/kg): 100

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
2001	2101	C	4	P
2002	2102	C	3	P
2003	2103	C	2	P
2004	2104	C	4	P
2005	2105	C	4	P
2006	2106	C	4	P
2007	2107	C	1	P
2008	2108	C	3	P
2009	2109	C	3	P
2010	2110	C	1	P
2011	2111	C	2	P
2012	2112	C	2	P

C: Copulated P: Pregnant

Appendix 11-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual mating and fertility of animals

Dose (mg/kg): 300

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
3001	3101	C	1	P
3002	3102	C	5	P
3003	3103	C	4	P
3004	3104	C	1	P
3005	3105	C	3	P
3006	3106	C	2	P
3007	3107	C	1	P
3008	3108	C	1	P
3009	3109	C	1	P
3010	3110	C	1	P
3011	3111	C	1	NP
3012	3112	C	2	P

C: Copulated P: Pregnant NP: Non-pregnant

Appendix 11-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual mating and fertility of animals

Dose (mg/kg): 1000

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
4001	4101	C	2	P
4002	4102	C	3	P
4003	4103	C	4	P
4004	4104	C	1	P
4005	4105	C	4	P
4006	4106	C	1	P
4007	4107	C	4	P
4008	4108	C	4	P
4009	4109	C	1	P
4010	4110	C	4	P
4011	4111	C	1	P
4012	4112	C	1	P

C: Copulated P: Pregnant

Appendix 12-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Delivery data on dams

Dose (mg/kg): 0

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	No. of stillborns (%)b)	No. of liveborns	External c) abnor-malities(%)d)	Live birth index % e)
1101	22	14	14	100.0	0(0.0)	14	0(0.0)	100.0
1102	22	20	16	80.0	0(0.0)	15	0(0.0)	93.8
1103	21	16	16	100.0	0(0.0)	12	0(0.0)	75.0
1104	22	16	16	100.0	0(0.0)	15	0(0.0)	93.8
1105	21	20	19	95.0	0(0.0)	17	0(0.0)	89.5
1106	22	17	17	100.0	1(5.9)	16	0(0.0)	94.1
1107	22	13	13	100.0	0(0.0)	13	0(0.0)	100.0
1108	22	17	17	100.0	0(0.0)	13	0(0.0)	76.5
1109	21	19	19	100.0	0(0.0)	17	0(0.0)	89.5
1110	21	17	17	100.0	0(0.0)	17	0(0.0)	100.0
1111	22	14	14	100.0	0(0.0)	14	0(0.0)	100.0
1112	22	15	15	100.0	1(7.1)	13	0(0.0)	86.7
Total		198	193		2	176	0	
Mean	21.7	16.5	16.1	97.9	(1.1)	14.7	(0.0)	91.6
S.D.	0.5	2.3	1.9	5.8	(2.5)	1.8	(0.0)	8.7

a): (No. of implantation sites / No. of corpora lutea) × 100
b): (No. of stillborns / No. of liveborns and stillborns) × 100
c): No. of delivered pups with external abnormalities
d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100
e): (No. of liveborns / No. of implantation sites) × 100

Appendix 12-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Delivery data on dams

Dose (mg/kg): 100

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	No. of stillborns (%)b)	No. of liveborns	External c) abnor-malities(%)d)	Live birth index % e)
2101	22	15	14	93.3	0(0.0)	12	0(0.0)	85.7
2102	22	18	18	100.0	0(0.0)	15	0(0.0)	83.3
2103	22	15	15	100.0	0(0.0)	15	0(0.0)	100.0
2104	21	16	14	87.5	0(0.0)	14	0(0.0)	100.0
2105	21	16	15	93.8	0(0.0)	14	0(0.0)	93.3
2106	22	14	14	100.0	0(0.0)	14	0(0.0)	100.0
2107	22	16	15	93.8	0(0.0)	8	0(0.0)	53.3
2108	22	18	16	88.9	0(0.0)	15	0(0.0)	93.8
2109	22	17	17	100.0	0(0.0)	16	0(0.0)	94.1
2110	22	16	15	93.8	0(0.0)	12	0(0.0)	80.0
2111	21	15	13	86.7	0(0.0)	10	0(0.0)	76.9
2112	22	14	14	100.0	0(0.0)	14	0(0.0)	100.0
Total		190	180		0	159	0	
Mean	21.8	15.8	15.0	94.8	(0.0)	13.3	(0.0)	88.4
S.D.	0.5	1.3	1.4	5.2	(0.0)	2.3	(0.0)	13.8

a): (No. of implantation sites / No. of corpora lutea) × 100
b): (No. of stillborns / No. of liveborns and stillborns) × 100
c): No. of delivered pups with external abnormalities
d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100
e): (No. of liveborns / No. of implantation sites) × 100

