Study No. 502227

# 1,8-ジクロロオクタンのラットを用いる 28 日間反復経口投与毒性試験及び 14 日間回復試験

## 最 終 報 告 書

作成日: 2011年9月13日

株式会社日本バイオリサーチセンター
羽島研究所

# 1. 目次

Tables

Appendices

## 2. 試験責任者陳述書

試験番号：502227

表　題：1,8-ジクロロオクタンのラットを用いる 28 日間反復経口投与毒性試験及び 14 日間回復試験

本試験は，新規化学物質等に係る試験を実施する試験施設に関する基準について (平成 15 年 11 月 21 日，薬食発第 1121003 号，平成 15・11・17 製局第 3 号，環保企発第 031121004 号，平成 20 年 7 月 4 日最終改正) 及び OECD PRINCIPLES OF GOOD LABORATORY PRACTICE (OECD 化学物質の安全性試験の実施に関する基準，1997 年 11 月 26 日) に従って実施したものである．

2011 年 9 月 13 日

株式会社日本バイオリサーチセンター　羽島研究所

試験責任者 [redacted]

## 3. 最終報告書作成者署名

試験番号：502227

表　　題：1,8-ジクロロオクタンのラットを用いる 28 日間反復経口投与毒性試験及び 14 日間回復試験

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試験責任者 [redacted]

## 4. 試験概要

試 験 番 号：502227

表　　題：1,8-ジクロロオクタンのラットを用いる 28 日間反復経口投与毒性試験及び 14 日間回復試験

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一丁目 2 番 2 号

試 験 施 設：株式会社日本バイオリサーチセンター 羽島研究所
〒501-6251 岐阜県羽島市福寿町間島六丁目 104 番地

試 験 目 的 ：1,8-ジクロロオクタンが継続的に人に摂取された場合の健康への影響を推定するために，1,8-ジクロロオクタンを雌雄ラットに 28 日間反復経口投与し，さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性学的影響を検討した.

準拠したガイドライン：
新規化学物質等に係る試験の方法について (平成 15 年 11 月 21 日，薬食発第 1121002 号，平成 15・11・13 製局第 2 号，環保企発第 031121002 号，平成 18 年 11 月 20 日最終改正) 及び OECD Guideline for Testing of Chemicals for Repeated Dose 28-day Oral Toxicity Study in Rodents (407)

遵守した GLP：
新規化学物質等に係る試験を実施する試験施設に関する基準について (平成 15 年 11 月 21 日, 薬食発第 1121003 号, 平成 15・11・17 製局第 3 号, 環保企発第 031121004 号，平成 20 年 7 月 4 日最終改正) 及び OECD PRINCIPLES OF GOOD LABORATORY PRACTICE (OECD 化学物質の安全性試験の実施に関する基準, 1997 年 11 月 26 日)

遵守した動物の福祉に関する法令など：
法律第 105 号 (昭和 48 年 10 月 1 日，平成 18 年 6 月 2 日最終改正)「動物の愛護及び管理に関する法律」，環境省告示第 88 号 (平成 18 年 4 月 28 日)「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」，厚生労働省通知　科発第 0601005 号 (平成 18 年 6 月 1 日)「厚生労働省の所管する実施機関における動物実験等の実施に関する基本指針」及び株式会社日本バイオリサーチセンター「動物実験倫理委員会規則」

本試験は，試験施設の動物実験倫理委員会で審査され，試験施設の運営管理者により承認されたものである．

試験開始日：2008 年 8 月 19 日

試験終了日：2011 年 9 月 13 日

試験実施日：

| | |
|---|---|
| 動物入手日 | 2008 年 8 月 20 日 |
| 雄の群分け日 | 2008 年 9 月 1 日 |
| 実験開始日 (雄の投与開始日) | 2008 年 9 月 2 日 |
| 雌の群分け日 | 2008 年 9 月 4 日 |
| 雌の投与開始日 | 2008 年 9 月 5 日 |
| 雄の投与期間終了日 | 2008 年 9 月 29 日 |
| 雄投与期間終了時の剖検日 | 2008 年 9 月 30 日 |
| 雌の投与期間終了日 | 2008 年 10 月 2 日 |
| 雌投与期間終了時の剖検日 | 2008 年 10 月 3 日 |
| 雄回復期間終了時の剖検日 | 2008 年 10 月 14 日 |
| 雌回復期間終了時の剖検日 | 2008 年 10 月 17 日 |
| 実験終了日 (病理組織所見最終化日) | 2009 年 1 月 9 日 |

資料，標本及び保管すべき被験物質の保管場所：

資料 (試験計画書の原本及びその変更書の原本，生データ，最終報告書の原本)，標本及び保管すべき被験物質は試験施設の資料保存施設に最終報告書提出後 10 年間保管する．その後の処置は，試験委託者と協議の上，決定する．

SOP 及び試験計画書に従わなかったこと：

1) HE 染色組織標本作製において，1000 mg/kg 群の雌 2 例 (No. F04455 及び F04456) では薄切プレパラート上に上皮小体は認められなかった．SOP に従い，それら 2 例について，甲状腺及び上皮小体のパラフィン包埋を再薄切して HE 染色組織標本を作製したが，プレパラート上に上皮小体は認められなかった．しかし，その他の動物の上皮小体で被験物質の毒性評価は十分可能であったことから，試験成績への影響はないと判断した．なお，甲状腺の病理組織学的評価は，初回作製時におけるプレパラートの観察結果を対象とした．
2) 投与期間終了時に 1000 mg/kg 群の雌で腎臓重量の高値がみられたこと，1000 mg/kg 群の雄で腎臓に病理組織学的変化が認められたことから，200 及び 40 mg/kg 群の投与期間終了時及び回復期間終了時の雌の腎臓についても HE 染色組織標本を作製し，病理組織学検査を実施した．被験物質の毒性学的評価をより詳細に確認するためである．

その他に SOP 又は試験計画書に従わなかったことはなかった．

予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態：

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

## 5. 試験従事者及び業務分担

試 験 責 任 者 : [redacted]

試 験 従 事 者 : [redacted]

## 6. 要約

1,8-ジクロロオクタンが継続的に人に摂取された場合の健康への影響を推定するために，1,8-ジクロロオクタンを雌雄ラットに 28 日間反復経口投与し，さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性学的影響を検討した．投与量は，1000 mg/kg を高用量とし，以下，200 及び 40 mg/kg を設定した．媒体にはトウモロコシ油を用い，対照群には被験物質投与群と同容量のトウモロコシ油を投与した．各群の使用動物数は対照群，200 及び 1000 mg/kg 群を雌雄各 12 例とし，各群ともそのうち半数を回復群とした．40 mg/kg 群は雌雄各 6 例とした．

1) 一般状態及び死亡状況

死亡例は，雌では 1000 mg/kg 群で投与 2 日に 1 例に認められたが，前日に一般状態に異常はみられなかった．

雌では，1000 mg/kg 群で口の周囲の汚れ及び下腹部被毛の汚れが 1 例にみられた．なお，雌雄とも，1000 及び 200 mg/kg 群で投与後に一過性の流涎がみられたが，毒性症状とはみなさなかった．

2) 体重，摂餌量及び摂水量

体重は，雄では 1000 mg/kg 群で投与期間の初期に低値がみられたが，雌ではいずれの投与群とも投与に起因する変化は認められなかった．摂餌量は，雌雄とも 1000 mg/kg 群で投与期間の初期に低値，投与期間の後期に高値がみられた．摂水量は，雌雄とも 1000 mg/kg 群でほぼ投与期間を通して高値がみられた．回復期間中には，雌では 1000 mg/kg 群で摂水量の一過性の高値がみられたが，雄では投与に起因する変化は認められなかった．

3) 行動機能 (FOB)，感覚反応，握力及び自発運動量

握力では，雄では 1000 mg/kg 群で前肢及び後肢の握力の低値，200 及び 40 mg/kg 群で後肢の握力の低値がみられたが，雌ではいずれの投与群とも投与に起因する変化は認められなかった．FOB，感覚反応及び自発運動量では，雌雄とも投与に起因する変化はみられなかった．

4) 尿検査，血液学検査及び血液生化学検査

尿検査において，投与期間終了時に雄では 1000 mg/kg 群で摂水量の増加に起因した尿量の高値がみられたが，雌ではいずれの投与群とも投与に起因する変化は認められなかった．回復期間終了時の尿検査では，雌雄とも投与に起因する変化は認められなかった．

血液学検査において，投与期間終了時及び回復期間終了時に雌雄とも投与に起因する変化は認められなかった．

血液生化学検査において，投与期間終了時に雌では 1000 及び 200 mg/kg 群で無機リンの高値，1000 mg/kg 群で総コレステロールの高値がみられたが，雄ではいずれの投与群とも投与に起因する変化は認められなかった．回復期間終了時にも雌では 1000 mg/kg 群で総コレステロールの高値がみられたが，雄では投与に起因する変化は認められなかった．

5) 剖検所見及び器官重量

剖検において，投与期間終了時に雌雄とも 1000 及び 200 mg/kg 群で肝臓の褪色がみられた．回復期間終了時には，雄では 200 mg/kg 群で肝臓の褪色がみられたが，雌では投与に起因する変化は認められなかった．

器官重量において，投与期間終了時に雄では 1000 及び 200 mg/kg 群で肝臓及び腎臓の絶対重量及び相対重量の高値，雌では 1000，200 及び 40 mg/kg 群で肝臓の相対重量の高値，1000 及び 200 mg/kg 群で肝臓の絶対重量の高値，1000 mg/kg 群で腎臓の絶対重量及び相対重量の高値がみられた．回復期間終了時には，雄では 1000 及び 200 mg/kg 群で腎臓の相対重量の高値，雌では 1000 mg/kg 群で肝臓の絶対重量及び相対重量の高値がみられた．

6) 病理組織学検査

投与期間終了時には，雄では肝臓に門脈周囲性の肝細胞腫大，膵臓にチモーゲン顆粒の減少及び腎臓に尿細管上皮の硝子滴が 1000，200 及び 40 mg/kg 群でみられた．雌では，肝臓に門脈周囲性の肝細胞腫大及び膵臓にチモーゲン顆粒の減少が 1000，200 及び 40 mg/kg 群，肝臓に微小肉芽腫が 1000 及び 200 mg/kg 群でみられた．

回復期間終了時には，雄では投与に起因する変化は認められなかった．雌では，肝臓に門脈周囲性の肝細胞腫大及び膵臓にチモーゲン顆粒の減少が 1000 及び 200 mg/kg 群でみられた．

以上のように，1,8-ジクロロオクタンの無影響量は，雄では 40 mg/kg 投与で後肢の握力の低値，肝臓に門脈周囲性の肝細胞腫大，膵臓にチモーゲン顆粒の減少が認められたことから 40 mg/kg/day 未満，雌では 40 mg/kg 投与で肝臓の相対重量の高値及び門脈周囲性の肝細胞腫大，膵臓にチモーゲン顆粒の減少が認められたことから 40 mg/kg/day 未満と考えられる．

## 7. 緒言

1,8-ジクロロオクタンが継続的に人に摂取された場合の健康への影響を推定するために，新規化学物質等に係る試験の方法について (平成 15 年 11 月 21 日, 薬食発第 1121002 号, 平成 15・11・13 製局第 2 号, 環保企発第 031121002 号, 平成 18 年 11 月 20 日最終改正) 及び OECD Guideline for Testing of Chemicals for Repeated Dose 28-day Oral Toxicity Study in Rodents (407) に基づいて 1,8-ジクロロオクタンを雌雄ラットに 28 日間反復経口投与し，さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性学的影響を検討した.

## 8. 方法

### 8.1. 被験物質及び媒体

被験物質 1,8-ジクロロオクタン (英語名称: 1,8-dichlorooctane，CAS No. 2162-99-4，Fig. 1) は，化学式: $Cl(CH_2)_8Cl$，分子量: 183.12，物性・性状: 無色透明液体，引火点: 118℃，発火点: 215℃，比重: 1.0280 である[1]. 当試験には, 東京化成工業株式会社から入手したものを用いた [製造元: 東京化成工業株式会社 (東京都)，Lot No. FGN01，純度 (GC): 99.9%]. 入手後は，被験物質保管室の保管庫に冷蔵・遮光・密閉の条件下で保管した. 被験物質を保管した保管庫 (冷蔵庫: BMS-500F3, 日本フリーザー株式会社) の温度 [設定温度: 4℃ (許容範囲: 2.0～8.0℃; 実測値: 2.1～6.4℃)] に問題はなかった.

投与期間終了後，試験施設で保存する被験物質 (1.0032 g) を除いた残余被験物質は東京化成工業株式会社へ返却した.

当試験の投与期間終了後に実施した試験施設で保管した被験物質 (Lot No. FGN01) の品質試験成績から，使用期間中の安定性が確認された.

媒体には，トウモロコシ油 (以下，Corn oil，Lot No.: V8F7016，使用期限: 2013 年 7 月 14 日，製造元: ナカライテスク株式会社，保管条件: 室温，保管場所: 被験物質保管室の保管庫) を用いた. Corn oil を保管した被験物質保管室の保管庫の温度 [設定温度: 23℃ (許容範囲: 18.0～28.0℃; 実測値: 21.7～24.4℃)] 及び湿度 [設定湿度: 55% (許容範囲: 40.0～70.0%; 実測値: 50.8～64.0%)] に問題はなかった.

### 8.2. 投与検体及び濃度測定

最高濃度の投与検体を調製するために, 1,8-ジクロロオクタンは必要量 (純度による補正は実施しなかった) を秤取 (電子天秤: PM2500，メトラー・トレド株式会社) 後，Corn oil で 200 mg/mL 濃度となるように溶解し，調製した. 40 及び 8 mg/mL 濃度の各投与検体は，200 mg/mL 濃度液を Corn oil で段階希釈して調製した.

調製検体の安定性については，2，20 及び 200 mg/mLの濃度で調製後，冷蔵 (設定温度 4℃，冷蔵庫: BMS-500F3，日本フリーザー株式会社)・遮光 8 日間とその後，室温 (設定温度: 23℃)・遮光で 6 時間まで問題がないことが確認されている[2](Attachment 1). 従って，各投与検体は，ディスポーザブルポリプロピレン製容器に 1 日分ごとに小分け後，冷蔵 (冷蔵庫: BMS-500F3，日本フ

リーザー株式会社)・遮光の条件下で保管し，調製後 7 日以内に使用した。各投与検体を保管した冷蔵庫の温度 [設定温度: 4°C (許容範囲: 2.0～8.0°C; 実測値: 3.4～5.8°C)] に問題はなかった。保管した各投与検体は，冷蔵庫から持ち出し後 5 時間 6 分以内に使用した。

雄投与開始日 (投与 1 日) 及び雌投与終了日に使用した各投与検体中の被験物質濃度をガスクロマトグラフ (GC-2010，株式会社島津製作所) で測定した．その結果，被験物質濃度は表示濃度の 95.2～102.9%であり，規定値 (100 ± 10%) の範囲内であった (Attachments 2 及び 3).

## 8.3. 試験動物及び飼育条件

### 8.3.1. 動物種及び系統

試験には，毒性試験に一般的に用いられている動物種で，その系統維持が明らかである Crl:CD (SD) 雌雄ラット (SPF) を用いた．動物は，2008 年 8 月 20 日に日本チャールス・リバー株式会社 日野飼育センターから 4 週齢で雌雄各 52 匹を入手した．入手後 1 日の体重範囲は，雄が 83～93 g，雌が 63～77 g であった．

### 8.3.2. 検疫及び馴化，群分け並びに個体識別

入手した動物には，検疫期間 (2008 年 8 月 20 日～25 日) と馴化期間 (雄: 2008 年 8 月 26 日～2008 年 9 月 1 日，雌: 2008 年 8 月 26 日～2008 年 9 月 4 日) を設け，この間に一般状態の観察を 1 日 1 回，体重測定 (電子天秤: PG2002-S，メトラー・トレド株式会社) を雄は 3 回と雌は 4 回，行動機能 (FOB) 観察を 1 回行った．検疫・馴化期間中の一般状態及び体重推移に異常が認められなかった動物を群分けした (Attachments 4-1～4-3，5-1～5-3，6-1～6-3 及び 7-1～7-3).

投与開始前日にコンピュータを用いて体重を層別に分けた後に無作為抽出法により各群の平均体重及び分散がほぼ等しくなるように群分けした．但し，個々の動物の体重が平均値の ±20% 以内であるものを選んで群分けした．群分け日の体重範囲は，雄が 172～205 g，雌が 135～173 g であった．群分け残余雄のうち，検疫・馴化動物番号の若い順に 2 匹を雌の回復期間終了日に実施した微生物モニタリング検査用動物とした．微生物モニタリング検査において，感染を示唆するような異常はみられなかった．群分け残余雄のうち微生物モニタリング検査に用いなかった雄及び群分け残余雌は，群分け日にジエチルエーテルによる麻酔下で腹大動脈から放血して安楽死させた．

動物の個体識別は，動物入手日に黒色油性インクを用いて尾へ検疫・馴化動物番号 (下 3 桁) を記入して行った．

動物の検疫・馴化期間中の各ケージには試験番号，入手年月日及び検疫・馴化動物番号を記入したラベルを，群分け後の各ケージには試験番号，投与量，検疫・馴化動物番号及び動物番号を記入し，群ごとに色分けしたラベルをそれぞれ取り付けた．なお，FOB 観察は Blind で検査するため，試験番号及び検疫・馴化動物番号を記入したラベルを取り付けた．

### 8.3.3. 環境条件及び飼育管理

動物は，設定温度: 23°C，設定湿度: 55%，明暗各 12 時間 (照明: 午前 6 時～午後 6 時)，換気回数 12 回/時 (中性能フィルターを通した新鮮空気) に維持された動物飼育室 (E 棟 5 号室) で飼育

した．動物飼育室の温度 (許容範囲: 20.0～26.0°C; 実測値: 21.6～22.8°C) 及び湿度 (許容範囲: 40.0～70.0%; 実測値: 42.5～59.4%) に問題はなかった．

動物は，検疫・馴化期間中はステンレス製懸垂式ケージ (W: 240 × D: 380 × H: 200 mm) を用いて 1 ケージ当たり 2 匹の雌雄別群飼育とし，群分け後はステンレス製懸垂式ケージを用いて個別飼育した．ステンレス製懸垂式ケージ及び給餌器の交換は 2 週間に 1 回以上行い，給水瓶及びステンレス製懸垂式ケージの受皿の交換は 1 週間に 2 回以上行った．動物飼育室の清掃 (床の掃き掃除) 及び 0.02%次亜塩素酸ナトリウム水溶液での床のモップ拭きによる消毒は毎日 1 回実施した．

### 8.3.4. 飼料及び飲料水

飼料は製造後 5 箇月以内の固型飼料 (CRF-1, オリエンタル酵母工業株式会社) を自由に摂取させた．但し，剖検前日には午後 4 時頃から給水・絶食させた．使用した飼料と同一ロットの分析結果は，Eurofins Scientific Analytics 及びオリエンタル酵母工業株式会社で実施したものを入手した．飼料の分析結果は，当試験施設で設定した基準値の範囲内であった．

飲料水は水道水を自由に摂取させた．飲料水の水質検査結果は，株式会社環境公害センターで約 6 箇月ごとに実施したものを入手した．飲料水の検査結果は，当試験施設で設定した基準値の範囲内であった．

## 8.4. 投与経路，投与方法，群構成，投与量及び投与期間

### 8.4.1. 投与経路及び投与方法

1,8-ジクロロオクタンは，継続して経口的に人に摂取される可能性が考えられるため，投与経路として経口を選択した．

投与は，ディスポーザブルラット用金属製経口胃ゾンデ (有限会社フチガミ器械) を取り付けたディスポーザブルポリプロピレン製注射筒 (テルモ株式会社) を用いて強制的に行った．

投与液量は，投与日に最も近い測定日の体重を基準とし，5 mL/kg で算出した．

投与時刻は午前 8 時 30 分～11 時 46 分までの間で，投与回数は 1 日 1 回とした．

投与開始日の週齢は雌雄とも 6 週齢であり，体重範囲は雄が 184～209 g，雌が 148～173 g であった．

### 8.4.2. 群構成及び投与量

群構成は, 以下に示したように被験物質投与群として 3 群を設定し, その他に対照群を設けた. 各群の動物数は, 対照群, 200 及び 1000 mg/kg 群を雌雄各 12 例, 40 mg/kg 群を雌雄各 6 例とした.

| | 群 | 投与量 (mg/kg/day) | 濃度 (mg/mL) | ラベルの色 | 動物数 (動物番号) | |
|---|---|---|---|---|---|---|
| | | | | | 雄 | 雌 |
| 1群 | 対照 (Corn oil) | 0 | 0 | 白色 | 6[1]+6[2] (M01101 ~ M01112) | 6[1]+6[2] (F01151 ~ F01162) |
| 2群 | 1,8-ｼﾞｸﾛﾛｵｸﾀﾝ | 40 | 8 | 茶色 | 6[1] (M02201 ~ M02206) | 6[1] (F02251 ~ F02256) |
| 3群 | 1,8-ｼﾞｸﾛﾛｵｸﾀﾝ | 200 | 40 | 青色 | 6[1]+6[2] (M03301 ~ M03312) | 6[1]+6[2] (F03351 ~ F03362) |
| 4群 | 1,8-ｼﾞｸﾛﾛｵｸﾀﾝ | 1000 | 200 | 紫色 | 6[1]+6[2] (M04401 ~ M04412) | 6[1]+6[2] (F04451 ~ F04462) |

[1]投与期間終了時に剖検

[2]回復期間終了時に剖検

1,8-ジクロロオクタンの投与量は, 当試験の予備試験[3] (投与段階: 0, 100, 200, 500 及び 1000 mg/kg, 使用動物数: 各群雌雄各 5 例) の結果から決定した. 予備試験において, 体重の有意な低値が 1000 mg/kg群の雄, 摂餌量の有意な低値が 1000 mg/kg群の雌雄でみられた. 尿素窒素の有意な高値が 1000, 500, 200 及び 100 mg/kg群の雄と 1000, 500 及び 100 mg/kg群の雌, A/Gの有意な高値が 1000, 500, 200 及び 100 mg/kg群の雌, K及び無機リンの有意な高値が 1000 及び 500 mg/kg群の雄, γ-GTP及びA/Gの有意な高値が 1000 mg/kg群の雄, 総蛋白, アルブミン及び無機リンの有意な高値が 1000 mg/kg群の雌でみられた. 肝臓の褪色が 1000, 500 及び 200 mg/kg群の雌雄と 100 mg/kg群の雌でみられた. また, 肝臓の絶対重量の有意な高値が 1000, 500 及び 200 mg/kg群の雄と 1000 及び 500 mg/kg群の雌, 肝臓の相対重量の有意な高値が 1000, 500, 200 及び 100 mg/kg群の雌雄, 腎臓の絶対重量の有意な高値が 1000, 500 及び 200 mg/kg群の雄と 1000 mg/kg群の雌, 腎臓の相対重量の有意な高値が 1000 及び 500 mg/kg群の雌雄でみられた. そこで, 当本試験では, 1000 mg/kgを高用量とし, 以下公比 5 で 200 及び 40 mg/kgの 3 投与群を設定した.

対照として媒体 (Corn oil) のみを被験物質投与群と同容量投与する群を設けた.

### 8.4.3. 投与期間

投与期間は, 新規化学物質等に係る試験の方法について (平成 15 年 11 月 21 日, 薬食発第 1121002 号, 平成 15・11・13 製局第 2 号, 環保企発第 031121002 号, 平成 18 年 11 月 20 日最終改正) 及び OECD Guideline for Testing of Chemicals for Repeated Dose 28-day Oral Toxicity Study in

Rodents (407) に従って, 雌雄とも 28 日間とした. 28 日間の投与後に, 対照群, 200 及び 1000 mg/kg 群の雌雄各半数の動物について 14 日間の回復期間を設けた.

投与開始日を投与 1 日と規定し，最終投与の翌日を回復 1 日とした.

### 8.5. 観察及び検査項目

#### 8.5.1. 一般状態

死亡の有無の確認及び一般状態の観察は，投与期間中に投与前及び投与後の 1 日 2 回，回復期間中に毎日 1 回及び剖検日に 1 回行った.

後述するように雌 1 例が死亡した．死亡例は，可能な限り生存例の剖検時と同様の器官重量の測定及び病理組織学検査を行った.

#### 8.5.2. 体重

体重は，1 週間に 2 回測定した [測定日: 投与 1，4，8，11，15，18，22，25，28 日及び 29 日 (回復 1 日)，回復 4，8，11，14 及び 15 日 (電子天秤: PB3002 又は PG2002-S，メトラー・トレド株式会社)].

#### 8.5.3. 摂餌量

摂餌量は，1 週間に 2 回 1 日量を測定した [残量測定日: 投与 2，5，9，12，16，19，23 及び 26 日，回復 2，5，9 及び 12 日 (電子天秤: PB3002，PG2002-S 又は PB3002-S/FACT，メトラー・トレド株式会社)]．摂餌量の Tables，Figs 及び Appendices の表示は残量の測定日とした.

#### 8.5.4. 摂水量

摂水量は，1 週間に 2 回 1 日量を測定した [残量測定日: 投与 2，5，9，12，16，19，23 及び 26 日，回復 2，5，9 及び 12 日 (電子天秤: PB3002，PG2002-S 又は PB3002-S/FACT，メトラー・トレド株式会社)]．摂水量の Tables，Figs 及び Appendices の表示は残量の測定日とした.

#### 8.5.5. FOB

全例について投与開始 4 日前，投与期間終了時剖検例について投与 7，14，21 及び 27 日に下記の 1) ～ 3)の項目を観察した．観察時刻は，投与後 1 時間とした．なお，観察者はほぼ固定し，Blind で実施した.

1) 姿勢，眼瞼閉鎖状態，かみつき行動及び痙攣はケージ内で観察した.
2) ケージからの出し易さ，扱い易さ，筋の緊張，毛の状態，流涙，流涎及び呼吸は手に持って観察した.
3) 立ち上がり回数及び毛づくろい回数はオープンフィールド内で 2 分間観察した．また，同時に歩行状態，眼瞼閉鎖状態，覚醒度，行動異常及び正向反射をオープンフィールド内で観察した.

### 8.5.6. 感覚反応

投与期間終了時剖検例について，投与 27 日の FOB 観察後に瞳孔反射，接近反射，触覚反射，聴覚反射及び痛覚反射を作業台の上で検査した.

### 8.5.7. 握力

投与期間終了時剖検例について, 投与 27 日の感覚反応検査終了後に Animal Grip Strength System (San Diego Instruments Inc.) を用いて，前肢及び後肢の握力を 5 回測定し，最高値と最低値を除いた中央の 3 測定値の平均値を採用した.

### 8.5.8. 自発運動量

投与期間終了時剖検例について，投与 26 日に Activity Monitor (MED Associates Inc.) を使用し，歩行量及び立ち上がり回数について投与後 1 時間から 2 時間まで 10 分間隔で測定した.

### 8.5.9. 尿検査

投与期間終了前 (投与 23 日) の投与検体投与前に投与期間終了時の剖検用動物，回復期間終了前 (回復 9 日) に回復期間終了時の剖検用動物について，採尿ケージを用いて絶食・給水下で新鮮尿を採取した. その後, 引き続いて給餌・給水下で 24 時間尿を採取した. 採取した尿について，以下の検査を実施した．検査後の尿は廃棄した.

新鮮尿: 色調は，外観判定とした．pH，蛋白質，ブドウ糖，ケトン体，ビリルビン，潜血及びウロビリノーゲンは，尿検査試験紙 (シーメンスメディカルソリューションズ・ダイアグノスティクス株式会社) に尿を滴下後，反射分光光度法により尿化学分析装置 (クリニテック アドバンタス，シーメンスメディカルソリューションズ・ダイアグノスティクス株式会社) を用いて検査した．尿沈渣は，沈渣を尿沈渣染色液 (新 Sternheimer 法，Sysmex 株式会社) で染色後に顕微鏡下で観察した.

24 時間尿: 尿量 (UV) は，尿比重 (S.G.) と重量 (電子天秤: PB3002，メトラー・トレド株式会社) から算出した．尿比重は，屈折率により屈折型尿比重計 (ユリペット-IID，株式会社ニコン) を用いて測定した.

### 8.5.10. 血液学検査

最終投与の翌日 (投与 29 日) 及び回復期間終了後 (回復 15 日) にペントバルビタールナトリウムの腹腔内投与 (40 mg/kg) による麻酔下で腹大動脈から EDTA-2K コーティングチューブ (ベノジェクト®II 真空採血管，VP-DK052K05，テルモ株式会社) に血液を採取し，以下の血液学検査を実施した．測定後の残余血液は廃棄した.

赤血球数 (RBC) はシースフローDC 検出法，ヘモグロビン量は SLS ヘモグロビン法，ヘマトクリット値は赤血球パルス波高値検出法, 血小板数はシースフローDC 検出法, 白血球数 (WBC), 白血球分類及び網状赤血球比率はフローサイトメトリー法によりいずれも多項目自動血球分析装置 (XT-2000iV，シスメックス株式会社) を用いて測定した．平均赤血球容積 (MCV) は赤血球数とヘマトクリット値から，平均赤血球血色素量 (MCH) は赤血球数とヘモグロビン量から，平均

赤血球血色素濃度 (MCHC) はヘマトクリット値とヘモグロビン量から多項目自動血球分析装置 (XT-2000iV，シスメックス株式会社) を用いて算出した.

プロトロンビン時間 (PT), 活性化部分トロンボプラスチン時間 (APTT) 及びフィブリノーゲン濃度は，血液を 3.2 w/v%クエン酸ナトリウムで処理後，遠心分離 [約 4℃，3000 rpm (約 1972×g), 15 分間，遠心機: CF 8DL，日立工機株式会社] して得た血漿について，光散乱検出方式により全自動血液凝固測定装置 (CA-530，シスメックス株式会社) を用いて測定した.

### 8.5.11. 血液生化学検査

血液学検査用の血液と同時期に腹大動脈から採取した血液から遠心分離 [約 4℃，3000 rpm (約 1972×g)，15 分間，遠心機: CF 8DL，日立工機株式会社] して得た血清は，測定用血清と保管用血清に分けて分取して，測定用血清について以下の血液生化学検査を実施した．測定後の残余血清は廃棄し，保管用血清は冷凍庫 (-80℃設定，超低温フリーザー: ULT1786-9JD，Kendro Laboratory Products) 内に保管したが，再測定の必要がないことを確認後廃棄した.

AST は MDH-UV 法，ALT は LDH-UV 法，ALP は p-ニトロフェニルリン酸基質法，γ-GTP は L-γ-グルタミル-3-カルボキシ-4-ニトロアニリド基質法，総蛋白は Biuret 法，総ビリルビンはジアゾ法，尿素窒素はウレアーゼ･GlDH 法，クレアチニンはクレアチニナーゼ・F-DAOS 法，ブドウ糖はヘキソキナーゼ・G-6-PDH 法，総コレステロールは COD･HDAOS 法，トリグリセライドは GPO･HDAOS 法，Ca は o-CPC 法，無機リンは PNP・XDH 法，Na，K 及び Cl はイオン選択電極法によりいずれも生化学自動分析装置 (AU 400，オリンパス株式会社) を用いて測定した.

アルブミンは総蛋白及び蛋白分画値 [電気泳動法，自動電気泳動装置 (AES 310，オリンパス株式会社)] から，A/G (アルブミン/グロブリン) は蛋白分画値から算出した.

### 8.5.12. 剖検及び器官重量

上記の 8.5.10.及び 8.5.11.の項で採血した動物をさらに放血して安楽死させた後，剖検した．脳 (大脳，小脳，延髄)，下垂体，唾液腺 (舌下腺・顎下腺)，甲状腺，胸腺，心臓，肝臓，脾臓，腎臓，副腎，精巣，精巣上体及び卵巣は重量を測定した (電子天秤: AB204，メトラー・トレド株式会社)．各器官重量を最終体重で除して相対重量も算出した．下垂体及び甲状腺重量は，20 vol%中性緩衝ホルマリンで 1 晩固定後，測定した．これらの器官は，肺，気管，膵臓，食道，胃，十二指腸，空腸，回腸，盲腸，結腸，直腸，リンパ節 (下顎・腸間膜)，膀胱，精嚢，前立腺，子宮，膣，上皮小体，脊髄，坐骨神経，眼球，ハーダー腺，胸骨，大腿骨，大腿筋，乳腺 (雌のみ) とともに 20 vol%中性緩衝ホルマリンで固定した．ただし，精巣及び精巣上体はブアン液で 2～3 時間固定後，10 vol%中性緩衝ホルマリンに再固定し，眼球はグルタールアルデヒド・ホルマリンで 1 晩固定後，20 vol%中性緩衝ホルマリンに再固定した.

### 8.5.13. 病理組織学検査

対照群及び 1000 mg/kg 群の投与期間終了時に剖検した例について，心臓，肺，気管，肝臓，膵臓，唾液腺 (舌下腺・顎下腺)，食道，胃，十二指腸，空腸，回腸，盲腸，結腸，直腸，胸腺，脾臓，リンパ節 (下顎・腸間膜)，腎臓，膀胱，精巣，精巣上体，精嚢，前立腺，卵巣，子宮，膣，

下垂体，副腎，甲状腺，上皮小体，脳 (大脳・小脳・延髄)，脊髄，坐骨神経，眼球，ハーダー腺，骨髄 (胸骨・大腿骨)，骨 (胸骨・大腿骨)，大腿筋，乳腺 (雌のみ) の HE 染色組織標本を作製し，病理組織学検査を実施した．なお，精巣については，PAS-ヘマトキシリン染色組織標本も作製した．

1000 mg/kg 群の雄の検査において対照群と比べて異常を示す動物数に差があった肝臓，膵臓及び腎臓については，200 及び 40 mg/kg 群の雄並びに回復群の雄についても HE 染色組織標本を作製し，病理組織学検査を実施した．1000 mg/kg 群の雌の検査において対照群と比べて異常を示す動物数に差があった肝臓及び膵臓については，200 及び 40 mg/kg 群の雌並びに回復群の雌についても HE 染色組織標本を作製し，病理組織学検査を実施した．また，1000 mg/kg 群の雌では腎臓重量の高値が認められたこと，1000 mg/kg 群の雄で腎臓に病理組織学的変化が認められたことから，200 及び 40 mg/kg 群の雌並びに回復群の雌の腎臓について HE 染色組織標本を作製し，病理組織学検査を実施した．切り出し後の器官・組織は，10 vol%中性緩衝ホルマリンで保管した．

### 8.6. 統計学的方法

測定値の統計学的解析は，下記のように行った．有意水準は，両側 5%及び 1%とした．一般状態及び剖検所見は統計学的解析を行わなかった．

体重，摂餌量，摂水量，毛づくろい及び立ち上がり回数 (FOB)，握力，自発運動量，尿量，尿比重，血液学検査，血液生化学検査及び器官重量 (相対重量を含む) については，各群で平均値及び標準偏差を算出した．次に，Bartlett検定[4]により分散の一様性を検定した．その結果，等分散の場合には対照群と各被験物質投与群との間でDunnett検定[5]を実施した．不等分散の場合には，対照群と各被験物質投与群との間でSteel検定[6]を実施した．

行動機能 (FOB) (但し，毛づくろい及び立ち上がり回数を除く) 及び感覚反応は，各群で平均値及び範囲を算出した．その後，Steel 検定を実施した．

病理組織学検査において，1000 mg/kg群で毒性学的影響が示唆され，200 及び 40 mg/kg群についても検査を実施した器官・組織の所見については，対照群との群間比較を上記のSteel検定を用いて行った．1000 mg/kg群において対照群との間に有意差が認められた場合は，Cochran・Armitageの傾向検定[7,8]を用いて用量反応性の検定を行った．

Dunnett検定及びSteel検定には，統計パッケージSASのPROBMC関数[9]を使用した．

## 9. 試験結果

### 9.1. 一般状態

#### 9.1.1. 雄 (Table 1; Appendices 1-1 - 1-4)

死亡例及び瀕死例はいずれの群にも認められなかった.

投与期間中には, 1000 mg/kg 群で投与後に一過性の流涎が 12 例, 200 mg/kg 群で投与後に一過性の流涎が 4 例にみられた. 40 mg/kg 群及び対照群では, 一般状態の異常はみられなかった.

回復期間中には, いずれの群とも一般状態の異常はみられなかった.

#### 9.1.2. 雌 (Table 2; Appendices 2-1 - 2-4)

死亡例は, 1000 mg/kg 群で 1 例 (No. F04454: 投与 2 日死亡) に認められたが, 前日に一般状態に異常はみられなかった. 200 及び 40 mg/kg 群並びに対照群では, 死亡例及び瀕死例は認められなかった.

投与期間中には, 1000 mg/kg 群で投与後に一過性の流涎が 11 例, 口の周囲の汚れ及び下腹部被毛の汚れが 1 例, 200 mg/kg 群で投与後に一過性の流涎が 3 例にみられた. 40 mg/kg 群及び対照群では, 一般状態の異常はみられなかった.

回復期間中には, いずれの群とも一般状態の異常はみられなかった.

### 9.2. 体重

#### 9.2.1. 雄 (Table 3; Fig. 2; Appendices 3-1 - 3-4)

投与期間中には, 1000 mg/kg 群では対照群と比べて投与 4, 8, 11 及び 15 日に体重の有意な低値がみられた. 200 及び 40 mg/kg 群では, 対照群と比べて各測定日の体重に有意差はみられなかった.

回復期間中には, 各投与群とも対照群と比べて各測定日の体重に有意差はみられなかった.

#### 9.2.2. 雌 (Table 4; Fig. 3; Appendices 4-1 - 4-4)

投与期間中には, 1000 mg/kg 群では対照群と比べて投与 18 及び 22 日に体重の有意な高値がみられたが, 一過性の変化であることから, 被験物質による影響とは考えられない. 200 及び 40 mg/kg 群では, 対照群と比べて各測定日の体重に有意差はみられなかった.

回復期間中には, 各投与群とも対照群と比べて各測定日の体重に有意差はみられなかった.

### 9.3. 摂餌量

#### 9.3.1. 雄 (Table 5; Fig. 4; Appendices 5-1 - 5-4)

投与期間中には, 1000 mg/kg 群では対照群と比べて投与 2 及び 5 日に摂餌量の有意な低値, 投与 19 及び 23 日に摂餌量の有意な高値がみられた. 200 及び 40 mg/kg 群では, 対照群と比べて各測定日の摂餌量に有意差はみられなかった.

回復期間中には, 各投与群とも対照群と比べて各測定日の摂餌量に有意差はみられなかった.

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

投与期間中には，1000 mg/kg 群では対照群と比べて投与 2 日に摂餌量の有意な低値，投与 16 及び 23 日に有意な高値がみられた．40 mg/kg 群では，対照群と比べて投与 19 日に摂餌量の有意な高値がみられたが，投与量に依存した変化ではなかった．200 mg/kg 群では，対照群と比べて各測定日の摂餌量に有意差はみられなかった．

回復期間中には，各投与群とも対照群と比べて各測定日の摂餌量に有意差はみられなかった．

9.4. 摂水量

9.4.1. 雄 (Table 7; Fig. 6; Appendices 7-1 - 7-4)

投与期間中には，1000 mg/kg 群では対照群と比べて投与 9，12，16，19，23 及び 26 日に摂水量の有意な高値がみられた．200 及び 40 mg/kg 群では，対照群と比べて各測定日の摂水量に有意差はみられなかった．

回復期間中には，各投与群とも対照群と比べて各測定日の摂水量に有意差はみられなかった．

9.4.2. 雌 (Table 8; Fig. 7; Appendices 8-1 - 8-4)

投与期間中には，1000 mg/kg 群では対照群と比べて投与 5，9，12，16，19，23 及び 26 日に摂水量の有意な高値がみられた．200 mg/kg 群では，対照群と比べて投与 9 日に摂水量の有意な高値がみられた．40 mg/kg 群では，対照群と比べて各測定日の摂水量に有意差はみられなかった．

回復期間中には，1000 mg/kg 群では対照群と比べて回復 2 日に摂水量の有意な高値がみられた．200 mg/kg 群では，対照群と比べて各測定日の摂水量に有意差はみられなかった．

9.5. FOB

9.5.1. 雄 (Table 9; Appendices 9-1 - 9-4)

1000 mg/kg 群では，流涎がみられたが，投与後の流涎が継続したものと考えられる．200 及び 40 mg/kg 群では，各測定日のいずれの項目にも異常はみられなかった．

9.5.2. 雌 (Table 10; Appendices 10-1 - 10-4)

1000 mg/kg 群では，流涎がみられたが，投与後の流涎が継続したものと考えられる．1000 mg/kg 群では，対照群と比べて投与 7 日に立ち上がり回数の有意な低値がみられたが，一過性の変化であること，その他の観察項目に異常は認められないことから，毒性学的影響とは考えられない．200 mg/kg 群では，対照群と比べて投与開始 4 日前に立ち上がり回数の有意な低値がみられたが，被験物質による影響ではなかった．40 mg/kg 群では，各測定日のいずれの項目にも異常はみられなかった．

9.6. 感覚反応

9.6.1. 雄 (Table 11; Appendices 11-1 - 11-4)

各投与群とも，いずれの項目にも異常はみられなかった．

9.6.2. 雌 (Table 12; Appendices 12-1 - 12-4)

各投与群とも，いずれの項目にも異常はみられなかった.

9.7. 握力

9.7.1. 雄 (Table 13; Appendices 13-1 - 13-4)

1000 mg/kg群では，対照群と比べて前肢及び後肢の握力の有意な低値がみられた．200及び40 mg/kg群では，対照群と比べて後肢の握力の有意な低値がみられた.

9.7.2. 雌 (Table 14; Appendices 14-1 - 14-4)

各投与群とも，対照群と比べて前肢及び後肢の握力に有意差はみられなかった.

9.8. 自発運動量

9.8.1. 雄 (Table 15; Appendices 15-1 - 15-4)

各投与群とも，対照群と比べて各測定項目に有意差はみられなかった.

9.8.2. 雌 (Table 16; Appendices 16-1 - 16-4)

各投与群とも，対照群と比べて各測定項目に有意差はみられなかった.

9.9. 尿検査

9.9.1. 投与期間終了時雄 (Table 17; Appendices 17-1 - 17-4)

1000 mg/kg 群では，対照群と比べて尿量の有意な高値がみられた．200 及び 40 mg/kg 群では，対照群と比べて尿量及び尿比重に有意差はみられなかった.

各投与群とも，色調，pH，蛋白質，ブドウ糖，ケトン体，ビリルビン，潜血，ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった.

9.9.2. 投与期間終了時雌 (Table 18; Appendices 18-1 - 18-4)

各投与群とも，対照群と比べて尿量及び尿比重に有意差はみられなかった.

各投与群とも，色調，pH，蛋白質，ブドウ糖，ケトン体，ビリルビン，潜血，ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった.

9.9.3. 回復期間終了時雄 (Table 19; Appendices 19-1 - 19-3)

各投与群とも，対照群と比べて尿量及び尿比重に有意差はみられなかった.

各投与群とも，色調，pH，蛋白質，ブドウ糖，ケトン体，ビリルビン，潜血，ウロビリノーゲン及び沈渣は対照群とほぼ同程度であった.

9.9.4. 回復期間終了時雌 (Table 20; Appendices 20-1 - 20-3)

各投与群とも，対照群と比べて尿量及び尿比重に有意差はみられなかった.

各投与群とも，色調，pH，蛋白質，ブドウ糖，ケトン体，ビリルビン，潜血，ウロビリノーゲ

ン及び沈渣は対照群とほぼ同程度であった.

### 9.10. 血液学検査

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

1000 及び 200 mg/kg 群では，対照群と比べて活性化部分トロンボプラスチン時間の有意な低値がみられたが，対照群との差はわずかであること及び当所の背景データの範囲 [22.6 ± 2.1 (sec); Attachment 8] 内の変化であることから，被験物質による影響とは考えられない．1000 mg/kg 群では，対照群と比べて単球比率の有意な高値及び好中球比率の有意な低値がみられたが，対照群との差はわずかであること及び当所の背景データの範囲 [単球比率: 2.5 ± 0.7 (%)，好中球比率: 17.6 ± 6.7 (%); Attachment 8] 内の変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べてプロトロンビン時間の有意な低値がみられたが，投与量に関連した変化ではないことから，被験物質による影響とは考えられない．40 mg/kg 群では，対照群と比べて各測定項目に有意差はみられなかった.

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

1000 mg/kg 群では，対照群と比べて MCHC の有意な低値がみられたが，対照群との差はわずかであること，ヘモグロビン量及びヘマトクリット値に有意差が認められないことから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べてプロトロンビン時間の有意な高値がみられたが，投与量に関連した変化ではないことから，被験物質による影響とは考えられない．40 mg/kg 群では，対照群と比べて各測定項目に有意差はみられなかった.

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

1000 mg/kg 群では，対照群と比べてヘモグロビン量の有意な低値がみられたが，対照群との差はわずかであること及び当所の背景データの範囲 [ヘモグロビン量: 15.1 ± 0.5 (g/dL); Attachment 8] 内の変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べて各測定項目に有意差はみられなかった.

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

1000 mg/kg 群では，対照群と比べて MCHC の有意な低値がみられたが，対照群との差はわずかであること，ヘモグロビン量及びヘマトクリット値に有意差が認められないことから，被験物質による影響とは考えられない．1000 mg/kg 群では，対照群と比べてフィブリノーゲン濃度の有意な高値がみられたが，対照群との差はわずかであること及び当所の背景データの範囲 [185.6 ± 12.6 (mg/dL); Attachment 9] 内の変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べて各測定項目に有意差はみられなかった.