Appendix 12-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Delivery data on dams

Dose (mg/kg): 300

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	No. of stillborns (%)b)	No. of liveborns	External c) abnor-malities(%)d)	Live birth index % e)
3101	22	16	15	93.8	0(0.0)	13	0(0.0)	86.7
3102	22	17	14	82.4	0(0.0)	13	0(0.0)	92.9
3103	21	15	15	100.0	0(0.0)	15	0(0.0)	100.0
3104	22	15	14	93.3	0(0.0)	13	0(0.0)	92.9
3105	22	19	17	89.5	0(0.0)	16	0(0.0)	94.1
3106	22	14	14	100.0	0(0.0)	12	0(0.0)	85.7
3107	21	19	19	100.0	0(0.0)	19	0(0.0)	100.0
3108	21	18	17	94.4	0(0.0)	16	0(0.0)	94.1
3109	22	15	14	93.3	0(0.0)	11	0(0.0)	78.6
3110	21	14	14	100.0	0(0.0)	13	0(0.0)	92.9
3111	Non-pregnant							
3112	21	19	19	100.0	0(0.0)	18	0(0.0)	94.7
Total		181	172		0	159	0	
Mean	21.5	16.5	15.6	95.2	(0.0)	14.5	(0.0)	92.1
S.D.	0.5	2.0	2.0	5.7	(0.0)	2.5	(0.0)	6.3

a): (No. of implantation sites / No. of corpora lutea) × 100
b): (No. of stillborns / No. of liveborns and stillborns) × 100
c): No. of delivered pups with external abnormalities
d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100
e): (No. of liveborns / No. of implantation sites) × 100

Appendix 12-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Delivery data on dams

Dose (mg/kg): 1000

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	No. of stillborns (%)b)	No. of liveborns	External c) abnor-malities(%)d)	Live birth index % e)
4101	22	16	15	93.8	0(0.0)	15	0(0.0)	100.0
4102	22	16	16	100.0	0(0.0)	15	0(0.0)	93.8
4103	22	14	13	92.9	0(0.0)	13	0(0.0)	100.0
4104	21	18	17	94.4	0(0.0)	15	0(0.0)	88.2
4105	22	16	15	93.8	0(0.0)	15	0(0.0)	100.0
4106	21	16	15	93.8	0(0.0)	14	0(0.0)	93.3
4107	21	14	14	100.0	0(0.0)	14	0(0.0)	100.0
4108	21	15	15	100.0	0(0.0)	15	0(0.0)	100.0
4109	21	16	16	100.0	0(0.0)	16	0(0.0)	100.0
4110	22	17	17	100.0	0(0.0)	16	0(0.0)	94.1
4111	22	19	16	84.2	0(0.0)	16	0(0.0)	100.0
4112	22	16	16	100.0	0(0.0)	16	0(0.0)	100.0
Total		193	185		0	180	0	
Mean	21.6	16.1	15.4	96.1	(0.0)	15.0	(0.0)	97.5
S.D.	0.5	1.4	1.2	4.9	(0.0)	1.0	(0.0)	4.0

a): (No. of implantation sites / No. of corpora lutea) × 100
b): (No. of stillborns / No. of liveborns and stillborns) × 100
c): No. of delivered pups with external abnormalities
d): (No. of delivered pups with external abnormalities / No. of liveborns and stillborns) × 100
e): (No. of liveborns / No. of implantation sites) × 100

Appendix 13-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual viability index of pups