### 9.11. 血液生化学検査

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

1000 及び 200 mg/kg 群では，対照群と比べて K の有意な高値がみられた．1000 mg/kg 群では，

対照群と比べてクレアチニンの有意な低値がみられた．しかし，いずれも対照群との差はわずかであること及び当所の背景データの範囲 [K: 4.21 ± 0.26 (mEq/L)，クレアチニン: 0.23 ± 0.03 (mg/dL); Attachment 10] 内の変化であることから，被験物質による影響とは考えられない．40 mg/kg 群では，対照群と比べて Cl の有意な高値がみられたが，投与量に関連した変化ではないことから，被験物質による影響とは考えられない．

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

1000 mg/kg 群では，対照群と比べて総コレステロール及び無機リンの有意な高値がみられた．200 mg/kg 群では，対照群と比べて無機リンの有意な高値がみられた．

1000，200 及び 40 mg/kg 群では，対照群と比べて K の有意な高値及び Ca の有意な低値がみられた．1000 mg/kg 群では，対照群と比べてクレアチニンの有意な低値がみられた．しかし，いずれも対照群との差はわずかであること及び当所の背景データの範囲 [K: 4.09 ± 0.20 (mEq/L); Ca: 10.0 ± 0.4 (mg/dL); クレアチニン: 0.27 ± 0.03 (mg/dL); Attachment 11] 内の変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べてアルブミン，A/G 及び尿素窒素の有意な高値並びに総コレステロールの有意な低値がみられたが，投与量に関連した変化ではないことから，被験物質による影響とは考えられない．

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

1000 mg/kg 群では，対照群と比べて無機リンの有意な高値がみられたが，投与期間終了時には認められなかった変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べて各測定項目にも有意差はみられなかった．

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

1000 mg/kg 群では，対照群と比べて総コレステロールの有意な高値がみられた．

1000 mg/kg 群では，対照群と比べて γ-GTP 及びトリグリセライドの有意な高値がみられたが，投与期間終了時には認められなかった変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べてクレアチニンの有意な低値がみられたが，投与量に関連した変化ではないことから，被験物質による影響とは考えられない．

## 9.12. 剖検所見

### 9.12.1. 死亡例雌 (Table 29; Appendix 29)

1000 mg/kg 群の 1 例では，胃に赤色点及び糜爛がみられた．

### 9.12.2. 投与期間終了時雄 (Table 30; Appendices 30-1 - 30-4)

肝臓の褪色が 1000 及び 200 mg/kg 群で 4 及び 6 例にみられた．40 mg/kg 群及び対照群では，異常はみられなかった．

9.12.3. 投与期間終了時雌 (Table 31; Appendices 31-1 - 31-4)

肝臓の褪色が 1000 及び 200 mg/kg 群で各 2 例にみられた．40 mg/kg 群及び対照群では，異常はみられなかった．

9.12.4. 回復期間終了時雄 (Table 32; Appendices 32-1 - 32-3)

肝臓の褪色が 200 mg/kg 群で 1 例にみられた．1000 mg/kg 群及び対照群では，異常はみられなかった．

9.12.5. 回復期間終了時雌 (Table 33; Appendices 33-1 - 33-3)

いずれの群とも，異常はみられなかった．

9.13. 器官重量

9.13.1. 死亡例雌 (Table 34; Appendix 34)

1000 mg/kg 群の雌の死亡例では，特記すべき変化はみられなかった．

9.13.2. 投与期間終了時雄 (Table 35; Appendices 35-1 - 35-4)

剖検日の体重は，各投与群とも対照群と比べて有意差はみられなかった．

1000 及び 200 mg/kg 群では，対照群と比べて肝臓及び腎臓の絶対及び相対重量の有意な高値がみられた．

1000 mg/kg 群では，対照群と比べて精巣の絶対重量の有意な高値がみられたが，その相対重量に有意差が認められないことから，被験物質による影響とは考えられない．40 mg/kg 群では，対照群と比べて精巣の相対重量の有意な高値がみられたが，投与量に依存した変化ではないことから，被験物質による影響とは考えられない．

9.13.3. 投与期間終了時雌 (Table 36; Appendices 36-1 - 36-4)

剖検日の体重は，各投与群とも対照群と比べて有意差はみられなかった．

1000，200 及び 40 mg/kg 群では対照群と比べて肝臓の相対重量の有意な高値，1000 及び 200 mg/kg 群では肝臓の絶対重量の有意な高値，1000 mg/kg 群では腎臓の絶対及び相対重量の有意な高値がみられた．

200 mg/kg 群では，対照群と比べて脾臓の相対重量の有意な低値がみられたが，絶対重量に差が認められないことから，被験物質による影響とは考えられない．

9.13.4. 回復期間終了時雄 (Table 37; Appendices 37-1 - 37-3)

剖検日の体重は，各投与群とも対照群と比べて有意差はみられなかった．

1000 及び 200 mg/kg 群では，対照群と比べて腎臓の相対重量の有意な高値がみられた．

9.13.5. 回復期間終了時雌 (Table 38; Appendices 38-1 - 38-3)

剖検日の体重は，各投与群とも対照群と比べて有意差はみられなかった．

1000 mg/kg 群では，対照群と比べて肝臓の絶対及び相対重量の有意な高値がみられた．

1000 mg/kg 群では，対照群と比べて胸腺の絶対及び相対重量の有意な高値がみられたが，投与期間終了時には認められなかった変化であることから，被験物質による影響とは考えられない．200 mg/kg 群では，対照群と比べて下垂体の相対重量の有意な低値がみられたが，投与量に依存した変化ではないことから，被験物質による影響とは考えられない．

### 9.14. 病理組織学所見

#### 9.14.1. 死亡例雌 (Table 39; Appendix 39)

全器官・組織: 死後変化が軽度にみられた．

#### 9.14.2. 投与期間終了時雄 (Table 40; Appendices 40-1 - 40-4)

肝臓: 門脈周囲性の肝細胞腫大が 1000，200 及び 40 mg/kg 群で 6 例全例にみられ，その程度は 1000 及び 200 mg/kg 群で軽度，40 mg/kg 群でごく軽度であった．門脈周囲性の肝細胞腫大は，1000，200 及び 40 mg/kg 群で対照群と比べて有意差が認められ，かつ，用量反応性も確認された．

膵臓: チモーゲン顆粒の減少が 1000，200 及び 40 mg/kg 群で 6 例全例にみられ，その程度は 1000，200 及び 40 mg/kg 群ともごく軽度又は軽度であった．チモーゲン顆粒の減少は，1000，200 及び 40 mg/kg 群で対照群と比べて有意差が認められ，かつ，用量反応性も確認された．

腎臓: 尿細管上皮の硝子滴が 1000 mg/kg 群で 6 例全例，200 mg/kg 群で 4 例，40 mg/kg 群で 1 例にみられ，その程度は 1000 mg/kg 群でごく軽度又は軽度，200 及び 40 mg/kg 群でごく軽度であった．尿細管上皮の硝子滴は，1000 mg/kg 群で対照群と比べて有意差が認められ，かつ，用量反応性も確認された．

その他の変化として以下に示した所見が得られた．

肺: 血管壁への鉱質沈着が 1000 mg/kg 群で 1 例にみられた．

腎臓: 嚢胞が対照群で 1 例にみられた．

下垂体: 異所性頭蓋咽頭管組織が 1000 mg/kg 群で 1 例にみられた．

なお，これらの変化は対照群でも通常観察される変化であること，それらの程度はいずれもごく軽度であること，投与群のそれらの出現頻度は対照群と比べて差がないことから，偶発的変化と判断される．

その他には，1000 mg/kg 群及び対照群では，心臓，気管，舌下腺，顎下腺，食道，胃，十二指腸，空腸，回腸，盲腸，結腸，直腸，胸腺，脾臓，下顎リンパ節，腸管膜リンパ節，膀胱，精巣，精巣上体，精嚢，前立腺，副腎，甲状腺，上皮小体，大脳，小脳，延髄，脊髄，坐骨神経，眼球，ハーダー腺，骨髄 (胸骨・大腿骨)，骨 (胸骨・大腿骨) 及び大腿筋に異常はみられなかった．

#### 9.14.3. 投与期間終了時雌 (Table 41; Appendices 41-1 - 41-4)

肝臓: 門脈周囲性の肝細胞腫大が 1000 mg/kg 群で 5 例全例，200 及び 40 mg/kg 群で 6 例全例にみられ，その程度は 1000 及び 200 mg/kg 群で軽度，40 mg/kg 群でごく軽度であった．門脈周囲性の肝細胞腫大は，1000，200 及び 40 mg/kg 群で対照群と比べて有意差が認められ，かつ，用量反応性も確認された．微小肉芽腫が 1000 mg/kg 群で 2 例と 200 mg/kg 群で 3 例にみられ，その程度

はいずれもごく軽度であった.

膵臓: チモーゲン顆粒の減少が 1000 mg/kg 群で 5 例全例, 200 及び 40 mg/kg 群で 6 例全例にみられ, その程度は 1000 及び 200 mg/kg 群で軽度, 40 mg/kg 群でごく軽度又は軽度であった. チモーゲン顆粒の減少は, 1000, 200 及び 40 mg/kg 群で対照群と比べて有意差が認められ, かつ, 用量反応性も確認された.

その他の変化として以下に示した所見が得られた.

肺: 血管壁への鉱質沈着が対照群で 1 例にみられた.

腎臓: 嚢胞が 40 mg/kg 群で 1 例にみられた.

眼球: 網膜異形成が 1000 mg/kg 群と対照群で各 1 例にみられた.

なお, これらの変化は対照群でも通常観察される変化であること, それらの程度はいずれもごく軽度であること, 投与群のそれらの出現頻度は対照群と比べて差がないことから, 偶発的変化と判断される.

その他には, 1000 mg/kg 群及び対照群では, 心臓, 気管, 舌下腺, 顎下腺, 食道, 胃, 十二指腸, 空腸, 回腸, 盲腸, 結腸, 直腸, 胸腺, 脾臓, 下顎リンパ節, 腸管膜リンパ節, 膀胱, 卵巣, 子宮, 膣, 下垂体, 副腎, 甲状腺, 上皮小体, 大脳, 小脳, 延髄, 脊髄, 坐骨神経, ハーダー腺, 骨髄 (胸骨・大腿骨), 骨 (胸骨・大腿骨), 大腿筋及び乳腺に異常はみられなかった.

### 9.14.4. 回復期間終了時雄 (Table 42; Appendices 42-1 - 42-3)

腎臓: 尿細管上皮の硝子滴が 1000 mg/kg 群で 3 例, 200 mg/kg 群で 1 例及び対照群で 2 例にみられ, その程度はいずれもごく軽度であった. 尿細管上皮の硝子滴は, 1000 及び 200 mg/kg 群とも対照群と比べて有意差は認められなかった. その他には, 嚢胞が対照群で 1 例にみられた.

その他には, 1000 及び 200 mg/kg 群並びに対照群では, 肝臓及び膵臓に異常はみられなかった.

### 9.14.5. 回復期間終了時雌 (Table 43; Appendices 43-1 - 43-3)

肝臓: 門脈周囲性の肝細胞腫大が 1000 mg/kg 群で 4 例と 200 mg/kg 群で 1 例にみられ, その程度はいずれもごく軽度であった. 門脈周囲性の肝細胞腫大は, 1000 mg/kg 群で対照群と比べて有意差が認められ, かつ, 用量反応性も確認された.

膵臓: チモーゲン顆粒の減少が 1000 及び 200 mg/kg 群で各 2 例にみられ, その程度はいずれもごく軽度であった. チモーゲン顆粒の減少は, 1000 及び 200 mg/kg 群とも対照群と比べて有意差は認められなかった.

その他には, 1000 及び 200 mg/kg 群並びに対照群では, 腎臓に異常はみられなかった.

## 10. 考察

1,8-ジクロロオクタンを雌雄ラットに 28 日間反復経口投与し，さらに一部の動物には 14 日間の回復期間を設けた反復投与による毒性学的影響を検討した．

死亡例が 1000 mg/kg 群で投与 2 日に雌 1 例に認められたが，前日に一般状態に異常はみられなかった．死亡例の病理組織学検査では，全器官・組織は死後変化のため，精査できなかったが，1,8-ジクロロオクタンによる急性毒性により死に至ったと考えられる．

一般状態の変化としては，1000 mg/kg 群で口の周囲の汚れ及び下腹部被毛の汚れが雌 1 例にみられた．なお，雌雄とも，1000 及び 200 mg/kg 群で流涎がみられたが，投与後に一過性に認められたのみであり，痙攣などの神経症状あるいは唾液腺の重量及び形態学的変化は認められないことから，被験物質の刺激性に基づく変化と判断され，毒性症状とはみなさなかった．

体重は，雄では 1000 mg/kg 群で投与期間の初期に有意な低値がみられたが，雌ではいずれの投与群にも投与に起因する変化は認められなかった．

摂餌量は，雌雄とも 1000 mg/kg群で投与期間の初期に有意な低値がみられた．また，摂餌量は，雌雄とも 1000 mg/kg群で投与期間の後期に有意な高値がみられた．膵臓の病理組織学検査において，投与期間終了時にチモーゲン顆粒の減少が雌雄とも 1000，200 及び 40 mg/kg群でみられた．膵腺房細胞の酵素原顆粒 (チモーゲン顆粒) にはアミラーゼ，リパーゼ，キモトリプシン，トリプシンなどの消化酵素が含まれている[10]．1,8-ジクロロオクタンにより，消化酵素分泌が減少し，代償性に摂餌量が増加した可能性が考えられる．回復期間中には雌雄とも摂餌量に変化はみられないこと，回復期間終了時に膵臓のチモーゲン顆粒の減少は雄では認められないこと，雌では軽減傾向にあることから，回復傾向にあったと考えられる．

摂水量は，雌雄とも 1000 mg/kg 群でほぼ投与期間を通して有意な高値がみられた．回復期間中には，雌では 1000 mg/kg 群で摂水量の一過性の有意な高値がみられたが，雄では投与に起因する変化は認められなかった．

握力では，雄では 1000 mg/kg 群で前肢及び後肢の握力の有意な低値，200 及び 40 mg/kg 群で後肢の握力の有意な低値がみられたが，雌ではいずれの投与群にも投与に起因する変化は認められなかった．FOB，感覚反応及び自発運動量では，雌雄ともいずれの投与群にも投与に起因する変化はみられなかった．

尿検査において，投与期間終了時に雄では 1000 mg/kg 群で尿量の有意な高値がみられたが，この変化は摂水量の増加に起因したものと考えられる．しかし，雌ではいずれの投与群にも投与に起因する変化は認められなかった．回復期間終了時の尿検査では，雌雄とも投与に起因する変化は認められなかった．

投与期間終了時に雄では 1000 及び 200 mg/kg群で腎臓の絶対及び相対重量の有意な高値，雌では 1000 mg/kg群で腎臓の絶対及び相対重量の有意な高値がみられた．回復期間終了時には，雄では 1000 及び 200 mg/kg群で腎臓の相対重量の有意な高値がみられたが，雌では腎臓重量に投与に起因する変化は認められなかった．血液生化学検査において，投与期間終了時に雌では 1000 及び 200 mg/kg群で無機リンの有意な高値がみられた．腎臓の病理組織学検査において，投与期間終了時に雄では 1000，200 及び 40 mg/kg群で用量に依存して尿細管上皮の硝子滴がみられたが，雌で

はいずれの投与群にも異常は認められなかった．尿細管上皮の硝子滴は，ラット雄において自然発生的にも認められる変化であるが[11]，種々の薬物及び化学物質によっても増強されることが報告されている[12]．当試験においても，回復期間終了時に対照群の雄2例で同程度の尿細管上皮の硝子滴がみられている．投与期間終了時に尿細管上皮の硝子滴が 1000 mg/kg群で 6 例全例，200 mg/kg群で4例及び40 mg/kg群で1例に認められていることから，1,8-ジクロロオクタンあるいはその代謝産物により自然発症病変が増悪したと考えられる．回復期間終了時には，1000及び200 mg/kg群の雄で腎臓の相対重量の有意な高値が認められたが，腎臓の尿細管上皮の硝子滴の出現例数は対照群とほぼ同じであったことから，回復傾向にあったと考えられる．

血液学検査において，投与期間終了時及び回復期間終了時に雌雄ともいずれの投与群にも投与に起因する変化は認められなかった．

血液生化学検査において，投与期間終了時に雌では1000 mg/kg群で総コレステロールの有意な高値がみられたが，雄ではいずれの投与群にも投与に起因する変化は認められなかった．回復期間終了時にも雌では1000 mg/kg群で総コレステロールの有意な高値がみられたが，雄では投与に起因する変化は認められなかった．投与期間終了時に雌雄とも1000及び200 mg/kg群で肝臓の褪色がみられた．回復期間終了時には，雄では200 mg/kg群で肝臓の褪色がみられたが，雌では投与に起因する変化は認められなかった．肝臓重量は，投与期間終了時に雄では1000及び200 mg/kg群で絶対重量及び相対重量の有意な高値，雌では1000，200及び40 mg/kg群で相対重量の有意な高値，1000及び200 mg/kg群で絶対重量の有意な高値がみられた．肝臓の病理組織学検査において，投与期間終了時に門脈周囲性の肝細胞腫大が雌雄とも1000, 200及び40 mg/kg群でみられた．肝細胞腫大は，細胞内小器官の増大によると考えられる．また，微小肉芽腫が雌の 1000 及び200 mg/kg 群でみられた．しかし，血液学検査及び血液生化学検査において肝機能障害を疑わせる異常は認められていないことから，重篤な影響とは考えられない．回復期間終了時には，雌では1000 mg/kg群で肝臓の絶対重量及び相対重量の有意な高値がみられ，門脈周囲性の肝細胞腫大が雌では1000及び200 mg/kg群でみられたものの，投与期間終了時に比べてその程度は軽減していること，雄では1000及び200 mg/kg群とも門脈周囲性の肝細胞腫大は認められなかったことから，回復傾向にあると考えられる．

以上のように，1,8-ジクロロオクタンの無影響量は，雄では40 mg/kg投与で後肢の握力の低値，肝臓に門脈周囲性の肝細胞腫大，膵臓にチモーゲン顆粒の減少が認められたことから40 mg/kg/day 未満，雌では 40 mg/kg 投与で肝臓の相対重量の高値及び門脈周囲性の肝細胞腫大，膵臓にチモーゲン顆粒の減少が認められたことから40 mg/kg/day未満と考えられる．

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Table 1. General signs in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | mg/kg | Number of males and general signs | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | | | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| Control | 0 | Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| 1,8-dichlorooctane | 40 | Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 200 | Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Salivation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 | Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 10 | 12 | 8 | 12 | 7 | 12 | 10 | 12 | 6 | 12 | 5 | 12 | 5 | 12 | 0 | 12 | 2 | 12 | 5 |
| | | Salivation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 4 | 0 | 5 | 0 | 2 | 0 | 6 | 0 | 7 | 0 | 7 | 0 | 12 | 0 | 10 | 0 | 7 |

Pre: Before administration, Post: after administration.

(Continued)

Table 1. (Continued) General signs in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | mg/kg | Number of males and general signs | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Total[a)] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | | |
| | | | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| Control | 0 | Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | - |
| 1,8-dichlorooctane | 40 | Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | - |
| | 200 | Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 12 | 12 | 11 | 12 | 10 | 6 | - |
| | | Salivation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 4 |
| | 1000 | Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 12 |
| | | Normal | 12 | 6 | 12 | 5 | 12 | 0 | 12 | 1 | 12 | 0 | 12 | 0 | 12 | 3 | 12 | 2 | 12 | 3 | 12 | 2 | 12 | 5 | 12 | 4 | 12 | 6 | 12 | 3 | 6 | - |
| | | Salivation | 0 | 6 | 0 | 7 | 0 | 12 | 0 | 11 | 0 | 12 | 0 | 12 | 0 | 9 | 0 | 10 | 0 | 9 | 0 | 10 | 0 | 7 | 0 | 8 | 0 | 6 | 0 | 9 | 0 | 12 |

Pre: Before administration, Post: after administration. (Continued)

a): Number of males showing abnormal signs at least once between Days 1 and 29 of administration.

Table 1. (Continued) General signs in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | mg/kg | Number of males and general signs | Days of recovery | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| Control | 0 | Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| 1,8-dichlorooctane | 200 | Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 1000 | Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

Table 2. General signs in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | mg/kg | Number of females and general signs | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | | | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| Control | 0 | Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| 1,8-dichlorooctane | 40 | Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 200 | Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| | | Salivation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 | Number of females | 12 | 12 | 12 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 |
| | | Normal | 12 | 12 | 11 | 11 | 11 | 11 | 11 | 10 | 11 | 9 | 11 | 8 | 11 | 9 | 11 | 7 | 11 | 6 | 11 | 6 | 11 | 5 | 11 | 3 | 11 | 7 | 11 | 5 |
| | | Salivation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 3 | 0 | 2 | 0 | 4 | 0 | 5 | 0 | 5 | 0 | 6 | 0 | 8 | 0 | 4 | 0 | 6 |
| | | Perioral smudge | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Soiled hair | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Death | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Pre: Before administration, Post: after administration.

(Continued)

Table 2. (Continued) General signs in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | mg/kg | Number of females and general signs | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Total[a)] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | |
| | | | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| Control | 0 | Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | - |
| 1,8-dichlorooctane | 40 | Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | - |
| | 200 | Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 12 |
| | | Normal | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 10 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 11 | 6 | - |
| | | Salivation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 3 |
| | 1000 | Number of females | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 5 | 12 |
| | | Normal | 11 | 3 | 11 | 1 | 11 | 2 | 11 | 6 | 11 | 5 | 11 | 1 | 11 | 5 | 11 | 5 | 11 | 6 | 11 | 4 | 10 | 4 | 10 | 4 | 11 | 2 | 11 | 2 | 5 | - |
| | | Salivation | 0 | 8 | 0 | 10 | 0 | 9 | 0 | 5 | 0 | 6 | 0 | 10 | 0 | 6 | 0 | 6 | 0 | 5 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 9 | 0 | 9 | 0 | 11 |
| | | Perioral smudge | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| | | Soiled hair | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| | | Death | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |

Pre: Before administration, Post: after administration. (Continued)

a): Number of females showing abnormal signs at least once between Days 1 and 29 of administration.

Table 2. (Continued) General signs in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | mg/kg | Number of females and general signs | Days of recovery | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| Control | 0 | Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| 1,8-dichlorooctane | 200 | Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 1000 | Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | | Normal | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

Table 3. Body weights of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 12 | 6 | 12 | 12 |
| Days of administration | | | | |
| 1 | 197 ± 5 | 199 ± 6 | 197 ± 7 | 198 ± 5 |
| 4 | 219 ± 9 | 223 ± 11 | 217 ± 8 | 207 ± 7 ** |
| 8 | 250 ± 11 | 250 ± 8 | 245 ± 8 | 236 ± 12 ** |
| 11 | 277 ± 13 | 275 ± 9 | 272 ± 10 | 264 ± 15 * |
| 15 | 310 ± 14 | 304 ± 11 | 304 ± 11 | 295 ± 18 * |
| 18 | 330 ± 20 | 327 ± 10 | 326 ± 9 | 318 ± 20 |
| 22 | 361 ± 16 | 352 ± 12 | 354 ± 12 | 348 ± 24 |
| 25 | 377 ± 17 | 368 ± 12 | 371 ± 14 | 363 ± 25 |
| 28 | 392 ± 22 | 375 ± 14 | 381 ± 17 | 372 ± 27 |
| Number of males | 6 | 0 | 6 | 6 |
| Days of recovery | | | | |
| 1 | 402 ± 25 | - | 389 ± 14 | 372 ± 29 |
| 4 | 417 ± 28 | - | 397 ± 17 | 381 ± 31 |
| 8 | 433 ± 30 | - | 414 ± 19 | 395 ± 34 |
| 11 | 440 ± 31 | - | 419 ± 22 | 406 ± 37 |
| 14 | 453 ± 32 | - | 429 ± 23 | 416 ± 37 |

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Table 4. Body weights of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 12 | 6 | 12 | 12 |
| Days of administration | | | | |
| 1 | 159 ± 5 | 162 ± 8 | 161 ± 5 | 162 ± 6 |
| 4 | 170 ± 6 | 169 ± 9 | 173 ± 7 | 162 ± 9 (11) |
| 8 | 183 ± 8 | 183 ± 10 | 184 ± 8 | 183 ± 9 (11) |
| 11 | 194 ± 10 | 199 ± 12 | 200 ± 11 | 199 ± 9 (11) |
| 15 | 205 ± 12 | 210 ± 11 | 210 ± 12 | 214 ± 11 (11) |
| 18 | 212 ± 11 | 223 ± 13 | 219 ± 15 | 229 ± 13 * (11) |
| 22 | 223 ± 13 | 235 ± 15 | 230 ± 15 | 239 ± 14 * (11) |
| 25 | 229 ± 14 | 242 ± 16 | 237 ± 15 | 241 ± 18 (11) |
| 28 | 241 ± 15 | 249 ± 15 | 245 ± 16 | 248 ± 14 (11) |
| Number of females | 6 | 0 | 6 | 6 |
| Days of recovery | | | | |
| 1 | 237 ± 20 | - | 244 ± 14 | 251 ± 11 |
| 4 | 247 ± 22 | - | 249 ± 14 | 254 ± 11 |
| 8 | 254 ± 23 | - | 259 ± 14 | 258 ± 12 |
| 11 | 259 ± 22 | - | 265 ± 16 | 263 ± 11 |
| 14 | 260 ± 22 | - | 270 ± 15 | 270 ± 11 |

Each value shows mean (g) ± S.D.

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

Figures in parentheses indicate number of females.

Table 5. Food consumption in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 12 | 6 | 12 | 12 |
| Days of administration | | | | |
| 2 | 21 ± 2 | 22 ± 3 | 22 ± 2 | 17 ± 3 ** |
| 5 | 22 ± 2 | 23 ± 2 | 22 ± 2 | 16 ± 4 ## |
| 9 | 24 ± 2 | 24 ± 0 | 24 ± 2 | 23 ± 3 |
| 12 | 24 ± 2 | 25 ± 2 | 24 ± 2 | 24 ± 4 |
| 16 | 27 ± 2 | 27 ± 2 | 27 ± 2 | 27 ± 3 |
| 19 | 24 ± 2 | 25 ± 2 | 26 ± 2 | 28 ± 3 ** |
| 23 | 24 ± 2 | 26 ± 2 | 26 ± 2 | 27 ± 2 ** |
| 26 | 24 ± 3 | 23 ± 2 | 25 ± 2 | 26 ± 3 |
| Number of males | 6 | 0 | 6 | 6 |
| Days of recovery | | | | |
| 2 | 26 ± 2 | - | 26 ± 1 | 26 ± 3 |
| 5 | 29 ± 2 | - | 28 ± 2 | 26 ± 3 |
| 9 | 29 ± 3 | - | 27 ± 3 | 28 ± 4 |
| 12 | 29 ± 2 | - | 28 ± 3 | 29 ± 3 |

Each value shows mean (g/day) ± S.D.

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Table 6. Food consumption in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 12 | 6 | 12 | 11 |
| Days of administration | | | | |
| 2 | 15 ± 2 | 15 ± 4 | 16 ± 3 | 10 ± 5 ** |
| 5 | 15 ± 2 | 18 ± 3 | 17 ± 2 | 16 ± 4 |
| 9 | 14 ± 3 | 17 ± 4 | 16 ± 2 | 17 ± 4 |
| 12 | 17 ± 2 | 17 ± 4 | 18 ± 2 | 19 ± 3 |
| 16 | 17 ± 1 | 17 ± 3 | 17 ± 2 | 20 ± 2 ** |
| 19 | 17 ± 2 | 20 ± 2 * | 19 ± 2 | 17 ± 3 |
| 23 | 16 ± 1 | 19 ± 2 | 17 ± 2 | 19 ± 3 ** |
| 26 | 16 ± 2 | 19 ± 2 | 16 ± 3 | 17 ± 4 |
| Number of females | 6 | 0 | 6 | 6 |
| Days of recovery | | | | |
| 2 | 19 ± 2 | - | 20 ± 4 | 22 ± 3 |
| 5 | 18 ± 5 | - | 21 ± 3 | 21 ± 3 |
| 9 | 16 ± 3 | - | 19 ± 3 | 21 ± 5 |
| 12 | 20 ± 1 | - | 21 ± 2 | 21 ± 3 |

Each value shows mean (g/day) ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Table 7. Water consumption in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 12 | 6 | 12 | 12 |
| Days of administration | | | | |
| 2 | 30 ± 3 | 31 ± 4 | 31 ± 2 | 28 ± 5 |
| 5 | 32 ± 4 | 30 ± 4 | 31 ± 3 | 32 ± 12 |
| 9 | 32 ± 4 | 33 ± 4 | 31 ± 4 | 38 ± 4 ** |
| 12 | 34 ± 5 | 34 ± 4 | 33 ± 4 | 43 ± 5 ** |
| 16 | 36 ± 4 | 36 ± 5 | 36 ± 5 | 48 ± 7 ** |
| 19 | 37 ± 5 | 36 ± 5 | 39 ± 5 | 54 ± 8 ** |
| 23 | 35 ± 4 | 35 ± 3 | 37 ± 4 | 51 ± 6 ** |
| 26 | 35 ± 6 | 37 ± 4 | 39 ± 5 | 53 ± 7 ** |
| Number of males | 6 | 0 | 6 | 6 |
| Days of recovery | | | | |
| 2 | 35 ± 3 | - | 35 ± 4 | 41 ± 8 |
| 5 | 36 ± 4 | - | 36 ± 2 | 39 ± 6 |
| 9 | 36 ± 5 | - | 32 ± 4 | 35 ± 6 |
| 12 | 35 ± 4 | - | 34 ± 3 | 37 ± 5 |

Each value shows mean (g/day) ± S.D.

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

Table 8. Water consumption in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 12 | 6 | 12 | 11 |
| Days of administration | | | | |
| 2 | 24 ± 3 | 24 ± 5 | 27 ± 5 | 21 ± 13 |
| 5 | 23 ± 3 | 26 ± 4 | 27 ± 5 | 49 ± 27 ## |
| 9 | 19 ± 5 | 23 ± 7 | 25 ± 5 * | 34 ± 6 ** |
| 12 | 28 ± 3 | 28 ± 4 | 30 ± 4 | 43 ± 11 ## |
| 16 | 24 ± 3 | 25 ± 6 | 27 ± 6 | 42 ± 12 ## |
| 19 | 27 ± 3 | 31 ± 5 | 31 ± 4 | 41 ± 14 # |
| 23 | 27 ± 3 | 30 ± 5 | 31 ± 3 | 42 ± 9 ## |
| 26 | 22 ± 3 | 27 ± 5 | 24 ± 5 | 40 ± 11 ## |
| Number of females | 6 | 0 | 6 | 6 |
| Days of recovery | | | | |
| 2 | 26 ± 4 | - | 28 ± 7 | 40 ± 7 ** |
| 5 | 22 ± 7 | - | 29 ± 7 | 31 ± 5 |
| 9 | 22 ± 9 | - | 25 ± 6 | 32 ± 9 |
| 12 | 27 ± 4 | - | 28 ± 4 | 33 ± 7 |

Each value shows mean (g/day) ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Significantly different from the control group (#: $p<0.05$, ##: $p<0.01$ by Steel's test).

Table 9. FOB of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Observation of animals in cages | | | | | |
| Posture | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Palpebral closure | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Biting behavior | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Clonic convulsions | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |

Findings were graded as follows: (Continued)

Posture: 1: Prone or recumbent position, 2: resting normally, 3: moving or running about, 4: jumping.
Palpebral closure: 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.
Biting behavior: 1: Not observed, 2: observed.
Clonic convulsions: 1: Not observed, 2: jaw convulsions, 3: tremor.

Table 9. (Continued) FOB of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Observation of animals in cages | | | | | |
| Tonic convulsions | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |

Findings were graded as follows: (Continued)

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

Table 9. (Continued) FOB of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Observation of animals on observer's palm | | | | | |
| Ease of removal from cage | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Ease of handling | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Muscle tone | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Fur conditions | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |

(Continued)

Findings were graded as follows:

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

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

Muscle tone: 1: Decreased, 2: normal, 3: increased.

Fur conditions: 1: Normal, 2: slightly soiled, 3: markedly soiled.

Table 9. (Continued) FOB of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Observation of animals on observer's palm | | | | | |
| Lacrimation | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Salivation | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.3 ( 1-2 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.3 ( 1-2 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.7 ( 1-2 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.3 ( 1-2 ) |
| Respiration | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |

Findings were graded as follows: (Continued)

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Table 9. (Continued) FOB of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Open-field test | | | | | |
| Frequency of rearing | Pre | 2.3 ± 2.3 | 3.7 ± 2.0 | 2.0 ± 2.1 | 4.8 ± 4.0 |
| Mean ± S.D. | Day 7 | 1.5 ± 1.4 | 3.3 ± 2.8 | 5.3 ± 4.0 | 5.7 ± 4.3 |
| | Day 14 | 1.2 ± 1.2 | 1.0 ± 1.3 | 1.0 ± 1.1 | 2.5 ± 2.3 |
| | Day 21 | 1.8 ± 2.6 | 6.2 ± 5.5 | 5.3 ± 2.7 | 5.5 ± 4.6 |
| | Day 27 | 0.8 ± 1.6 | 2.0 ± 3.5 | 2.2 ± 1.9 | 5.0 ± 5.7 |
| Frequency of grooming | Pre | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Mean ± S.D. | Day 7 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| | Day 14 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| | Day 21 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.2 ± 0.4 | 0.0 ± 0.0 |
| | Day 27 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Gait | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Palpebral closure | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |

Frequency of rearing (during a 2-minute period).

Frequency of grooming (during a 2-minute period).

Findings were graded as follows:

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

Palpebral closure: 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

(Continued)

Table 9. (Continued) FOB of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Open-field test | | | | | |
| Consciousness | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Behavioral abnormalities | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Righting reflex | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |

Findings were graded as follows:

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

Behavioral abnormalities: 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

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

Table 10. FOB of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | | |
|---|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 | |
| Number of females | | 6 | 6 | 6 | 6 | |
| Observation of animals in cages | | | | | | |
| Posture | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| Palpebral closure | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| Biting behavior | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| Clonic convulsions | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |

Figures in brackets indicate number of females. (Continued)

Findings were graded as follows:

| | |
|---|---|
| Posture | 1: Prone or recumbent position, 2: resting normally, 3: moving or running about, 4: jumping. |
| Palpebral closure | 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed. |
| Biting behavior | 1: Not observed, 2: observed. |
| Clonic convulsions | 1: Not observed, 2: jaw convulsions, 3: tremor. |

Table 10. (Continued) FOB of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | | |
|---|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 | |
| Number of females | | 6 | 6 | 6 | 6 | |
| Observation of animals in cages | | | | | | |
| Tonic convulsions | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |

Figures in brackets indicate number of females. (Continued)

Findings were graded as follows:

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

Table 10. (Continued) FOB of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | | |
|---|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 | |
| Number of females | | 6 | 6 | 6 | 6 | |
| Observation of animals on observer's palm | | | | | | |
| Ease of removal from cage | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| Ease of handling | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| Muscle tone | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| Fur conditions | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |

Figures in brackets indicate number of females. (Continued)

Findings were graded as follows:

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

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

Muscle tone: 1: Decreased, 2: normal, 3: increased.

Fur conditions: 1: Normal, 2: slightly soiled, 3: markedly soiled.

Table 10. (Continued) FOB of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | | |
|---|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 | |
| Number of females | | 6 | 6 | 6 | 6 | |
| Observation of animals on observer's palm | | | | | | |
| Lacrimation | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| Salivation | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.2 ( 1-2 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.6 ( 1-2 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.6 ( 1-2 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.8 ( 1-3 ) | [5] |
| Respiration | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |

Figures in brackets indicate number of females. (Continued)

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Table 10. (Continued) FOB of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | | |
|---|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 | |
| Number of females | | 6 | 6 | 6 | 6 | |
| Open-field test | | | | | | |
| Frequency of rearing | Pre | 4.3 ± 1.9 | 4.2 ± 2.9 | 0.8 ± 0.8 * | 3.8 ± 2.5 | |
| Mean ± S.D. | Day 7 | 10.0 ± 4.1 | 5.8 ± 3.3 | 7.8 ± 2.6 | 5.0 ± 2.1 * | [5] |
| | Day 14 | 8.5 ± 4.6 | 6.5 ± 3.1 | 6.2 ± 4.0 | 5.2 ± 2.2 | [5] |
| | Day 21 | 9.2 ± 4.0 | 6.0 ± 3.3 | 5.3 ± 6.5 | 5.8 ± 7.2 | [5] |
| | Day 27 | 5.7 ± 3.1 | 5.0 ± 4.3 | 2.3 ± 2.9 | 4.4 ± 1.9 | [5] |
| Frequency of grooming | Pre | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | |
| Mean ± S.D. | Day 7 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | [5] |
| | Day 14 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | [5] |
| | Day 21 | 0.0 ± 0.0 | 0.2 ± 0.4 | 0.2 ± 0.4 | 0.2 ± 0.4 | [5] |
| | Day 27 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | [5] |
| Gait | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| Palpebral closure | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |

Frequency of rearing (during a 2-minute period).

(Continued)

Frequency of grooming (during a 2-minute period).

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

Figures in brackets indicate number of females.

Findings were graded as follows:

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

Palpebral closure: 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Table 10. (Continued) FOB of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | | |
|---|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 | |
| Number of females | | 6 | 6 | 6 | 6 | |
| Open-field test | | | | | | |
| Consciousness | Pre | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | |
| Mean (range) | Day 7 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 14 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 21 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| | Day 27 | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | [5] |
| Behavioral abnormalities | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| Righting reflex | Pre | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | |
| Mean (range) | Day 7 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 14 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 21 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |
| | Day 27 | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | [5] |

Figures in brackets indicate number of females.
Findings were graded as follows:
Consciousness 1: Comatose; no response, 2: exploring behavior, 3: excited and moving spasmodically.
Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.
Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Table 11. Sensory response of male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 6 | 6 | 6 | 6 |
| Pupillary reflex | | | | |
| Mean (range) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Approaching behavior | | | | |
| Mean (range) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Response to touch | | | | |
| Mean (range) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Auditory reflex | | | | |
| Mean (range) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Pain reflex | | | | |
| Mean (range) | 3.0 ( 3 ) | 3.0 ( 3 ) | 3.0 ( 3 ) | 3.0 ( 3 ) |

Findings were graded as follows:

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

Table 12. Sensory response of female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 6 | 6 | 6 | 5 |
| Pupillary reflex | | | | |
| Mean (range) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) | 1.0 ( 1 ) |
| Approaching behavior | | | | |
| Mean (range) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Response to touch | | | | |
| Mean (range) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Auditory reflex | | | | |
| Mean (range) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) | 2.0 ( 2 ) |
| Pain reflex | | | | |
| Mean (range) | 3.0 ( 3 ) | 3.0 ( 3 ) | 3.0 ( 3 ) | 3.0 ( 3 ) |

Findings were graded as follows:

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

Table 13. Grip strength of male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 6 | 6 | 6 | 6 |
| Forelimb | 1407 ± 177 | 1295 ± 112 | 1262 ± 84 | 1145 ± 202 * |
| Hindlimb | 399 ± 45 | 329 ± 33 * | 329 ± 41 * | 286 ± 52 ** |

Each value shows mean (g) ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Table 14. Grip strength of female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 6 | 6 | 6 | 5 |
| Forelimb | 1053 ± 82 | 1089 ± 142 | 1005 ± 162 | 949 ± 179 |
| Hindlimb | 272 ± 14 | 246 ± 60 | 265 ± 35 | 227 ± 44 |

Each value shows mean (g) ± S.D.

Table 15. Spontaneous motor activity of male rats on termination of administration priod in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 6 | 6 | 6 | 6 |
| Ambulatory counts | | | | |
| Minutes after administration | | | | |
| 70 | 299 ± 120 | 307 ± 209 | 294 ± 115 | 428 ± 92 |
| 80 | 163 ± 106 | 197 ± 167 | 278 ± 108 | 282 ± 131 |
| 90 | 134 ± 126 | 109 ± 112 | 106 ± 55 | 154 ± 165 |
| 100 | 47 ± 60 | 73 ± 88 | 261 ± 533 | 78 ± 91 |
| 110 | 80 ± 133 | 123 ± 106 | 227 ± 394 | 4 ± 11 |
| 120 | 3 ± 6 | 44 ± 63 | 57 ± 68 | 56 ± 137 |
| Total | 725 ± 432 | 852 ± 617 | 1223 ± 955 | 1003 ± 503 |
| Vertical counts | | | | |
| Minutes after administration | | | | |
| 70 | 44 ± 15 | 45 ± 33 | 58 ± 24 | 63 ± 8 |
| 80 | 22 ± 11 | 27 ± 23 | 42 ± 24 | 33 ± 13 |
| 90 | 19 ± 8 | 20 ± 21 | 22 ± 14 | 19 ± 21 |
| 100 | 4 ± 6 | 12 ± 17 | 6 ± 9 | 12 ± 16 |
| 110 | 10 ± 16 | 15 ± 12 | 8 ± 8 | 2 ± 4 |
| 120 | 0 ± 1 | 10 ± 16 | 9 ± 10 | 10 ± 23 |
| Total | 99 ± 41 | 128 ± 113 | 144 ± 65 | 138 ± 74 |

Each value shows mean ± S.D.

Table 16. Spontaneous motor activity of female rats on termination of administration priod in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 6 | 6 | 6 | 5 |
| Ambulatory counts | | | | |
| Minutes after administration | | | | |
| 70 | 387 ± 261 | 352 ± 240 | 404 ± 89 | 107 ± 89 |
| 80 | 264 ± 136 | 203 ± 78 | 165 ± 140 | 119 ± 142 |
| 90 | 45 ± 66 | 91 ± 102 | 94 ± 116 | 97 ± 90 |
| 100 | 37 ± 91 | 77 ± 111 | 145 ± 170 | 19 ± 25 |
| 110 | 12 ± 30 | 31 ± 74 | 59 ± 100 | 36 ± 80 |
| 120 | 18 ± 20 | 10 ± 24 | 70 ± 172 | 44 ± 96 |
| Total | 763 ± 480 | 763 ± 428 | 938 ± 398 | 422 ± 295 |
| Vertical counts | | | | |
| Minutes after administration | | | | |
| 70 | 50 ± 27 | 48 ± 28 | 58 ± 24 | 21 ± 24 |
| 80 | 29 ± 19 | 26 ± 11 | 22 ± 18 | 14 ± 14 |
| 90 | 4 ± 7 | 15 ± 19 | 17 ± 23 | 7 ± 6 |
| 100 | 4 ± 9 | 11 ± 16 | 16 ± 18 | 1 ± 3 |
| 110 | 1 ± 2 | 3 ± 6 | 9 ± 14 | 3 ± 7 |
| 120 | 3 ± 5 | 2 ± 3 | 17 ± 41 | 7 ± 15 |
| Total | 90 ± 51 | 105 ± 39 | 139 ± 66 | 53 ± 43 |

Each value shows mean ± S.D.

Table 17. Urinary findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 6 | 6 | 6 | 6 |
| Volume (mL): Mean±S.D. | 10.8 ± 4.2 | 10.2 ± 3.0 | 13.9 ± 4.7 | 18.6 ± 4.7 * |
| Specific gravity: Mean±S.D. | 1.056 ± 0.012 | 1.057 ± 0.012 | 1.051 ± 0.014 | 1.046 ± 0.007 |
| Color | | | | |
| Light yellow | 6 | 6 | 6 | 6 |
| pH | | | | |
| 7.5 | 1 | 0 | 0 | 0 |
| 8.0 | 0 | 0 | 0 | 1 |
| 8.5 | 5 | 5 | 5 | 5 |
| ≧9.0 | 0 | 1 | 1 | 0 |
| Protein | | | | |
| Trace | 2 | 0 | 2 | 1 |
| 30 mg/dL | 4 | 6 | 4 | 5 |
| Glucose | | | | |
| Negative | 6 | 6 | 6 | 6 |
| Ketone body | | | | |
| Negative | 1 | 0 | 0 | 0 |
| Trace | 1 | 1 | 1 | 0 |
| Slight | 4 | 5 | 5 | 6 |
| Bilirubin | | | | |
| Negative | 6 | 6 | 6 | 6 |
| Occult blood | | | | |
| Negative | 6 | 5 | 6 | 6 |
| Marked | 0 | 1 | 0 | 0 |
| Urobilinogen | | | | |
| 0.1 E.U./dL | 5 | 6 | 5 | 6 |
| 1.0 E.U./dL | 1 | 0 | 1 | 0 |

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

Table 17. (Continued) Urinary findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 6 | 6 | 6 | 6 |
| Urinary sediments | | | | |
| Epithelial cells | | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 | 6 |
| Erythrocytes | | | | |
| 0-20 cells/100 fields | 6 | 5 | 6 | 6 |
| 21-100 cells/100fields | 0 | 1 | 0 | 0 |
| Leukocytes | | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 | 6 |
| Casts | | | | |
| Not observed | 6 | 6 | 6 | 6 |
| Crystals | | | | |
| Not observed | 1 | 2 | 2 | 2 |
| Observed | 5 | 4 | 4 | 4 |

Table 18. Urinary findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 6 | 6 | 6 | 5 |
| Volume (mL): Mean±S.D. | 9.2 ± 2.0 | 6.6 ± 1.7 | 10.7 ± 2.5 | 11.9 ± 6.4 |
| Specific gravity: Mean±S.D. | 1.047 ± 0.008 | 1.057 ± 0.012 | 1.047 ± 0.006 | 1.048 ± 0.009 |
| Color | | | | |
| Light yellow | 6 | 6 | 6 | 5 |
| pH | | | | |
| 7.5 | 0 | 1 | 0 | 0 |
| 8.0 | 2 | 2 | 2 | 2 |
| 8.5 | 2 | 3 | 4 | 3 |
| ≧9.0 | 2 | 0 | 0 | 0 |
| Protein | | | | |
| Negative | 2 | 1 | 5 | 5 |
| Trace | 3 | 5 | 1 | 0 |
| 30 mg/dL | 1 | 0 | 0 | 0 |
| Glucose | | | | |
| Negative | 6 | 6 | 6 | 5 |
| Ketone body | | | | |
| Negative | 1 | 1 | 1 | 0 |
| Trace | 5 | 2 | 5 | 3 |
| Slight | 0 | 3 | 0 | 2 |
| Bilirubin | | | | |
| Negative | 6 | 6 | 6 | 5 |
| Occult blood | | | | |
| Negative | 6 | 6 | 5 | 5 |
| Trace | 0 | 0 | 1 | 0 |
| Urobilinogen | | | | |
| 0.1 E.U./dL | 4 | 5 | 6 | 5 |
| 1.0 E.U./dL | 2 | 1 | 0 | 0 |

(Continued)

Table 18. (Continued) Urinary findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 6 | 6 | 6 | 5 |
| Urinary sediments | | | | |
| Epithelial cells | | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 | 5 |
| Erythrocytes | | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 | 5 |
| Leukocytes | | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 | 5 |
| Casts | | | | |
| Not observed | 6 | 6 | 6 | 5 |
| Crystals | | | | |
| Not observed | 2 | 2 | 2 | 1 |
| Observed | 4 | 4 | 4 | 4 |