Dose (mg/kg): 0

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
1101	14	14	100.0
1102	15	15	100.0
1103	12	12	100.0
1104	15	15	100.0
1105	17	17	100.0
1106	16	16	100.0
1107	13	13	100.0
1108	13	13	100.0
1109	17	17	100.0
1110	17	16	94.1
1111	14	14	100.0
1112	13	13	100.0
Total	176	175	
Mean	14.7	14.6	99.5
S.D.	1.8	1.7	1.7

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100

Appendix 13-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual viability index of pups

Dose (mg/kg): 100

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
2101	12	12	100.0
2102	15	15	100.0
2103	15	14	93.3
2104	14	14	100.0
2105	14	14	100.0
2106	14	14	100.0
2107	8	8	100.0
2108	15	15	100.0
2109	16	16	100.0
2110	12	12	100.0
2111	10	9	90.0
2112	14	14	100.0
Total	159	157	
Mean	13.3	13.1	98.6
S.D.	2.3	2.4	3.3

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100

Appendix 13-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual viability index of pups

Dose (mg/kg): 300

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
3101	13	13	100.0
3102	13	13	100.0
3103	15	15	100.0
3104	13	13	100.0
3105	16	16	100.0
3106	12	12	100.0
3107	19	15	78.9
3108	16	16	100.0
3109	11	11	100.0
3110	13	13	100.0
3111	Non-pregnant		
3112	18	18	100.0
Total	159	155	
Mean	14.5	14.1	98.1
S.D.	2.5	2.1	6.4

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100

Appendix 13-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual viability index of pups

Dose (mg/kg): 1000

Dam number	No. of live pups		Viability index on postnatal day 4 % a)
	Day 0	Day 4	
4101	15	15	100.0
4102	15	15	100.0
4103	13	12	92.3
4104	15	15	100.0
4105	15	15	100.0
4106	14	11	78.6
4107	14	11	78.6
4108	15	15	100.0
4109	16	16	100.0
4110	16	15	93.8
4111	16	16	100.0
4112	16	15	93.8
Total	180	171	
Mean	15.0	14.3	94.8
S.D.	1.0	1.8	8.1

a): (No. of live pups on postnatal day 4 / No. of liveborns) × 100

Appendix 14-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual sex ratio of pups

Dose (mg/kg): 0

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
1101	6	8	0.43	6	8	0.43
1102	4	11	0.27	4	11	0.27
1103	8	4	0.67	8	4	0.67
1104	6	9	0.40	6	9	0.40
1105	10	7	0.59	10	7	0.59
1106	8	8	0.50	8	8	0.50
1107	8	5	0.62	8	5	0.62
1108	6	7	0.46	6	7	0.46
1109	9	8	0.53	9	8	0.53
1110	10	7	0.59	10	6	0.63
1111	8	6	0.57	8	6	0.57
1112	5	8	0.38	5	8	0.38
Total	88	88		88	87	
Mean	7.3	7.3	0.50	7.3	7.3	0.50
S.D.	1.9	1.8	0.12	1.9	1.9	0.12

a): No. of liveborn males / No. of liveborns
b): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual sex ratio of pups

Dose (mg/kg): 100

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
2101	6	6	0.50	6	6	0.50
2102	8	7	0.53	8	7	0.53
2103	5	10	0.33	5	9	0.36
2104	7	7	0.50	7	7	0.50
2105	7	7	0.50	7	7	0.50
2106	7	7	0.50	7	7	0.50
2107	5	3	0.63	5	3	0.63
2108	5	10	0.33	5	10	0.33
2109	9	7	0.56	9	7	0.56
2110	7	5	0.58	7	5	0.58
2111	7	3	0.70	7	2	0.78
2112	9	5	0.64	9	5	0.64
Total	82	77		82	75	
Mean	6.8	6.4	0.53	6.8	6.3	0.53
S.D.	1.4	2.2	0.11	1.4	2.3	0.12

a): No. of liveborn males / No. of liveborns
b): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual sex ratio of pups