Table 19. Urinary findings in male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | |
|---|---|---|---|
| mg/kg | 0 | 200 | 1000 |
| Number of males | 6 | 6 | 6 |
| Volume (mL): Mean±S.D. | 16.7 ± 6.4 | 16.0 ± 7.0 | 14.5 ± 6.5 |
| Specific gravity: Mean±S.D. | 1.029 ± 0.006 | 1.031 ± 0.010 | 1.032 ± 0.007 |
| Color | | | |
| Light yellow | 6 | 6 | 6 |
| pH | | | |
| 8.5 | 6 | 5 | 5 |
| ≧9.0 | 0 | 1 | 1 |
| Protein | | | |
| Trace | 2 | 1 | 3 |
| 30 mg/dL | 3 | 4 | 3 |
| 100 mg/dL | 1 | 1 | 0 |
| Glucose | | | |
| Negative | 6 | 6 | 6 |
| Ketone body | | | |
| Negative | 0 | 0 | 1 |
| Trace | 4 | 3 | 5 |
| Slight | 2 | 3 | 0 |
| Bilirubin | | | |
| Negative | 6 | 5 | 6 |
| Slight | 0 | 1 | 0 |
| Occult blood | | | |
| Negative | 6 | 5 | 4 |
| Trace | 0 | 0 | 1 |
| Slight | 0 | 1 | 1 |
| Urobilinogen | | | |
| 0.1 E.U./dL | 6 | 6 | 6 |

(Continued)

Table 19. (Continued) Urinary findings in male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | |
|---|---|---|---|
| mg/kg | 0 | 200 | 1000 |
| Number of males | 6 | 6 | 6 |
| Urinary sediments | | | |
| Epithelial cells | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 |
| Erythrocytes | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 |
| Leukocytes | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 |
| Casts | | | |
| Not observed | 6 | 6 | 6 |
| Crystals | | | |
| Not observed | 2 | 2 | 2 |
| Observed | 4 | 4 | 4 |

Table 20. Urinary findings in female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | |
|---|---|---|---|
| mg/kg | 0 | 200 | 1000 |
| Number of females | 6 | 6 | 6 |
| Volume (mL): Mean±S.D. | 9.3 ± 1.7 | 11.5 ± 4.9 | 11.9 ± 2.9 |
| Specific gravity: Mean±S.D. | 1.053 ± 0.012 | 1.045 ± 0.011 | 1.042 ± 0.009 |
| Color | | | |
| Light yellow | 6 | 6 | 6 |
| pH | | | |
| 6.0 | 1 | 0 | 0 |
| 7.0 | 1 | 1 | 0 |
| 7.5 | 1 | 1 | 0 |
| 8.0 | 1 | 1 | 1 |
| 8.5 | 2 | 3 | 5 |
| Protein | | | |
| Negative | 1 | 2 | 6 |
| Trace | 3 | 3 | 0 |
| 30 mg/dL | 2 | 1 | 0 |
| Glucose | | | |
| Negative | 6 | 6 | 6 |
| Ketone body | | | |
| Negative | 4 | 2 | 6 |
| Trace | 2 | 4 | 0 |
| Bilirubin | | | |
| Negative | 6 | 6 | 6 |
| Occult blood | | | |
| Negative | 6 | 5 | 5 |
| Trace | 0 | 1 | 1 |
| Urobilinogen | | | |
| 0.1 E.U./dL | 5 | 5 | 6 |
| 1.0 E.U./dL | 1 | 1 | 0 |

(Continued)

Table 20. (Continued) Urinary findings in female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | |
|---|---|---|---|
| mg/kg | 0 | 200 | 1000 |
| Number of females | 6 | 6 | 6 |
| Urinary sediments | | | |
| Epithelial cells | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 |
| Erythrocytes | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 |
| Leukocytes | | | |
| 0-20 cells/100 fields | 6 | 6 | 6 |
| Casts | | | |
| Not observed | 6 | 6 | 6 |
| Crystals | | | |
| Not observed | 3 | 1 | 1 |
| Observed | 3 | 5 | 5 |

Table 21. Hematological findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| RBC | ($10^4$/μL) | 796 ± 46 | 792 ± 37 | 815 ± 32 | 784 ± 18 |
| Hemoglobin | (g/dL) | 15.2 ± 0.6 | 15.3 ± 0.7 | 15.6 ± 0.5 | 15.2 ± 0.6 |
| Hematocrit | (%) | 43.1 ± 1.9 | 43.4 ± 1.9 | 44.2 ± 1.2 | 43.8 ± 1.2 |
| MCV | (fL) | 54.3 ± 3.7 | 54.9 ± 1.7 | 54.3 ± 1.5 | 55.9 ± 2.3 |
| MCH | (pg) | 19.2 ± 1.2 | 19.3 ± 0.5 | 19.1 ± 0.6 | 19.4 ± 1.0 |
| MCHC | (g/dL) | 35.3 ± 0.2 | 35.2 ± 0.4 | 35.2 ± 0.2 | 34.8 ± 0.5 |
| Platelet | ($10^4$/μL) | 124.0 ± 9.2 | 115.6 ± 10.5 | 114.4 ± 14.6 | 115.2 ± 16.3 |
| Reticulocyte | (%) | 3.00 ± 0.54 | 3.09 ± 0.54 | 2.93 ± 0.14 | 3.00 ± 0.45 |
| PT | (sec.) | 27.2 ± 6.8 | 20.0 ± 3.6 | 18.1 ± 1.3 # | 18.6 ± 4.6 |
| APTT | (sec.) | 27.1 ± 1.4 | 23.9 ± 3.5 | 22.0 ± 1.7 ** | 20.8 ± 2.3 ** |
| Fibrinogen | (mg/dL) | 208.7 ± 20.7 | 203.6 ± 16.8 | 203.1 ± 12.6 | 214.2 ± 21.8 |
| WBC | ($10^2$/μL) | 77.5 ± 22.4 | 70.0 ± 12.7 | 55.2 ± 12.1 | 66.5 ± 18.4 |
| Differential leukocyte (%) | | | | | |
| Lymphocyte | | 78.8 ± 3.8 | 79.7 ± 6.8 | 82.3 ± 6.2 | 84.7 ± 2.2 |
| Neutrophil | | 17.7 ± 3.7 | 16.4 ± 6.6 | 14.0 ± 5.5 | 10.9 ± 1.6 # |
| Eosinophil | | 1.2 ± 0.4 | 1.2 ± 0.4 | 0.9 ± 0.4 | 0.9 ± 0.2 |
| Basophil | | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.1 |
| Monocyte | | 2.4 ± 0.7 | 2.8 ± 0.4 | 2.8 ± 0.8 | 3.5 ± 1.1 * |

Each value shows mean ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

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

Table 22. Hematological findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of females | | 6 | 6 | 6 | 5 |
| RBC | ($10^4$/μL) | 759 ± 50 | 767 ± 21 | 761 ± 25 | 737 ± 30 |
| Hemoglobin | (g/dL) | 14.4 ± 0.8 | 14.5 ± 0.5 | 14.6 ± 0.5 | 13.9 ± 0.7 |
| Hematocrit | (%) | 40.0 ± 1.8 | 40.5 ± 1.3 | 40.9 ± 1.1 | 39.8 ± 1.7 |
| MCV | (fL) | 52.7 ± 2.1 | 52.9 ± 1.8 | 53.8 ± 0.8 | 54.0 ± 0.8 |
| MCH | (pg) | 19.0 ± 0.8 | 18.9 ± 0.6 | 19.2 ± 0.4 | 18.8 ± 0.3 |
| MCHC | (g/dL) | 36.1 ± 0.6 | 35.7 ± 0.3 | 35.7 ± 0.4 | 34.8 ± 0.4 ** |
| Platelet | ($10^4$/μL) | 113.7 ± 10.5 | 120.6 ± 5.9 | 118.9 ± 5.4 | 114.4 ± 13.5 |
| Reticulocyte | (%) | 2.72 ± 0.53 | 3.01 ± 0.36 | 2.81 ± 0.29 | 2.78 ± 0.43 |
| PT | (sec.) | 15.1 ± 0.7 | 15.5 ± 0.6 | 17.2 ± 0.5 ** | 16.0 ± 1.0 |
| APTT | (sec.) | 17.5 ± 0.9 | 17.0 ± 0.6 | 17.3 ± 1.0 | 16.1 ± 1.4 |
| Fibrinogen | (mg/dL) | 180.5 ± 11.6 | 179.3 ± 11.9 | 168.0 ± 19.2 | 188.0 ± 11.7 |
| WBC | ($10^2$/μL) | 57.6 ± 26.0 | 59.5 ± 16.2 | 45.7 ± 10.1 | 44.3 ± 15.5 |
| Differential leukocyte (%) | | | | | |
| Lymphocyte | | 79.5 ± 5.6 | 81.8 ± 7.2 | 80.2 ± 3.9 | 85.2 ± 3.1 |
| Neutrophil | | 16.3 ± 5.1 | 14.6 ± 7.3 | 14.5 ± 3.3 | 9.8 ± 2.9 |
| Eosinophil | | 1.6 ± 0.5 | 1.7 ± 0.9 | 1.8 ± 0.7 | 1.5 ± 0.5 |
| Basophil | | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Monocyte | | 2.6 ± 0.7 | 1.9 ± 0.5 | 3.5 ± 1.2 | 3.5 ± 0.9 |

Each value shows mean ± S.D.

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

Table 23. Hematological findings in male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | |
|---|---|---|---|---|
| mg/kg | | 0 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 |
| RBC | ($10^4$/μL) | 854 ± 35 | 855 ± 18 | 846 ± 38 |
| Hemoglobin | (g/dL) | 15.6 ± 0.1 | 15.6 ± 0.4 | 15.0 ± 0.5 * |
| Hematocrit | (%) | 43.3 ± 0.7 | 43.4 ± 1.0 | 41.9 ± 1.5 |
| MCV | (fL) | 50.8 ± 2.8 | 50.8 ± 1.0 | 49.5 ± 1.1 |
| MCH | (pg) | 18.3 ± 0.8 | 18.2 ± 0.3 | 17.7 ± 0.4 |
| MCHC | (g/dL) | 36.1 ± 0.5 | 35.9 ± 0.4 | 35.8 ± 0.4 |
| Platelet | ($10^4$/μL) | 121.0 ± 8.1 | 117.9 ± 13.0 | 118.0 ± 4.1 |
| Reticulocyte | (%) | 3.26 ± 0.48 | 3.08 ± 0.61 | 3.11 ± 0.35 |
| PT | (sec.) | 19.2 ± 2.6 | 20.7 ± 2.6 | 18.5 ± 5.0 |
| APTT | (sec.) | 23.1 ± 2.1 | 23.2 ± 2.3 | 22.1 ± 2.4 |
| Fibrinogen | (mg/dL) | 209.1 ± 13.8 | 201.8 ± 11.8 | 200.1 ± 13.9 |
| WBC | ($10^2$/μL) | 69.3 ± 17.5 | 73.8 ± 28.1 | 58.8 ± 11.9 |
| Differential leukocyte (%) | | | | |
| Lymphocyte | | 77.3 ± 3.5 | 83.0 ± 5.8 | 80.2 ± 5.3 |
| Neutrophil | | 18.3 ± 3.3 | 13.1 ± 5.0 | 15.1 ± 3.9 |
| Eosinophil | | 1.8 ± 0.3 | 1.8 ± 0.8 | 1.8 ± 0.9 |
| Basophil | | 0.1 ± 0.1 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Monocyte | | 2.5 ± 0.8 | 2.1 ± 0.3 | 3.0 ± 1.1 |

Each value shows mean ± S.D.

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

Table 24. Hematological findings in female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | |
|---|---|---|---|---|
| mg/kg | | 0 | 200 | 1000 |
| Number of females | | 6 | 6 | 6 |
| RBC | ($10^4$/μL) | 793 ± 47 | 793 ± 41 | 772 ± 28 |
| Hemoglobin | (g/dL) | 14.4 ± 0.5 | 14.8 ± 0.7 | 14.3 ± 0.5 |
| Hematocrit | (%) | 39.7 ± 1.3 | 40.6 ± 2.0 | 39.9 ± 0.9 |
| MCV | (fL) | 50.2 ± 1.5 | 51.3 ± 1.0 | 51.6 ± 1.0 |
| MCH | (pg) | 18.2 ± 0.6 | 18.6 ± 0.2 | 18.5 ± 0.5 |
| MCHC | (g/dL) | 36.4 ± 0.2 | 36.4 ± 0.4 | 35.8 ± 0.4 * |
| Platelet | ($10^4$/μL) | 125.3 ± 13.9 | 106.4 ± 17.3 | 128.9 ± 14.5 |
| Reticulocyte | (%) | 3.00 ± 0.41 | 2.90 ± 0.37 | 2.94 ± 0.92 |
| PT | (sec.) | 15.1 ± 0.6 | 15.4 ± 0.5 | 14.9 ± 0.6 |
| APTT | (sec.) | 17.7 ± 0.6 | 17.4 ± 0.3 | 17.8 ± 1.0 |
| Fibrinogen | (mg/dL) | 175.2 ± 13.3 | 172.2 ± 9.0 | 196.5 ± 15.0 * |
| WBC | ($10^2$/μL) | 48.4 ± 16.7 | 48.9 ± 12.8 | 49.7 ± 14.4 |
| Differential leukocyte (%) | | | | |
| Lymphocyte | | 79.2 ± 6.6 | 80.8 ± 4.4 | 81.5 ± 5.8 |
| Neutrophil | | 15.7 ± 5.7 | 14.5 ± 3.8 | 14.1 ± 5.3 |
| Eosinophil | | 2.5 ± 1.4 | 2.2 ± 0.8 | 1.9 ± 0.5 |
| Basophil | | 0.0 ± 0.0 | 0.0 ± 0.0 | 0.0 ± 0.0 |
| Monocyte | | 2.7 ± 1.3 | 2.5 ± 0.8 | 2.6 ± 0.9 |

Each value shows mean ± S.D.

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

Table 25. Blood chemical findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| AST | (IU/L) | 76.1 ± 11.5 | 83.2 ± 19.3 | 90.0 ± 11.2 | 84.4 ± 12.0 |
| ALT | (IU/L) | 28.4 ± 14.4 | 27.4 ± 6.3 | 25.5 ± 3.5 | 36.7 ± 18.6 |
| ALP | (IU/L) | 555.0 ± 75.8 | 503.7 ± 96.0 | 549.4 ± 152.5 | 580.8 ± 155.6 |
| γ-GTP | (IU/L) | 0.69 ± 0.39 | 0.72 ± 0.16 | 0.76 ± 0.21 | 1.10 ± 0.32 |
| Total protein | (g/dL) | 5.38 ± 0.17 | 5.23 ± 0.23 | 5.41 ± 0.27 | 5.62 ± 0.44 |
| Albumin | (g/dL) | 2.87 ± 0.18 | 2.78 ± 0.13 | 2.91 ± 0.11 | 3.02 ± 0.22 |
| A/G | | 1.15 ± 0.09 | 1.14 ± 0.09 | 1.16 ± 0.05 | 1.17 ± 0.07 |
| Total bilirubin | (mg/dL) | 0.11 ± 0.01 | 0.10 ± 0.01 | 0.12 ± 0.01 | 0.12 ± 0.01 |
| Urea nitrogen | (mg/dL) | 15.4 ± 5.9 | 16.7 ± 3.3 | 20.2 ± 2.2 | 17.5 ± 3.7 |
| Creatinine | (mg/dL) | 0.25 ± 0.02 | 0.22 ± 0.03 | 0.22 ± 0.02 | 0.22 ± 0.02 * |
| Glucose | (mg/dL) | 111.3 ± 6.6 | 114.6 ± 9.3 | 121.7 ± 14.4 | 111.3 ± 8.5 |
| Total cholesterol | (mg/dL) | 47.3 ± 9.0 | 42.3 ± 12.9 | 44.2 ± 10.3 | 47.5 ± 19.1 |
| Triglyceride | (mg/dL) | 35.4 ± 14.1 | 18.3 ± 5.6 | 26.1 ± 8.5 | 36.2 ± 39.5 |
| Na | (mEq/L) | 144.2 ± 1.0 | 144.6 ± 1.0 | 143.4 ± 0.8 | 143.7 ± 0.7 |
| K | (mEq/L) | 4.14 ± 0.25 | 4.29 ± 0.14 | 4.48 ± 0.23 * | 4.49 ± 0.17 * |
| Cl | (mEq/L) | 104.7 ± 0.6 | 105.8 ± 0.5 # | 105.0 ± 0.6 | 104.0 ± 1.6 |
| Ca | (mg/dL) | 9.6 ± 0.3 | 9.3 ± 0.2 | 9.3 ± 0.3 | 9.6 ± 0.5 |
| Inorganic phosphate | (mg/dL) | 8.2 ± 0.7 | 8.5 ± 0.4 | 8.6 ± 0.4 | 8.5 ± 0.4 |

Each value shows mean ± S.D.

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

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

Table 26. Blood chemical findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of females | | 6 | 6 | 6 | 5 |
| AST | (IU/L) | 77.9 ± 13.2 | 87.6 ± 18.2 | 75.4 ± 3.2 | 64.7 ± 8.5 |
| ALT | (IU/L) | 22.6 ± 1.9 | 21.8 ± 2.4 | 23.3 ± 2.3 | 30.5 ± 7.6 |
| ALP | (IU/L) | 306.0 ± 103.1 | 342.4 ± 44.8 | 385.8 ± 37.3 | 347.7 ± 84.3 |
| γ-GTP | (IU/L) | 0.81 ± 0.20 | 1.03 ± 0.47 | 1.05 ± 0.31 | 1.24 ± 0.33 |
| Total protein | (g/dL) | 5.47 ± 0.18 | 5.54 ± 0.26 | 5.59 ± 0.18 | 5.62 ± 0.28 |
| Albumin | (g/dL) | 3.04 ± 0.13 | 3.07 ± 0.17 | 3.29 ± 0.10 * | 3.14 ± 0.19 |
| A/G | | 1.26 ± 0.11 | 1.24 ± 0.08 | 1.43 ± 0.07 ** | 1.27 ± 0.03 |
| Total bilirubin | (mg/dL) | 0.11 ± 0.01 | 0.10 ± 0.01 | 0.11 ± 0.01 | 0.11 ± 0.00 |
| Urea nitrogen | (mg/dL) | 15.2 ± 2.0 | 19.7 ± 3.0 | 21.1 ± 4.0 * | 18.4 ± 3.5 |
| Creatinine | (mg/dL) | 0.27 ± 0.01 | 0.27 ± 0.04 | 0.26 ± 0.02 | 0.24 ± 0.01 # |
| Glucose | (mg/dL) | 111.4 ± 10.1 | 110.6 ± 3.6 | 109.6 ± 6.3 | 103.7 ± 7.7 |
| Total cholesterol | (mg/dL) | 63.3 ± 8.5 | 57.8 ± 14.4 | 47.6 ± 8.7 * | 82.5 ± 4.3 * |
| Triglyceride | (mg/dL) | 26.9 ± 12.1 | 18.4 ± 7.4 | 27.7 ± 15.7 | 30.6 ± 13.0 |
| Na | (mEq/L) | 143.5 ± 0.9 | 142.7 ± 0.9 | 143.1 ± 1.4 | 142.8 ± 1.1 |
| K | (mEq/L) | 4.12 ± 0.14 | 4.38 ± 0.12 ** | 4.34 ± 0.11 * | 4.38 ± 0.18 * |
| Cl | (mEq/L) | 106.1 ± 0.7 | 107.4 ± 1.3 | 107.5 ± 1.1 | 106.2 ± 1.8 |
| Ca | (mg/dL) | 9.7 ± 0.1 | 9.3 ± 0.1 ** | 9.5 ± 0.1 * | 9.4 ± 0.1 ** |
| Inorganic phosphate | (mg/dL) | 6.9 ± 0.5 | 7.3 ± 0.6 | 7.6 ± 0.4 * | 8.1 ± 0.3 ** |

Each value shows mean ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

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

Table 27. Blood chemical findings in male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | |
|---|---|---|---|---|
| mg/kg | | 0 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 |
| AST | (IU/L) | 82.2 ± 15.2 | 81.4 ± 11.3 | 70.4 ± 8.0 |
| ALT | (IU/L) | 27.6 ± 4.5 | 29.5 ± 2.4 | 27.0 ± 3.2 |
| ALP | (IU/L) | 454.1 ± 139.0 | 477.8 ± 81.9 | 364.7 ± 26.1 |
| γ-GTP | (IU/L) | 0.68 ± 0.12 | 0.76 ± 0.23 | 0.59 ± 0.08 |
| Total protein | (g/dL) | 5.61 ± 0.17 | 5.68 ± 0.22 | 5.55 ± 0.25 |
| Albumin | (g/dL) | 2.86 ± 0.08 | 2.84 ± 0.15 | 2.83 ± 0.07 |
| A/G | | 1.04 ± 0.09 | 1.01 ± 0.10 | 1.04 ± 0.06 |
| Total bilirubin | (mg/dL) | 0.12 ± 0.02 | 0.12 ± 0.02 | 0.11 ± 0.01 |
| Urea nitrogen | (mg/dL) | 15.7 ± 1.6 | 15.8 ± 1.9 | 15.7 ± 1.8 |
| Creatinine | (mg/dL) | 0.26 ± 0.03 | 0.24 ± 0.02 | 0.25 ± 0.03 |
| Glucose | (mg/dL) | 135.4 ± 18.5 | 128.6 ± 16.4 | 119.3 ± 13.6 |
| Total cholesterol | (mg/dL) | 62.1 ± 13.5 | 55.7 ± 8.7 | 72.2 ± 18.5 |
| Triglyceride | (mg/dL) | 45.1 ± 13.8 | 37.5 ± 14.5 | 52.8 ± 15.6 |
| Na | (mEq/L) | 144.0 ± 1.4 | 144.1 ± 1.2 | 144.8 ± 1.1 |
| K | (mEq/L) | 4.23 ± 0.12 | 4.23 ± 0.22 | 4.19 ± 0.22 |
| Cl | (mEq/L) | 103.4 ± 1.2 | 103.8 ± 1.1 | 102.9 ± 1.2 |
| Ca | (mg/dL) | 9.5 ± 0.3 | 9.5 ± 0.3 | 9.7 ± 0.2 |
| Inorganic phosphate | (mg/dL) | 7.0 ± 0.5 | 7.3 ± 0.6 | 7.9 ± 0.7 * |

Each value shows mean ± S.D.

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

Table 28. Blood chemical findings in female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | |
|---|---|---|---|---|
| mg/kg | | 0 | 200 | 1000 |
| Number of females | | 6 | 6 | 6 |
| AST | (IU/L) | 85.7 ± 12.6 | 71.6 ± 7.5 | 76.1 ± 14.9 |
| ALT | (IU/L) | 24.1 ± 2.7 | 21.8 ± 3.0 | 21.0 ± 2.7 |
| ALP | (IU/L) | 248.0 ± 71.7 | 237.6 ± 66.8 | 255.4 ± 58.8 |
| γ-GTP | (IU/L) | 0.68 ± 0.22 | 0.51 ± 0.07 | 1.13 ± 0.20 ** |
| Total protein | (g/dL) | 5.88 ± 0.38 | 5.97 ± 0.41 | 5.99 ± 0.33 |
| Albumin | (g/dL) | 3.19 ± 0.26 | 3.30 ± 0.21 | 3.10 ± 0.17 |
| A/G | | 1.18 ± 0.06 | 1.24 ± 0.07 | 1.08 ± 0.09 |
| Total bilirubin | (mg/dL) | 0.15 ± 0.03 | 0.13 ± 0.02 | 0.14 ± 0.03 |
| Urea nitrogen | (mg/dL) | 17.6 ± 2.0 | 17.9 ± 2.2 | 16.4 ± 2.4 |
| Creatinine | (mg/dL) | 0.31 ± 0.03 | 0.26 ± 0.01 ## | 0.29 ± 0.04 |
| Glucose | (mg/dL) | 117.3 ± 8.7 | 128.7 ± 11.8 | 114.2 ± 13.6 |
| Total cholesterol | (mg/dL) | 68.1 ± 16.4 | 68.1 ± 14.5 | 100.7 ± 12.0 ** |
| Triglyceride | (mg/dL) | 18.7 ± 6.4 | 29.1 ± 11.3 | 37.7 ± 9.7 ** |
| Na | (mEq/L) | 141.6 ± 0.9 | 141.7 ± 1.2 | 142.1 ± 1.2 |
| K | (mEq/L) | 3.99 ± 0.35 | 4.04 ± 0.16 | 4.14 ± 0.09 |
| Cl | (mEq/L) | 105.1 ± 1.2 | 105.1 ± 1.8 | 104.8 ± 2.1 |
| Ca | (mg/dL) | 9.6 ± 0.2 | 9.7 ± 0.4 | 9.7 ± 0.2 |
| Inorganic phosphate | (mg/dL) | 5.9 ± 0.5 | 5.9 ± 0.6 | 6.5 ± 0.3 |

Each value shows mean ± S.D.

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Table 29. Necropsy findings in a dead female rat in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | 1,8-dichlorooctane |
|---|---|
| mg/kg | 1000 |
| Number of females | 1 |
| Findings | |
| Stomach | |
| Red dot | 1 |
| Erosion | 1 |

Table 30. Necropsy findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of males | 6 | 6 | 6 | 6 |
| Findings | | | | |
| Normal | 6 | 6 | 0 | 2 |
| Liver | | | | |
| Discoloration | 0 | 0 | 6 | 4 |

Table 31. Necropsy findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|
| mg/kg | 0 | 40 | 200 | 1000 |
| Number of females | 6 | 6 | 6 | 5 |
| Findings | | | | |
| Normal | 6 | 6 | 4 | 3 |
| Liver | | | | |
| Discoloration | 0 | 0 | 2 | 2 |

Table 32. Necropsy findings in male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | |
|---|---|---|---|
| mg/kg | 0 | 200 | 1000 |
| Number of males | 6 | 6 | 6 |
| Findings | | | |
| Normal | 6 | 5 | 6 |
| Liver | | | |
| Discoloration | 0 | 1 | 0 |

Table 33. Necropsy findings in female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | 1,8-dichlorooctane | |
|---|---|---|---|
| mg/kg | 0 | 200 | 1000 |
| Number of females | 6 | 6 | 6 |
| Findings | | | |
| Normal | 6 | 6 | 6 |

Table 34. Organ weights of a dead female rat in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | 1,8-dichlorooctane |
|---|---|---|
| mg/kg | | 1000 |
| Number of females | | 1 |
| Body weight | (g) | 149 |
| Brain | (g) | 1.61 |
| | (g%) | 1.08 |
| Pituitary | (mg) | 10.2 |
| | (mg%) | 6.8 |
| Salivary glands | (mg) | 318 |
| | (mg%) | 213 |
| Thyroids | (mg) | 19.0 |
| | (mg%) | 12.8 |
| Thymus | (mg) | 521 |
| | (mg%) | 350 |
| Heart | (g) | 0.70 |
| | (g%) | 0.47 |
| Liver | (g) | 6.80 |
| | (g%) | 4.56 |
| Spleen | (mg) | 356 |
| | (mg%) | 239 |
| Kidneys | (g) | 1.88 |
| | (g%) | 1.26 |
| Adrenals | (mg) | 54.0 |
| | (mg%) | 36.2 |
| Ovaries | (mg) | 58.5 |
| | (mg%) | 39.3 |

Table 35. Organ weights of male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 | 6 |
| Body weight | (g) | 358 ± 13 | 346 ± 13 | 343 ± 17 | 339 ± 29 |
| Brain | (g) | 2.03 ± 0.07 | 2.03 ± 0.08 | 1.99 ± 0.07 | 1.95 ± 0.05 |
| | (g%) | 0.57 ± 0.03 | 0.59 ± 0.03 | 0.58 ± 0.04 | 0.58 ± 0.05 |
| Pituitary | (mg) | 14.2 ± 2.5 | 13.8 ± 1.8 | 13.8 ± 2.3 | 14.8 ± 3.6 |
| | (mg%) | 4.0 ± 0.7 | 4.0 ± 0.7 | 4.0 ± 0.7 | 4.3 ± 0.8 |
| Salivary glands | (mg) | 639 ± 65 | 603 ± 49 | 558 ± 46 | 561 ± 59 |
| | (mg%) | 179 ± 17 | 175 ± 16 | 163 ± 12 | 166 ± 17 |
| Thyroids | (mg) | 19.7 ± 5.7 | 22.7 ± 4.1 | 18.2 ± 2.2 | 19.2 ± 2.6 |
| | (mg%) | 5.5 ± 1.6 | 6.5 ± 1.2 | 5.3 ± 0.7 | 5.7 ± 0.5 |
| Thymus | (mg) | 477 ± 107 | 578 ± 88 | 532 ± 83 | 431 ± 34 |
| | (mg%) | 133 ± 28 | 167 ± 25 | 155 ± 24 | 128 ± 16 |
| Heart | (g) | 1.25 ± 0.08 | 1.16 ± 0.06 | 1.16 ± 0.06 | 1.17 ± 0.08 |
| | (g%) | 0.35 ± 0.03 | 0.34 ± 0.02 | 0.34 ± 0.03 | 0.35 ± 0.03 |
| Liver | (g) | 10.31 ± 0.55 | 10.72 ± 0.78 | 13.27 ± 0.83 ** | 16.23 ± 1.52 ** |
| | (g%) | 2.88 ± 0.08 | 3.10 ± 0.25 | 3.88 ± 0.29 ** | 4.79 ± 0.18 ** |
| Spleen | (mg) | 628 ± 78 | 582 ± 91 | 569 ± 96 | 566 ± 122 |
| | (mg%) | 176 ± 23 | 169 ± 31 | 166 ± 31 | 168 ± 40 |
| Kidneys | (g) | 2.48 ± 0.23 | 2.70 ± 0.22 | 2.81 ± 0.17 * | 3.16 ± 0.17 ** |
| | (g%) | 0.69 ± 0.08 | 0.78 ± 0.07 | 0.82 ± 0.06 * | 0.94 ± 0.11 ** |
| Adrenals | (mg) | 64.9 ± 10.7 | 57.5 ± 5.8 | 53.7 ± 7.9 | 60.7 ± 8.4 |
| | (mg%) | 18.1 ± 2.8 | 16.6 ± 1.6 | 15.7 ± 2.2 | 18.0 ± 2.4 |
| Testes | (g) | 2.98 ± 0.09 | 3.26 ± 0.13 | 3.06 ± 0.18 | 3.36 ± 0.30 ** |
| | (g%) | 0.84 ± 0.03 | 0.94 ± 0.04 ## | 0.90 ± 0.08 | 1.00 ± 0.14 |
| Epididymides | (mg) | 808 ± 77 | 873 ± 44 | 849 ± 40 | 821 ± 53 |
| | (mg%) | 226 ± 23 | 253 ± 14 | 248 ± 21 | 244 ± 25 |

Each value shows mean ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Table 36. Organ weights of female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | | |
|---|---|---|---|---|---|
| mg/kg | | 0 | 40 | 200 | 1000 |
| Number of females | | 6 | 6 | 6 | 5 |
| Body weight | (g) | 226 ± 10 | 234 ± 13 | 229 ± 15 | 222 ± 16 |
| Brain | (g) | 1.84 ± 0.10 | 1.84 ± 0.05 | 1.83 ± 0.07 | 1.87 ± 0.05 |
| | (g%) | 0.82 ± 0.03 | 0.79 ± 0.04 | 0.81 ± 0.06 | 0.84 ± 0.06 |
| Pituitary | (mg) | 16.9 ± 4.7 | 14.7 ± 0.8 | 15.0 ± 3.9 | 15.9 ± 2.0 |
| | (mg%) | 7.5 ± 2.2 | 6.3 ± 0.4 | 6.6 ± 1.7 | 7.2 ± 0.9 |
| Salivary glands | (mg) | 410 ± 24 | 400 ± 49 | 403 ± 24 | 383 ± 46 |
| | (mg%) | 182 ± 8 | 171 ± 19 | 177 ± 11 | 172 ± 15 |
| Thyroids | (mg) | 18.4 ± 3.0 | 19.0 ± 3.5 | 17.2 ± 1.1 | 21.4 ± 2.7 |
| | (mg%) | 8.2 ± 1.0 | 8.1 ± 1.5 | 7.5 ± 0.2 | 9.7 ± 1.6 |
| Thymus | (mg) | 473 ± 92 | 476 ± 66 | 418 ± 66 | 408 ± 121 |
| | (mg%) | 209 ± 39 | 204 ± 29 | 183 ± 23 | 181 ± 44 |
| Heart | (g) | 0.82 ± 0.08 | 0.87 ± 0.09 | 0.80 ± 0.08 | 0.83 ± 0.07 |
| | (g%) | 0.36 ± 0.02 | 0.37 ± 0.02 | 0.35 ± 0.02 | 0.37 ± 0.03 |
| Liver | (g) | 6.97 ± 0.55 | 7.99 ± 0.58 | 9.07 ± 0.98 ** | 10.80 ± 0.85 ** |
| | (g%) | 3.08 ± 0.14 | 3.41 ± 0.09 * | 3.96 ± 0.23 ** | 4.87 ± 0.30 ** |
| Spleen | (mg) | 547 ± 122 | 470 ± 47 | 436 ± 65 | 448 ± 107 |
| | (mg%) | 241 ± 43 | 201 ± 19 | 191 ± 26 * | 200 ± 41 |
| Kidneys | (g) | 1.73 ± 0.15 | 1.78 ± 0.10 | 1.88 ± 0.10 | 2.04 ± 0.14 ** |
| | (g%) | 0.76 ± 0.04 | 0.76 ± 0.02 | 0.82 ± 0.05 | 0.92 ± 0.05 ** |
| Adrenals | (mg) | 71.6 ± 9.0 | 69.0 ± 9.1 | 63.9 ± 6.3 | 70.3 ± 10.4 |
| | (mg%) | 31.8 ± 4.5 | 29.4 ± 2.7 | 28.0 ± 2.4 | 31.9 ± 5.8 |
| Ovaries | (mg) | 82.3 ± 7.7 | 87.7 ± 9.5 | 81.5 ± 12.1 | 86.0 ± 12.5 |
| | (mg%) | 36.5 ± 3.4 | 37.4 ± 2.5 | 35.7 ± 5.2 | 39.2 ± 8.4 |

Each value shows mean ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Table 37. Organ weights of male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | |
|---|---|---|---|---|
| mg/kg | | 0 | 200 | 1000 |
| Number of males | | 6 | 6 | 6 |
| Body weight | (g) | 419 ± 30 | 399 ± 18 | 390 ± 36 |
| Brain | (g) | 2.05 ± 0.10 | 2.06 ± 0.06 | 2.02 ± 0.08 |
| | (g%) | 0.49 ± 0.02 | 0.52 ± 0.02 | 0.52 ± 0.05 |
| Pituitary | (mg) | 15.8 ± 3.8 | 14.5 ± 1.2 | 13.8 ± 1.7 |
| | (mg%) | 3.8 ± 0.7 | 3.6 ± 0.3 | 3.6 ± 0.7 |
| Salivary glands | (mg) | 670 ± 53 | 632 ± 49 | 619 ± 79 |
| | (mg%) | 160 ± 8 | 159 ± 16 | 159 ± 16 |
| Thyroids | (mg) | 22.7 ± 3.0 | 24.2 ± 2.8 | 22.2 ± 2.1 |
| | (mg%) | 5.5 ± 0.8 | 6.1 ± 0.5 | 5.7 ± 0.6 |
| Thymus | (mg) | 493 ± 123 | 470 ± 95 | 499 ± 129 |
| | (mg%) | 118 ± 28 | 118 ± 23 | 127 ± 24 |
| Heart | (g) | 1.42 ± 0.13 | 1.47 ± 0.18 | 1.37 ± 0.16 |
| | (g%) | 0.34 ± 0.02 | 0.37 ± 0.04 | 0.35 ± 0.04 |
| Liver | (g) | 12.14 ± 1.82 | 11.65 ± 0.82 | 11.64 ± 0.97 |
| | (g%) | 2.89 ± 0.29 | 2.92 ± 0.15 | 2.99 ± 0.23 |
| Spleen | (mg) | 700 ± 102 | 677 ± 59 | 690 ± 67 |
| | (mg%) | 167 ± 21 | 170 ± 15 | 177 ± 13 |
| Kidneys | (g) | 2.88 ± 0.33 | 2.98 ± 0.19 | 2.93 ± 0.15 |
| | (g%) | 0.69 ± 0.04 | 0.75 ± 0.04 * | 0.75 ± 0.04 * |
| Adrenals | (mg) | 60.1 ± 9.2 | 55.9 ± 8.6 | 60.7 ± 10.9 |
| | (mg%) | 14.3 ± 1.8 | 14.0 ± 1.8 | 15.7 ± 3.0 |
| Testes | (g) | 3.41 ± 0.28 | 3.27 ± 0.17 | 3.28 ± 0.28 |
| | (g%) | 0.82 ± 0.05 | 0.82 ± 0.06 | 0.85 ± 0.11 |
| Epididymides | (mg) | 1122 ± 77 | 1119 ± 48 | 1085 ± 77 |
| | (mg%) | 269 ± 17 | 281 ± 20 | 279 ± 15 |

Each value shows mean ± S.D.

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

Table 38. Organ weights of female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | | Control | 1,8-dichlorooctane | |
|---|---|---|---|---|
| mg/kg | | 0 | 200 | 1000 |
| Number of females | | 6 | 6 | 6 |
| Body weight | (g) | 244 ± 20 | 253 ± 14 | 250 ± 12 |
| Brain | (g) | 1.96 ± 0.14 | 1.86 ± 0.05 | 1.91 ± 0.06 |
| | (g%) | 0.80 ± 0.08 | 0.74 ± 0.05 | 0.76 ± 0.04 |
| Pituitary | (mg) | 16.3 ± 2.3 | 13.4 ± 0.7 | 14.6 ± 1.2 |
| | (mg%) | 6.7 ± 0.9 | 5.3 ± 0.2 ## | 5.8 ± 0.5 |
| Salivary glands | (mg) | 441 ± 49 | 407 ± 44 | 436 ± 56 |
| | (mg%) | 181 ± 22 | 161 ± 15 | 175 ± 19 |
| Thyroids | (mg) | 17.4 ± 2.8 | 15.8 ± 2.6 | 15.9 ± 1.4 |
| | (mg%) | 7.2 ± 1.5 | 6.3 ± 1.2 | 6.4 ± 0.6 |
| Thymus | (mg) | 416 ± 29 | 389 ± 65 | 498 ± 52 * |
| | (mg%) | 171 ± 16 | 154 ± 21 | 200 ± 23 * |
| Heart | (g) | 0.88 ± 0.07 | 0.92 ± 0.07 | 0.89 ± 0.04 |
| | (g%) | 0.36 ± 0.02 | 0.36 ± 0.03 | 0.36 ± 0.02 |
| Liver | (g) | 6.68 ± 0.72 | 7.24 ± 0.35 | 7.70 ± 0.41 ** |
| | (g%) | 2.73 ± 0.17 | 2.87 ± 0.12 | 3.08 ± 0.06 ** |
| Spleen | (mg) | 542 ± 119 | 482 ± 80 | 509 ± 52 |
| | (mg%) | 222 ± 46 | 192 ± 38 | 204 ± 16 |
| Kidneys | (g) | 1.76 ± 0.19 | 1.87 ± 0.13 | 1.89 ± 0.11 |
| | (g%) | 0.72 ± 0.03 | 0.74 ± 0.07 | 0.76 ± 0.04 |
| Adrenals | (mg) | 70.9 ± 10.4 | 63.6 ± 6.9 | 68.2 ± 7.8 |
| | (mg%) | 29.2 ± 4.8 | 25.3 ± 3.6 | 27.4 ± 3.2 |
| Ovaries | (mg) | 90.2 ± 7.4 | 78.8 ± 16.9 | 84.1 ± 11.7 |
| | (mg%) | 37.0 ± 3.1 | 31.4 ± 7.7 | 33.8 ± 5.5 |

Each value shows mean ± S.D.

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Table 39. Histopathological findings in a dead female rat in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | 1,8-dichlorooctane | | | | | |
|---|---|---|---|---|---|---|
| mg/kg | 1000 | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ |
| Findings | | | | | | |
| Heart | [1][c] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Lung | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Trachea | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Liver | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Pancreas | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Sublingual gland | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Submandibular gland | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Esophagus | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Stomach | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Duodenum | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |

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

a): No abnormality detected.

b): Abnormality detected.

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

Table 39. (Continued) Histopathological findings in a dead female rat in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | 1,8-dichlorooctane | | | | | |
|---|---|---|---|---|---|---|
| mg/kg | 1000 | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ |
| Findings | | | | | | |
| Jejunum | [1][c] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Ileum | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Cecum | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Colon | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Rectum | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Thymus | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Spleen | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Mandibular lymph node | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Mesenteric lymph node | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Kidney | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |

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

a): No abnormality detected.

b): Abnormality detected.

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

Table 39. (Continued) Histopathological findings in a dead female rat in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | 1,8-dichlorooctane | | | | | |
|---|---|---|---|---|---|---|
| mg/kg | 1000 | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ |
| Findings | | | | | | |
| Urinary bladder | [1][c] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Ovary | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Uterus | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Vagina | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Pituitary | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Adrenal | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Thyroid | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Parathyroid | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Cerebrum | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Cerebellum | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |

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

a): No abnormality detected.

b): Abnormality detected.

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

Table 39. (Continued) Histopathological findings in a dead female rat in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | 1,8-dichlorooctane | | | | | |
|---|---|---|---|---|---|---|
| mg/kg | 1000 | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ |
| Findings | | | | | | |
| Medulla oblongata | [1][c] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Spinal cord | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Sciatic nerve | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Eyeball | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Harderian gland | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Bone marrow (sternum, femur) | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Bone (sternum, femur) | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Femur muscle | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |
| Mammary gland | [1] | | | | | |
| Postmortal change | 0 | 1 | 0 | 1 | 0 | 0 |

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

a): No abnormality detected.

b): Abnormality detected.

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

Table 40. Histopathological findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | | | | | | 1,8-dichlorooctane | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | 0 | | | | | | 40 | | | | | | | 200 | | | | | | | 1000 | | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | | N[a] | A[b] | ± | + | 2+ | 3+ | | N[a] | A[b] | ± | + | 2+ | 3+ | |
| Findings | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | [6][c] | | | | | | [0][c] | | | | | | | [0][c] | | | | | | | [6][c] | | | | | | |
| Lung | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Mineralization, vascular wall, left | 6 | 0 | 0 | 0 | 0 | 0 | | | | | | | | | | | | | | | 5 | 1 | 1 | 0 | 0 | 0 | |
| Trachea | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Liver | [6] | | | | | | [6] | | | | | | | [6] | | | | | | | [6] | | | | | | |
| Swelling, hepatocyte, periportal | 6 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 6 | 0 | 0 | 0 | ## | 0 | 6 | 0 | 6 | 0 | 0 | ## | 0 | 6 | 0 | 6 | 0 | 0 | ## && |
| Pancreas | [6] | | | | | | [6] | | | | | | | [6] | | | | | | | [6] | | | | | | |
| Decreased, zymogen granules | 6 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 4 | 2 | 0 | 0 | ## | 0 | 6 | 3 | 3 | 0 | 0 | ## | 0 | 6 | 4 | 2 | 0 | 0 | ## && |
| Sublingual gland | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Submandibular gland | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Esophagus | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Stomach | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Duodenum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Jejunum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Ileum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Cecum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Colon | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Rectum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Thymus | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Spleen | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Mandibular lymph node | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |
| Mesenteric lymph node | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [6] | | | | | | |

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

a): No abnormality detected.

b): Abnormality detected.

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

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Significantly different by dose response test (&&: $p<0.01$ by Cochran-Armitage exact test).

Table 40. (Continued) Histopathological findings in male rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | | | | | | 1,8-dichlorooctane | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | 0 | | | | | | 40 | | | | | | 200 | | | | | | 1000 | | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | |
| Findings | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | [6][c] | | | | | | [6][c] | | | | | | [6][c] | | | | | | [6][c] | | | | | | |
| Hyaline droplet, tubular epithelium, bilateral | 6 | 0 | 0 | 0 | 0 | 0 | 5 | 1 | 1 | 0 | 0 | 0 | 2 | 4 | 4 | 0 | 0 | 0 | 0 | 6 | 2 | 4 | 0 | 0 | ## && |
| Cyst, left | 5 | 1 | 1 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | |
| Urinary bladder | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Testis | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Epididymis | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Seminal vesicle | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Prostate | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Pituitary | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Aberrant craniopharyngeal tissue | 6 | 0 | 0 | 0 | 0 | 0 | | | | | | | | | | | | | 5 | 1 | 1 | 0 | 0 | 0 | |
| Adrenal | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Thyroid | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Parathyroid | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Cerebrum | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Cerebellum | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Medulla oblongata | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Spinal cord | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Sciatic nerve | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Eyeball | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Harderian gland | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Bone marrow (sternum, femur) | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Bone (sternum, femur) | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |
| Femur muscle | [6] | | | | | | [0] | | | | | | [0] | | | | | | [6] | | | | | | |

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

a): No abnormality detected.

b): Abnormality detected.

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

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Significantly different by dose response test (&&: $p<0.01$ by Cochran-Armitage exact test).

Table 41. Histopathological findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | | | | | | 1,8-dichlorooctane | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | 0 | | | | | | 40 | | | | | | | 200 | | | | | | | 1000 | | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | | N[a] | A[b] | ± | + | 2+ | 3+ | | N[a] | A[b] | ± | + | 2+ | 3+ | |
| Findings | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | [6][c] | | | | | | [0][c] | | | | | | | [0][c] | | | | | | | [5][c] | | | | | | |
| Lung | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Mineralization, vascular wall, left | 5 | 1 | 1 | 0 | 0 | 0 | | | | | | | | | | | | | | | 5 | 0 | 0 | 0 | 0 | 0 | |
| Trachea | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Liver | [6] | | | | | | [6] | | | | | | | [6] | | | | | | | [5] | | | | | | |
| Swelling, hepatocyte, periportal | 6 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 6 | 0 | 0 | 0 | ## | 0 | 6 | 0 | 6 | 0 | 0 | ## | 0 | 5 | 0 | 5 | 0 | 0 | ## && |
| Microgranuloma | 6 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | | 3 | 3 | 3 | 0 | 0 | 0 | | 3 | 2 | 2 | 0 | 0 | 0 | |
| Pancreas | [6] | | | | | | [6] | | | | | | | [6] | | | | | | | [5] | | | | | | |
| Decreased, zymogen granules | 6 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 1 | 5 | 0 | 0 | ## | 0 | 6 | 0 | 6 | 0 | 0 | ## | 0 | 5 | 0 | 5 | 0 | 0 | ## & |
| Sublingual gland | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Submandibular gland | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Esophagus | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Stomach | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Duodenum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Jejunum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Ileum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Cecum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Colon | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Rectum | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Thymus | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Spleen | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Mandibular lymph node | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |
| Mesenteric lymph node | [6] | | | | | | [0] | | | | | | | [0] | | | | | | | [5] | | | | | | |

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

a): No abnormality detected.

b): Abnormality detected.