Dose (mg/kg): 300

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
3101	5	8	0.38	5	8	0.38
3102	6	7	0.46	6	7	0.46
3103	10	5	0.67	10	5	0.67
3104	5	8	0.38	5	8	0.38
3105	8	8	0.50	8	8	0.50
3106	8	4	0.67	8	4	0.67
3107	6	13	0.32	5	10	0.33
3108	9	7	0.56	9	7	0.56
3109	8	3	0.73	8	3	0.73
3110	4	9	0.31	4	9	0.31
3111	Non-pregnant					
3112	9	9	0.50	9	9	0.50
Total	78	81		77	78	
Mean	7.1	7.4	0.50	7.0	7.1	0.50
S.D.	2.0	2.7	0.15	2.0	2.2	0.14

a): No. of liveborn males / No. of liveborns
b): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual sex ratio of pups

Dose (mg/kg): 1000

Dam number	Liveborns		Sex ratio of liveborns at birth a)	Postnatal day 4		Sex ratio of live pups on day 4 b)
	No. of males	No. of females		No. of males	No. of females	
4101	9	6	0.60	9	6	0.60
4102	9	6	0.60	9	6	0.60
4103	4	9	0.31	4	8	0.33
4104	10	5	0.67	10	5	0.67
4105	9	6	0.60	9	6	0.60
4106	6	8	0.43	5	6	0.45
4107	8	6	0.57	5	6	0.45
4108	9	6	0.60	9	6	0.60
4109	11	5	0.69	11	5	0.69
4110	7	9	0.44	7	8	0.47
4111	11	5	0.69	11	5	0.69
4112	8	8	0.50	7	8	0.47
Total	101	79		96	75	
Mean	8.4	6.6	0.56	8.0	6.3	0.55
S.D.	2.0	1.5	0.12	2.4	1.1	0.11

a): No. of liveborn males / No. of liveborns
b): No. of live males on day 4 / No. of live pups on day 4

Appendix 15-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of pups

Dose (mg/kg): 0

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
1101	6.9	10.8	3.9	6.4	10.2	3.8
1102	6.5	9.6	3.1	6.4	9.4	3.0
1103	5.8	8.3	2.5	5.5	8.1	2.6
1104	6.1	9.6	3.5	6.0	9.3	3.3
1105	5.7	7.9	2.2	5.2	7.2	2.0
1106	6.7	9.9	3.2	6.2	9.1	2.9
1107	6.6	10.0	3.4	6.2	9.3	3.1
1108	7.5	11.0	3.5	6.8	10.0	3.2
1109	5.9	8.2	2.3	5.5	7.5	2.0
1110	6.2	9.0	2.8	5.8	8.5	2.7
1111	6.8	10.2	3.4	6.7	9.9	3.2
1112	7.0	11.4	4.4	5.8	9.2	3.4
Mean	6.5	9.7	3.2	6.0	9.0	2.9
S.D.	0.5	1.1	0.7	0.5	1.0	0.5

Unit: g
a): Postnatal day

Appendix 15-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of pups

Dose (mg/kg): 100

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
2101	6.7	11.1	4.4	6.3	10.7	4.4
2102	6.8	9.5	2.7	6.5	9.1	2.6
2103	6.7	9.8	3.1	6.4	9.7	3.3
2104	6.2	8.8	2.6	5.9	8.2	2.3
2105	6.0	8.4	2.4	5.7	8.2	2.5
2106	6.5	9.8	3.3	6.1	9.7	3.6
2107	8.0	11.4	3.4	7.4	11.0	3.6
2108	6.4	9.4	3.0	6.2	9.2	3.0
2109	6.8	10.0	3.2	6.5	9.6	3.1
2110	7.7	12.4	4.7	7.0	10.9	3.9
2111	6.4	11.4	5.0	5.3	10.1	4.8
2112	6.6	9.3	2.7	6.2	9.0	2.8
Mean	6.7	10.1	3.4	6.3	9.6	3.3
S.D.	0.6	1.2	0.9	0.6	0.9	0.8