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

Significantly different from the control group (##: $p<0.01$ by Steel's test).

Significantly different by dose response test (&: $p<0.05$, &&: $p<0.01$ by Cochran-Armitage exact test).

Table 41. (Continued) Histopathological findings in female rats on termination of administration period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | | | | | | 1,8-dichlorooctane | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | 0 | | | | | | 40 | | | | | | 200 | | | | | | 1000 | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ |
| Findings | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | [6][c] | | | | | | [6][c] | | | | | | [6][c] | | | | | | [5][c] | | | | | |
| Cyst, left | 6 | 0 | 0 | 0 | 0 | 0 | 5 | 1 | 1 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 |
| Urinary bladder | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Ovary | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Uterus | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Vagina | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Pituitary | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Adrenal | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Thyroid | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Parathyroid | [6] | | | | | | [0] | | | | | | [0] | | | | | | [3] | | | | | |
| Cerebrum | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Cerebellum | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Medulla oblongata | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Spinal cord | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Sciatic nerve | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Eyeball | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Dysplasia, retina | 5 | 1 | 1 | 0 | 0 | 0 | | | | | | | | | | | | | 4 | 1 | 1 | 0 | 0 | 0 |
| Harderian gland | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Bone marrow (sternum, femur) | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Bone (sternum, femur) | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Femur muscle | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |
| Mammary gland | [6] | | | | | | [0] | | | | | | [0] | | | | | | [5] | | | | | |

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

a): No abnormality detected.

b): Abnormality detected.

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

Table 42. Histopathological findings in male rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | | | | | | 1,8-dichlorooctane | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | 0 | | | | | | 200 | | | | | | 1000 | | | | | |
| Grade | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ | N[a] | A[b] | ± | + | 2+ | 3+ |
| Findings | | | | | | | | | | | | | | | | | | |
| Liver | [6][c] | | | | | | [6][c] | | | | | | [6][c] | | | | | |
| Pancreas | [6] | | | | | | [6] | | | | | | [6] | | | | | |
| Kidney | [6] | | | | | | [6] | | | | | | [6] | | | | | |
| Hyaline droplet, tubular epithelium, bilateral | 4 | 2 | 2 | 0 | 0 | 0 | 5 | 1 | 1 | 0 | 0 | 0 | 3 | 3 | 3 | 0 | 0 | 0 |
| Cyst, left | 5 | 1 | 1 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | 0 |

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

a): No abnormality detected.

b): Abnormality detected.

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

Table 43. Histopathological findings in female rats on termination of recovery period in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane

| Group | Control | | | | | | 1.8-dichlorooctane | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | 0 | | | | | | 200 | | | | | | 1000 | | | | | | | |
| Grade | N[a)] | A[b)] | ± | + | 2+ | 3+ | N[a)] | A[b)] | ± | + | 2+ | 3+ | N[a)] | A[b)] | ± | + | 2+ | 3+ | | |
| Findings | | | | | | | | | | | | | | | | | | | | |
| Liver | [6][c)] | | | | | | [6][c)] | | | | | | [6][c)] | | | | | | | |
| Swelling, hepatocyte, periportal | 6 | 0 | 0 | 0 | 0 | 0 | 5 | 1 | 1 | 0 | 0 | 0 | 2 | 4 | 4 | 0 | 0 | 0 | # | & |
| Pancreas | [6] | | | | | | [6] | | | | | | [6] | | | | | | | |
| Decreased, zymogen granules | 6 | 0 | 0 | 0 | 0 | 0 | 4 | 2 | 2 | 0 | 0 | 0 | 4 | 2 | 2 | 0 | 0 | 0 | | |
| Kidney | [6] | | | | | | [6] | | | | | | [6] | | | | | | | |

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

a): No abnormality detected.

b): Abnormality detected.

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

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

Significantly different by dose response test (&: $p<0.05$ by Cochran-Armitage exact test).

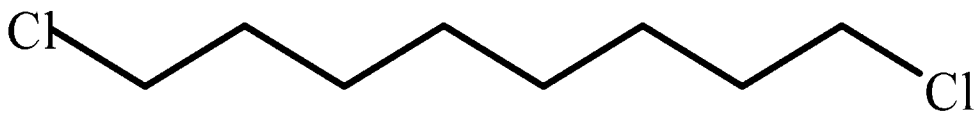


Fig. 1. Chemical structure of 1,8-dichlorooctane.

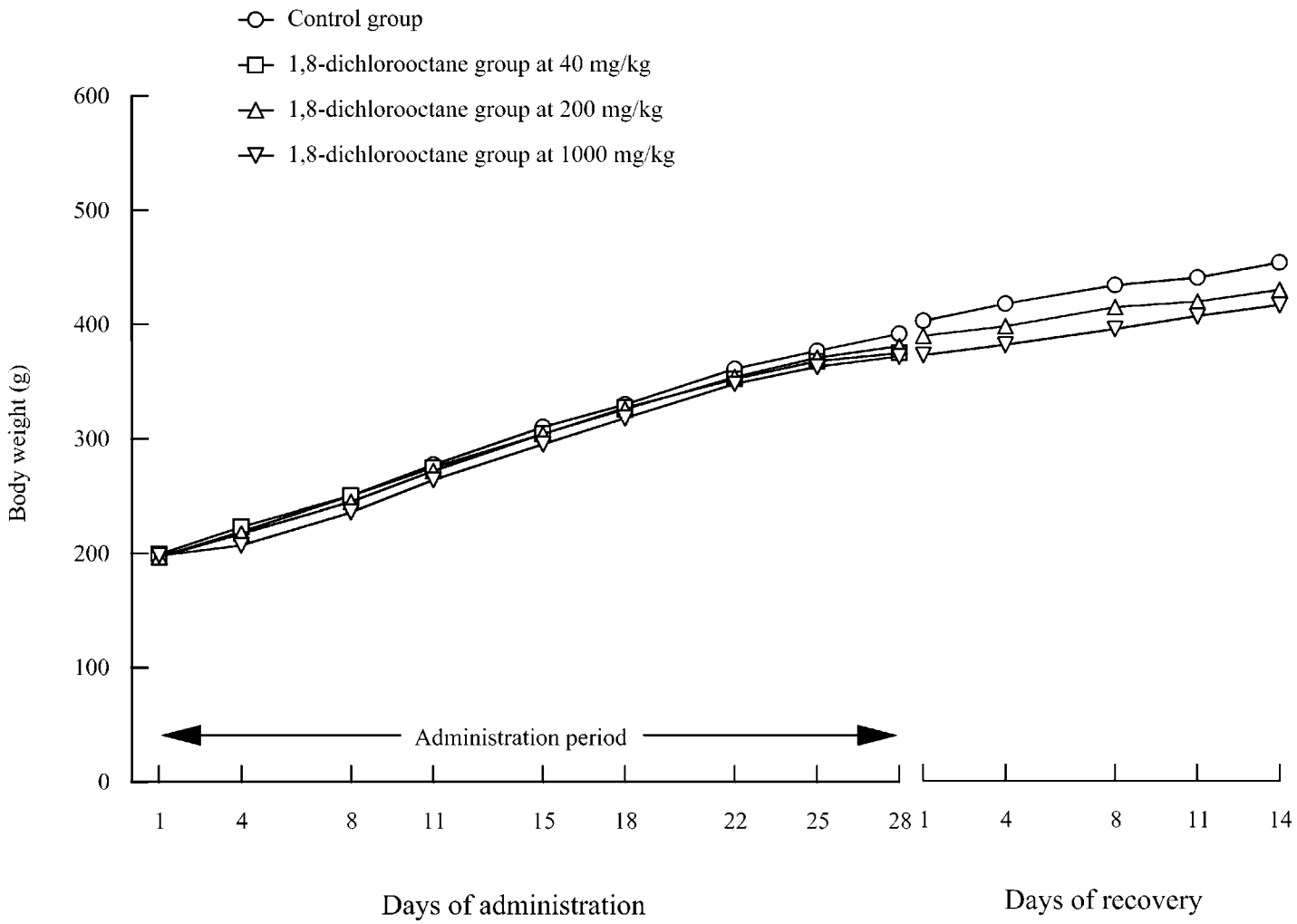


Fig. 2. Body weights of male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane.

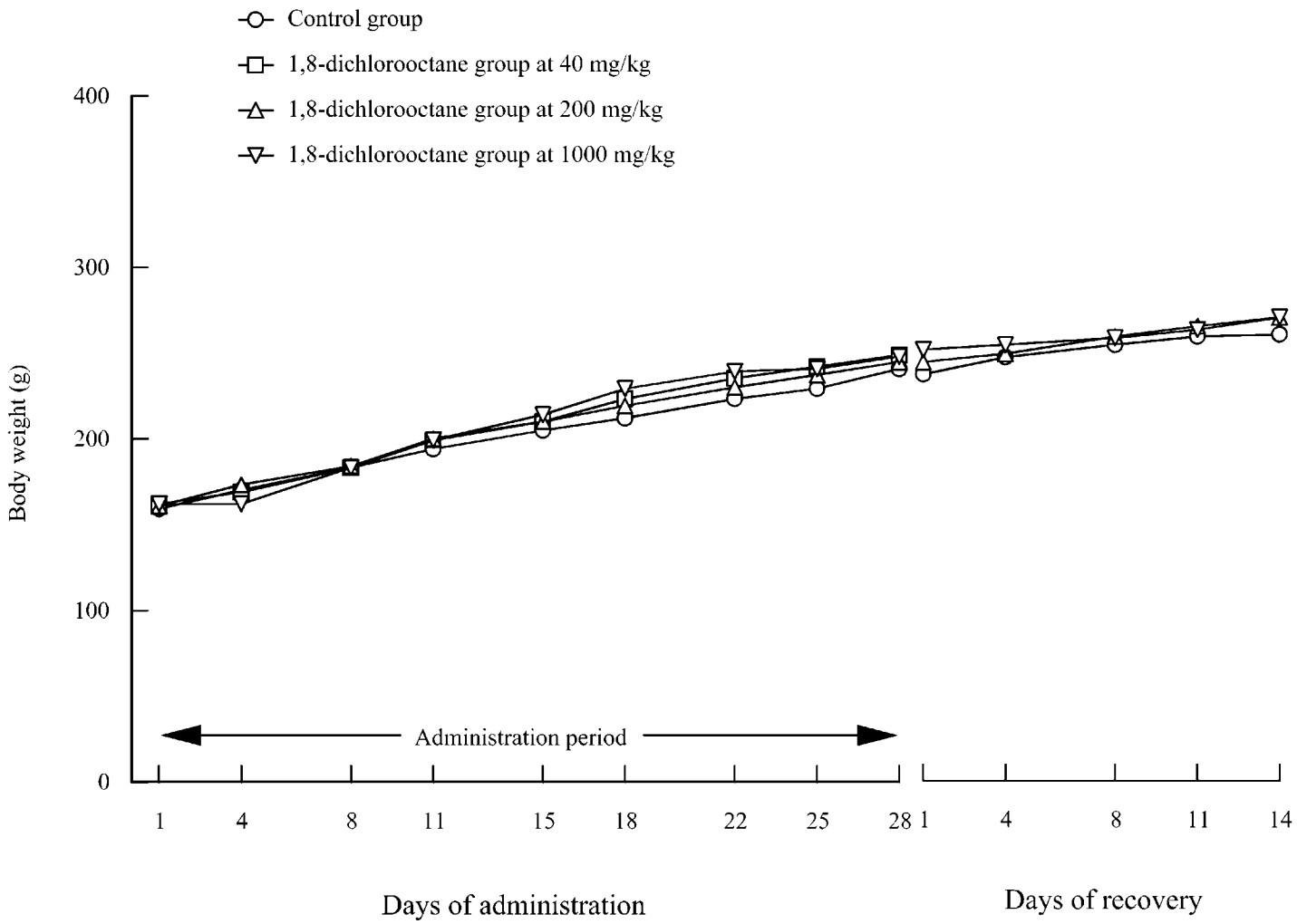


Fig. 3. Body weights of female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane.

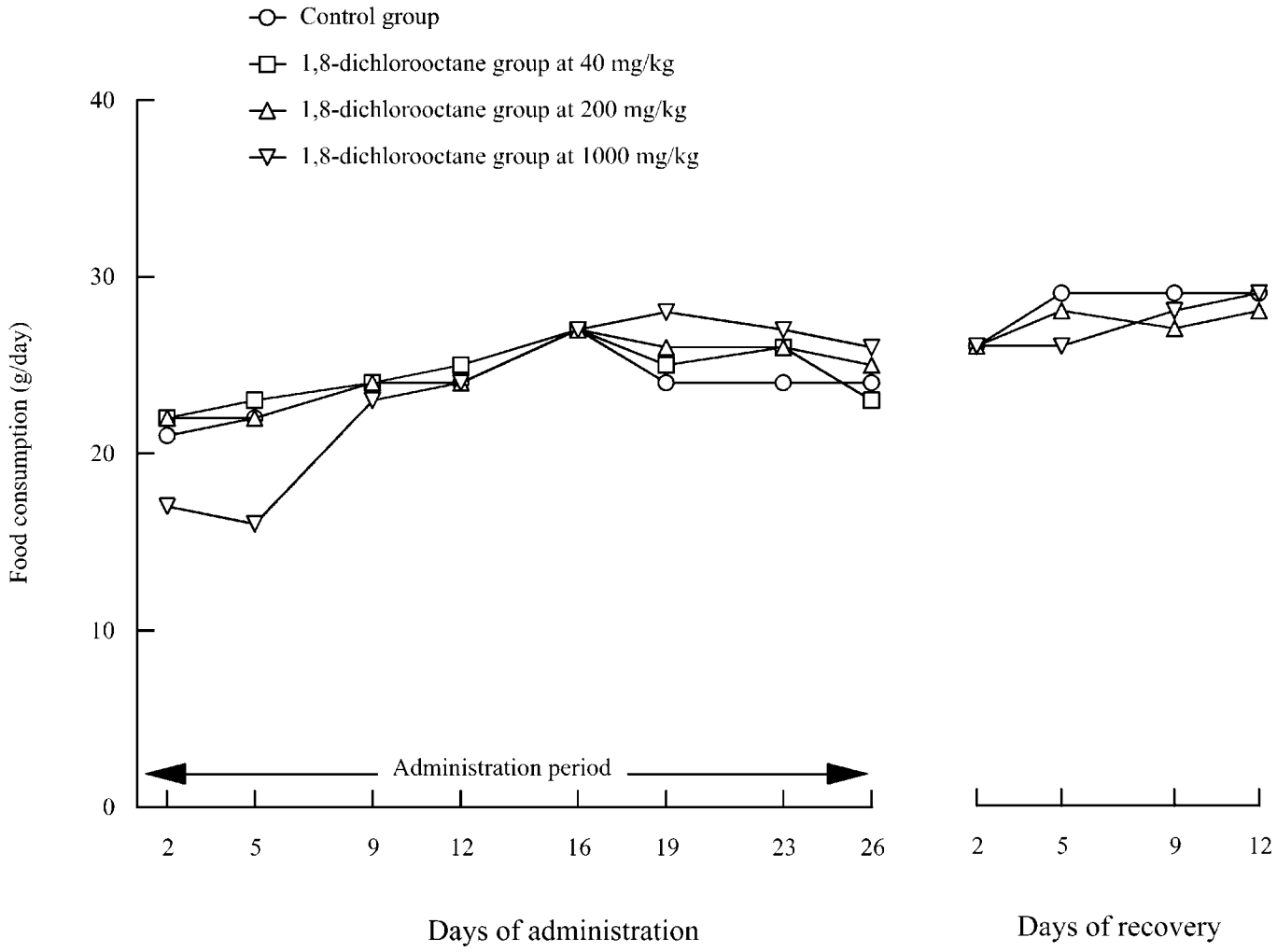


Fig. 4. Food consumption in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane.

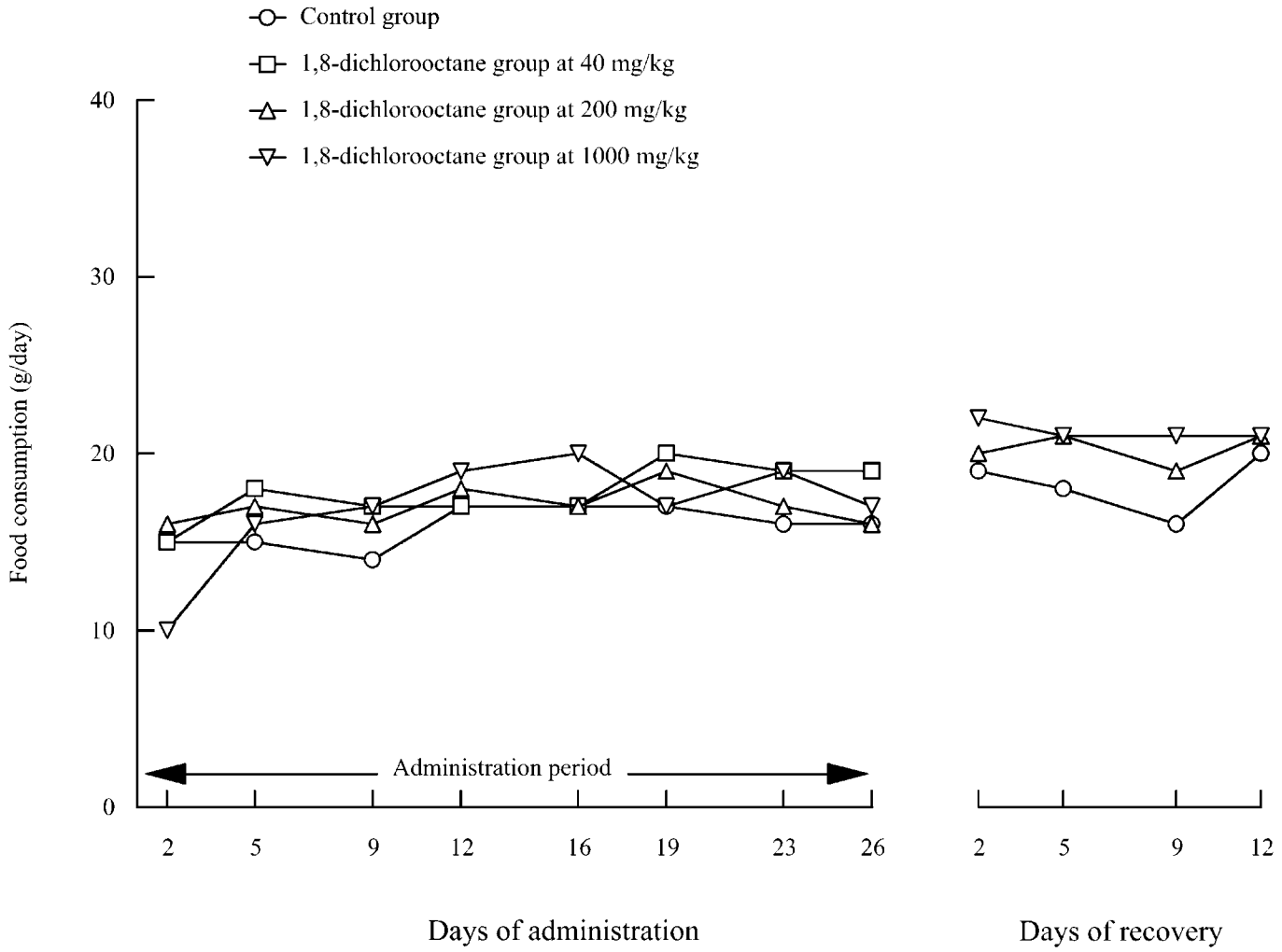


Fig. 5. Food consumption in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane.

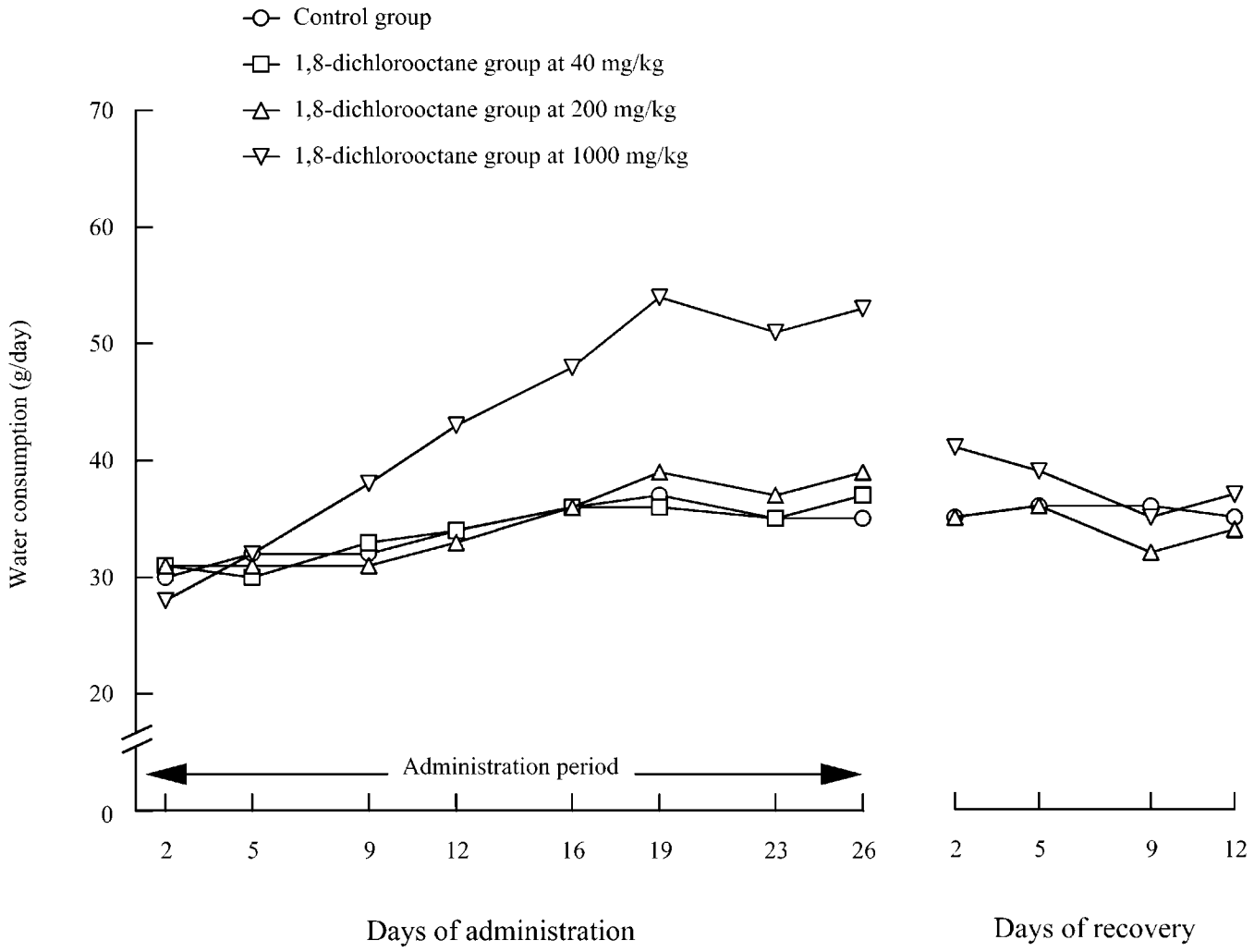


Fig. 6. Water consumption in male rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane.