Unit: g
a): Postnatal day

Appendix 15-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of pups

Dose (mg/kg): 300

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
3101	6.4	10.6	4.2	5.9	9.4	3.5
3102	6.6	10.5	3.9	6.2	10.3	4.1
3103	6.0	7.9	1.9	5.8	7.6	1.8
3104	7.8	11.9	4.1	7.3	11.2	3.9
3105	6.8	9.8	3.0	6.5	9.1	2.6
3106	7.5	10.6	3.1	7.1	9.8	2.7
3107	5.8	7.9	2.1	5.4	7.5	2.1
3108	6.0	9.6	3.6	6.0	9.1	3.1
3109	6.9	11.6	4.7	6.6	11.3	4.7
3110	5.8	9.1	3.3	5.6	8.5	2.9
3111	Non-pregnant					
3112	6.0	8.2	2.2	5.8	7.8	2.0
Mean	6.5	9.8	3.3	6.2	9.2	3.0
S.D.	0.7	1.4	0.9	0.6	1.3	0.9

Unit: g
a): Postnatal day

Appendix 15-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual body weight of pups

Dose (mg/kg): 1000

Dam number	Male			Female		
	0	4a)	Gain	0	4a)	Gain
4101	6.4	9.9	3.5	6.3	9.3	3.0
4102	6.7	9.7	3.0	6.3	9.4	3.1
4103	7.0	9.3	2.3	6.2	8.0	1.8
4104	6.0	8.6	2.6	5.5	7.8	2.3
4105	6.2	9.2	3.0	6.2	8.4	2.2
4106	6.2	9.8	3.6	5.8	9.0	3.2
4107	6.0	7.2	1.2	5.8	6.2	0.4
4108	6.1	9.2	3.1	5.8	9.0	3.2
4109	6.2	8.7	2.5	5.7	7.2	1.5
4110	7.3	10.9	3.6	6.7	10.6	3.9
4111	6.5	9.5	3.0	6.1	9.3	3.2
4112	6.5	10.3	3.8	6.3	9.3	3.0
Mean	6.4	9.4	2.9	6.1	8.6	2.6
S.D.	0.4	0.9	0.7	0.3	1.2	1.0

Unit: g
a): Postnatal day

Appendix 16-1

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 0

Dam number	No. of pups examined Total (Male + Female)	Findings
1101	14 (6 + 8)	NAF
1102	15 (4 + 11)	NAF
1103	12 (8 + 4)	NAF
1104	15 (6 + 9)	NAF
1105	17 (10 + 7)	NAF
1106	16 (8 + 8)	NAF
1107	13 (8 + 5)	NAF
1108	13 (6 + 7)	NAF
1109	17 (9 + 8)	NAF
1110	16 (10 + 6)	NAF
1111	14 (8 + 6)	NAF
1112	13 (5 + 8)	NAF

NAF: No abnormal findings

Appendix 16-2

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 100

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	12 (6 + 6)	NAF
2102	15 (8 + 7)	NAF
2103	14 (5 + 9)	NAF
2104	14 (7 + 7)	NAF
2105	14 (7 + 7)	NAF
2106	14 (7 + 7)	NAF
2107	8 (5 + 3)	NAF
2108	15 (5 + 10)	NAF
2109	16 (9 + 7)	NAF
2110	12 (7 + 5)	NAF
2111	9 (7 + 2)	NAF
2112	14 (9 + 5)	NAF

NAF: No abnormal findings

Appendix 16-3

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 300

Dam number	No. of pups examined Total (Male + Female)	Findings
3101	13 (5 + 8)	NAF
3102	13 (6 + 7)	NAF
3103	15 (10 + 5)	NAF
3104	13 (5 + 8)	NAF
3105	16 (8 + 8)	NAF
3106	12 (8 + 4)	NAF
3107	15 (5 + 10)	NAF
3108	16 (9 + 7)	NAF
3109	11 (8 + 3)	NAF
3110	13 (4 + 9)	NAF
3111	Non-pregnant	
3112	18 (9 + 9)	NAF

NAF: No abnormal findings

Appendix 16-4

A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of octadecanoic acid, 1,2-ethanediyl ester by oral administraion in rats

Individual externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg): 1000

Dam number	No. of pups examined Total	(Male	+ Female)	Findings
4101	15	9	6	NAF
4102	15	9	6	NAF
4103	12	4	8	NAF
4104	15	10	5	NAF
4105	15	9	6	NAF
4106	11	5	6	NAF
4107	11	5	6	NAF
4108	15	9	6	NAF
4109	16	11	5	NAF
4110	15	7	8	NAF
4111	16	11	5	NAF
4112	15	7	8	NAF

NAF: No abnormal findings