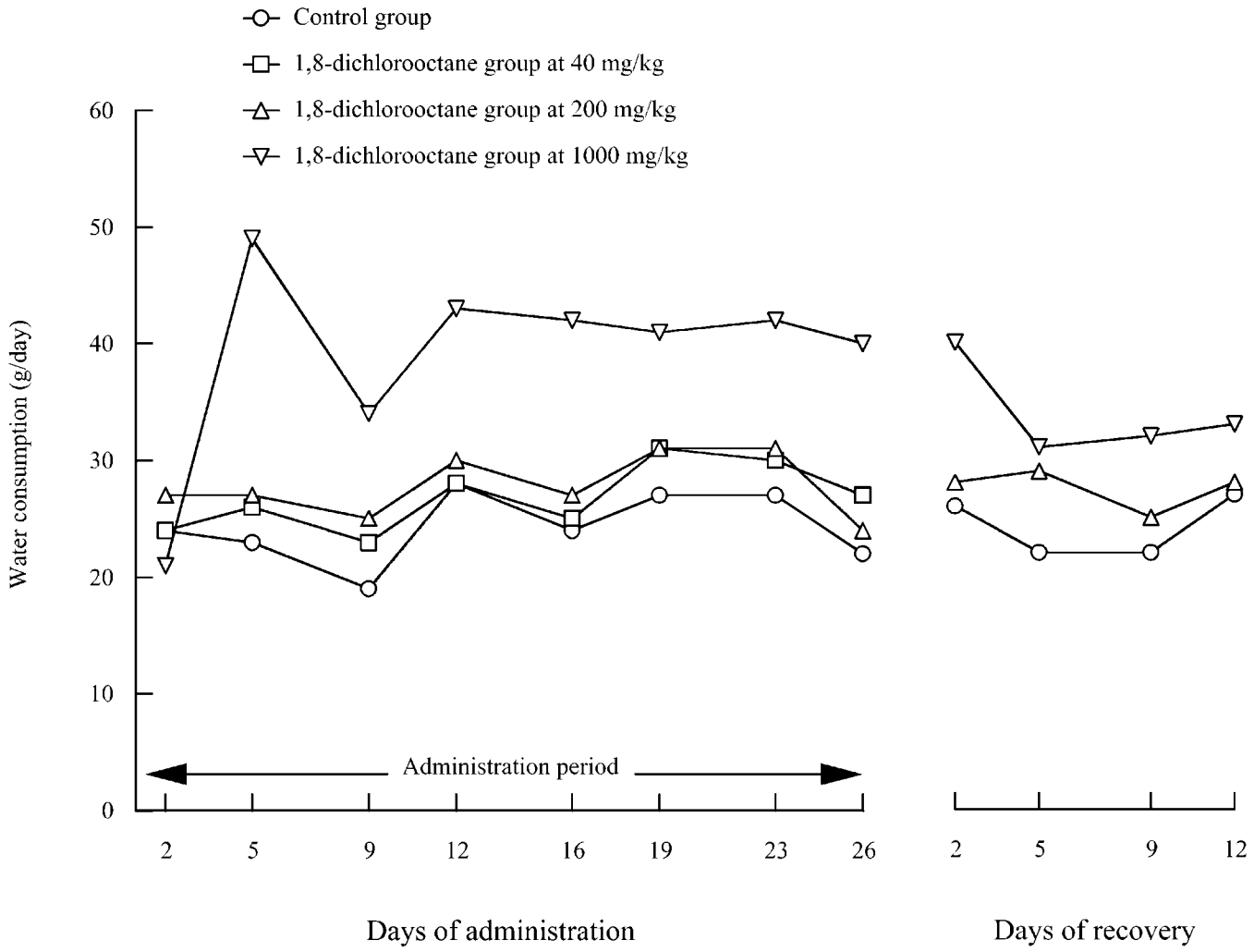


Fig. 7. Water consumption in female rats in repeated dose 28-day oral toxicity study of 1,8-dichlorooctane.

Appendix 1-1. Individual general signs in male rats

Control group

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| M01101 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01102 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01103 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01104 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01105 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01106 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01107 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01108 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01109 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01110 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01111 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M01112 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |

Pre: Before administration, Post: after administration. (Continued)

N: Normal.

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

Control group

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| M01101 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01102 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01103 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01104 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01105 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01106 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01107 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| M01108 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| M01109 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| M01110 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| M01111 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| M01112 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | |

Pre: Before administration, Post: after administration. (Continued)

*: Euthanized.

N: Normal.

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

Control group

| Male No. | Days of recovery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| M01107 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01108 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01109 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01110 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01111 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M01112 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

*: Euthanized.

N: Normal.

Appendix 1-2. Individual general signs in male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| M02201 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M02202 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M02203 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M02204 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M02205 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M02206 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

Pre: Before administration, Post: after administration. (Continued)

N: Normal.

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

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| M02201 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M02202 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M02203 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M02204 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M02205 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M02206 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

Pre: Before administration, Post: after administration.

*: Euthanized.

N: Normal.

Appendix 1-3. Individual general signs in male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| M03301 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03302 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03303 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03304 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03305 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03306 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03307 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03308 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03309 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03310 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03311 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| M03312 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| A | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

A: Salivation.

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

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Total[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | | A |
| M03301 | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | * | + |
| M03302 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| M03303 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| M03304 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| M03305 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| M03306 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| M03307 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| M03308 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| M03309 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | | | + |
| M03310 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| M03311 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | | | + |
| M03312 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | N | | | + |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 12 | 12 | 11 | 12 | 10 | 6 | | - |
| A | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | | 4 |

Pre: Before administration, Post: after administration.

(Continued)

*: Euthanized.

a): Number of males showing abnormal signs at least once between Days 1 and 29 of administration.

-: Not observed, +: observed.

N: Normal.

A: Salivation.

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

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Days of recovery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| M03307 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M03308 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M03309 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M03310 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M03311 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M03312 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

*: Euthanized.

N: Normal.

Appendix 1-4. Individual general signs in male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| M04401 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | A |
| M04402 | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | N | N | A | N | A | N | A |
| M04403 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | A |
| M04404 | N | N | N | N | N | N | N | N | N | A | N | N | N | A | N | N | N | A | N | A | N | A | N | A | N | A | N | A |
| M04405 | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | N |
| M04406 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | N |
| M04407 | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | A | N | A | N | A | N | A | N | N | N | A |
| M04408 | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | N | N | N | N | N | N | N | N | A | N | A | N | A |
| M04409 | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | A | N | N | N | A | N | A | N | A | N | A | N | A |
| M04410 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | N |
| M04411 | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | A | N | A | N | A | N | A | N | A | N | N |
| M04412 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | A | N | N |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 10 | 12 | 8 | 12 | 7 | 12 | 10 | 12 | 6 | 12 | 5 | 12 | 5 | 12 | 0 | 12 | 2 | 12 | 5 |
| A | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 4 | 0 | 5 | 0 | 2 | 0 | 6 | 0 | 7 | 0 | 7 | 0 | 12 | 0 | 10 | 0 | 7 |

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

A: Salivation.

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

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Total[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | | A |
| M04401 | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | N | N | N | N | N | N | N | N | A | N | N | N | * | + |
| M04402 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | N | N | A | N | N | N | A | N | * | + |
| M04403 | N | N | N | A | N | A | N | A | N | A | N | A | N | N | N | A | N | N | N | A | N | N | N | N | N | N | N | A | N | * | + |
| M04404 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | * | + |
| M04405 | N | A | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | N | N | A | N | * | + |
| M04406 | N | A | N | N | N | A | N | A | N | A | N | A | N | N | N | N | N | A | N | A | N | A | N | A | N | N | N | A | N | * | + |
| M04407 | N | N | N | A | N | A | N | N | N | A | N | A | N | A | N | A | N | N | N | N | N | N | N | N | N | A | N | A | | | + |
| M04408 | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | | | + |
| M04409 | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | | | + |
| M04410 | N | N | N | N | N | A | N | A | N | A | N | A | N | N | N | N | N | A | N | A | N | N | N | N | N | N | N | A | | | + |
| M04411 | N | A | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | N | | | + |
| M04412 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | N | N | N | | | + |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | | 12 |
| N | 12 | 6 | 12 | 5 | 12 | 0 | 12 | 1 | 12 | 0 | 12 | 0 | 12 | 3 | 12 | 2 | 12 | 3 | 12 | 2 | 12 | 5 | 12 | 4 | 12 | 6 | 12 | 3 | 6 | | - |
| A | 0 | 6 | 0 | 7 | 0 | 12 | 0 | 11 | 0 | 12 | 0 | 12 | 0 | 9 | 0 | 10 | 0 | 9 | 0 | 10 | 0 | 7 | 0 | 8 | 0 | 6 | 0 | 9 | 0 | | 12 |

Pre: Before administration, Post: after administration. (Continued)

*: Euthanized.

a): Number of males showing abnormal signs at least once between Days 1 and 29 of administration.

-: Not observed, +: observed.

N: Normal.

A: Salivation.

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

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Days of recovery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| M04407 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M04408 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M04409 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M04410 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M04411 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| M04412 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

*: Euthanized.

N: Normal.

Appendix 2-1. Individual general signs in female rats

Control group

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| F01151 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01152 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01153 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01154 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01155 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01156 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01157 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01158 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01159 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01160 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01161 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F01162 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |

Pre: Before administration, Post: after administration. (Continued)

N: Normal.

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

Control group

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| F01151 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01152 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01153 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01154 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01155 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01156 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01157 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| F01158 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| F01159 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| F01160 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| F01161 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| F01162 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | |

Pre: Before administration, Post: after administration. (Continued)

*: Euthanized.

N: Normal.

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

Control group

| Female No. | Days of recovery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| F01157 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01158 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01159 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01160 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01161 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F01162 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

*: Euthanized.

N: Normal.

Appendix 2-2. Individual general signs in female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| F02251 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F02252 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F02253 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F02254 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F02255 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F02256 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

Pre: Before administration, Post: after administration. (Continued)

N: Normal.

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

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | |
| F02251 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F02252 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F02253 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F02254 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F02255 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F02256 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

Prc: Bcforc administration, Post: aftcr administration.

*: Euthanized.

N: Normal.

Appendix 2-3. Individual general signs in female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| F03351 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03352 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03353 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03354 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03355 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03356 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03357 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03358 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03359 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03360 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03361 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F03362 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| A | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Pre: Before administration, Post: after administration.

(Continued)

N: Normal.

A: Salivation.

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

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Total[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | | A |
| F03351 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| F03352 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| F03353 | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | * | + |
| F03354 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| F03355 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| F03356 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | - |
| F03357 | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | + |
| F03358 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| F03359 | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | | | + |
| F03360 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| F03361 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| F03362 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | - |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | | 12 |
| N | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 10 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 12 | 12 | 12 | 12 | 11 | 12 | 11 | 6 | | - |
| A | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | | 3 |

Pre: Before administration, Post: after administration. (Continued)

*: Euthanized.

a): Number of females showing abnormal signs at least once between Days 1 and 29 of administration.

-: Not observed, +: observed.

N: Normal.

A: Salivation.

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

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Days of recovery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| F03357 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F03358 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F03359 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F03360 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F03361 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F03362 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

*: Euthanized.

N: Normal.

Appendix 2-4. Individual general signs in female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | | 13 | | 14 | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| F04451 | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | A | N | A | N | N | N | N |
| F04452 | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | N | N | N | N | A | N | N | N | A | N | A |
| F04453 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| F04454 | N | N | Z | | | | | | | | | | | | | | | | | | | | | | | | | |
| F04455 | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | A | N | A | N | A | N | A | N | N | N | A |
| F04456 | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | A |
| F04457 | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | A | N | A | N | A | N | A | N | N | N | A |
| F04458 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | A |
| F04459 | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | N | N | N | N | N | N | N | N | N | N | N |
| F04460 | N | N | N | N | N | N | N | N | N | A | N | A | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | A |
| F04461 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N |
| F04462 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | A | N | N | N | A | N | A | N | N |
| Number of females | 12 | 12 | 12 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 |
| N | 12 | 12 | 11 | 11 | 11 | 11 | 11 | 10 | 11 | 9 | 11 | 8 | 11 | 9 | 11 | 7 | 11 | 6 | 11 | 6 | 11 | 5 | 11 | 3 | 11 | 7 | 11 | 5 |
| A | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 3 | 0 | 2 | 0 | 4 | 0 | 5 | 0 | 5 | 0 | 6 | 0 | 8 | 0 | 4 | 0 | 6 |
| B | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Z | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Pre: Before administration, Post: after administration. (Continued)

N: Normal.

A: Salivation.

B: Perioral smudge.

C: Soiled hair.

Z: Death.

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

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Days of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | Total[a] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 | | 16 | | 17 | | 18 | | 19 | | 20 | | 21 | | 22 | | 23 | | 24 | | 25 | | 26 | | 27 | | 28 | | 29 | | | | | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | | | | | |
| F04451 | N | A | N | A | N | A | N | N | N | A | N | A | N | N | N | N | N | N | N | N | B,C | A,B,C | B,C | A,B,C | N | A | N | A | N | * | + | + | + | - |
| F04452 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | N | N | A | N | A | N | * | + | - | - | - |
| F04453 | N | N | N | N | N | N | N | N | N | N | N | A | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * | + | - | - | - |
| F04454 | Died on Day 2 of administration | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | - | - | - | + |
| F04455 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | * | + | - | - | - |
| F04456 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | * | + | - | - | - |
| F04457 | N | A | N | A | N | A | N | N | N | N | N | A | N | N | N | A | N | N | N | A | N | A | N | A | N | A | N | A | | | + | - | - | - |
| F04458 | N | A | N | A | N | A | N | N | N | N | N | A | N | A | N | A | N | A | N | A | N | N | N | N | N | A | N | A | | | + | - | - | - |
| F04459 | N | A | N | A | N | A | N | N | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | | | + | - | - | - |
| F04460 | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | N | A | | | + | - | - | - |
| F04461 | N | N | N | A | N | A | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | | | + | - | - | - |
| F04462 | N | N | N | A | N | N | N | A | N | N | N | A | N | N | N | N | N | N | N | N | N | N | N | A | N | A | N | A | | | + | - | - | - |
| Number of females | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 5 | | 12 | 12 | 12 | 12 |
| N | 11 | 3 | 11 | 1 | 11 | 2 | 11 | 6 | 11 | 5 | 11 | 1 | 11 | 5 | 11 | 5 | 11 | 6 | 11 | 4 | 10 | 4 | 10 | 4 | 11 | 2 | 11 | 2 | 5 | | - | - | - | - |
| A | 0 | 8 | 0 | 10 | 0 | 9 | 0 | 5 | 0 | 6 | 0 | 10 | 0 | 6 | 0 | 6 | 0 | 5 | 0 | 7 | 0 | 7 | 0 | 7 | 0 | 9 | 0 | 9 | 0 | | 11 | - | - | - |
| B | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | | - | 1 | - | - |
| C | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | | - | - | 1 | - |
| Z | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | - | - | - | 1 |

Pre: Before administration, Post: after administration. (Continued)

*: Euthanized.

a): Number of females showing abnormal signs at least once between Days 1 and 29 of administration.

-: Not observed, +: observed.

N: Normal.

A: Salivation.

B: Perioral smudge.

C: Soiled hair.

Z: Death.

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

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Days of recovery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
| F04457 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F04458 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F04459 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F04460 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F04461 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| F04462 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | * |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | |

*: Euthanized.

N: Normal.

Appendix 3-1. Individual body weights (g) of male rats

Control group

| Male No. | Days of administration | | | | | | | | | Days of recovery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 | 1 | 4 | 8 | 11 | 14 |
| M01101 | 197 | 213 | 248 | 268 | 298 | 318 | 349 | 366 | 372 | | | | | |
| M01102 | 209 | 239 | 263 | 291 | 318 | 337 | 357 | 374 | 384 | | | | | |
| M01103 | 194 | 213 | 244 | 274 | 310 | 337 | 369 | 386 | 399 | | | | | |
| M01104 | 204 | 226 | 257 | 285 | 317 | 336 | 365 | 383 | 394 | | | | | |
| M01105 | 198 | 219 | 238 | 258 | 289 | 293 | 337 | 355 | 362 | | | | | |
| M01106 | 196 | 224 | 252 | 283 | 315 | 342 | 361 | 384 | 391 | | | | | |
| M01107 | 195 | 209 | 231 | 260 | 289 | 307 | 340 | 353 | 367 | 370 | 386 | 402 | 407 | 425 |
| M01108 | 191 | 213 | 256 | 289 | 327 | 355 | 393 | 415 | 436 | 434 | 452 | 464 | 470 | 488 |
| M01109 | 199 | 221 | 256 | 284 | 318 | 342 | 370 | 386 | 410 | 413 | 428 | 443 | 459 | 465 |
| M01110 | 193 | 206 | 233 | 260 | 295 | 301 | 347 | 360 | 374 | 376 | 388 | 402 | 402 | 413 |
| M01111 | 198 | 225 | 258 | 285 | 318 | 338 | 366 | 381 | 396 | 398 | 407 | 421 | 430 | 439 |
| M01112 | 195 | 219 | 260 | 291 | 329 | 350 | 380 | 385 | 416 | 418 | 442 | 468 | 470 | 485 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 | 6 |
| Mean | 197 | 219 | 250 | 277 | 310 | 330 | 361 | 377 | 392 | 402 | 417 | 433 | 440 | 453 |
| S.D. | 5 | 9 | 11 | 13 | 14 | 20 | 16 | 17 | 22 | 25 | 28 | 30 | 31 | 32 |

Appendix 3-2. Individual body weights (g) of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Days of administration | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 |
| M02201 | 198 | 227 | 254 | 275 | 304 | 322 | 346 | 360 | 365 |
| M02202 | 206 | 236 | 255 | 279 | 307 | 329 | 358 | 374 | 380 |
| M02203 | 190 | 213 | 239 | 266 | 290 | 314 | 334 | 350 | 355 |
| M02204 | 194 | 207 | 241 | 263 | 291 | 321 | 344 | 362 | 370 |
| M02205 | 201 | 225 | 255 | 283 | 314 | 334 | 360 | 376 | 385 |
| M02206 | 204 | 228 | 258 | 284 | 315 | 342 | 367 | 384 | 394 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 199 | 223 | 250 | 275 | 304 | 327 | 352 | 368 | 375 |
| S.D. | 6 | 11 | 8 | 9 | 11 | 10 | 12 | 12 | 14 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 3-3. Individual body weights (g) of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Days of administration | | | | | | | | | Days of recovery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 | 1 | 4 | 8 | 11 | 14 |
| M03301 | 201 | 223 | 244 | 269 | 301 | 325 | 353 | 366 | 364 | | | | | |
| M03302 | 205 | 225 | 248 | 273 | 306 | 332 | 364 | 385 | 399 | | | | | |
| M03303 | 199 | 222 | 247 | 273 | 301 | 320 | 343 | 368 | 377 | | | | | |
| M03304 | 198 | 224 | 248 | 275 | 297 | 316 | 335 | 350 | 358 | | | | | |
| M03305 | 185 | 203 | 230 | 252 | 280 | 308 | 334 | 349 | 356 | | | | | |
| M03306 | 189 | 205 | 235 | 265 | 305 | 327 | 359 | 376 | 389 | | | | | |
| M03307 | 184 | 212 | 241 | 269 | 302 | 327 | 356 | 375 | 390 | 391 | 387 | 419 | 427 | 437 |
| M03308 | 205 | 215 | 241 | 266 | 306 | 327 | 357 | 375 | 387 | 391 | 398 | 416 | 420 | 431 |
| M03309 | 200 | 215 | 250 | 279 | 315 | 332 | 362 | 385 | 404 | 403 | 417 | 429 | 440 | 451 |
| M03310 | 190 | 211 | 244 | 267 | 297 | 321 | 347 | 356 | 364 | 365 | 377 | 390 | 389 | 397 |
| M03311 | 200 | 223 | 256 | 284 | 320 | 342 | 371 | 391 | 398 | 400 | 416 | 437 | 439 | 451 |
| M03312 | 202 | 228 | 260 | 292 | 316 | 338 | 361 | 375 | 384 | 382 | 387 | 394 | 396 | 406 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 | 6 |
| Mean | 197 | 217 | 245 | 272 | 304 | 326 | 354 | 371 | 381 | 389 | 397 | 414 | 419 | 429 |
| S.D. | 7 | 8 | 8 | 10 | 11 | 9 | 12 | 14 | 17 | 14 | 17 | 19 | 22 | 23 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 3-4. Individual body weights (g) of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Days of administration | | | | | | | | | Days of recovery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 | 1 | 4 | 8 | 11 | 14 |
| M04401 | 191 | 205 | 224 | 241 | 264 | 287 | 309 | 331 | 330 | | | | | |
| M04402 | 203 | 218 | 260 | 294 | 315 | 341 | 371 | 390 | 401 | | | | | |
| M04403 | 200 | 220 | 248 | 276 | 310 | 337 | 372 | 382 | 391 | | | | | |
| M04404 | 208 | 209 | 244 | 271 | 309 | 339 | 374 | 397 | 404 | | | | | |
| M04405 | 196 | 207 | 231 | 256 | 292 | 306 | 340 | 357 | 361 | | | | | |
| M04406 | 192 | 200 | 228 | 255 | 281 | 311 | 339 | 356 | 372 | | | | | |
| M04407 | 199 | 207 | 239 | 267 | 292 | 307 | 330 | 338 | 340 | 346 | 344 | 359 | 367 | 376 |
| M04408 | 203 | 217 | 247 | 281 | 326 | 349 | 380 | 399 | 406 | 417 | 419 | 435 | 452 | 457 |
| M04409 | 196 | 200 | 227 | 256 | 287 | 307 | 333 | 347 | 359 | 359 | 373 | 379 | 392 | 400 |
| M04410 | 195 | 205 | 230 | 267 | 301 | 322 | 361 | 370 | 386 | 390 | 402 | 422 | 433 | 440 |
| M04411 | 200 | 201 | 237 | 263 | 287 | 314 | 351 | 363 | 376 | 377 | 401 | 415 | 429 | 448 |
| M04412 | 195 | 199 | 218 | 244 | 274 | 292 | 318 | 330 | 338 | 340 | 346 | 358 | 364 | 374 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 | 6 |
| Mean | 198 | 207 | 236 | 264 | 295 | 318 | 348 | 363 | 372 | 372 | 381 | 395 | 406 | 416 |
| S.D. | 5 | 7 | 12 | 15 | 18 | 20 | 24 | 25 | 27 | 29 | 31 | 34 | 37 | 37 |
| Significance | NS | ** | ** | * | * | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 4-1. Individual body weights (g) of female rats

Control group

| Female No. | Days of administration | | | | | | | | | Days of recovery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 | 1 | 4 | 8 | 11 | 14 |
| F01151 | 160 | 167 | 177 | 187 | 198 | 203 | 213 | 228 | 239 | | | | | |
| F01152 | 166 | 174 | 184 | 196 | 205 | 210 | 221 | 224 | 239 | | | | | |
| F01153 | 157 | 172 | 183 | 196 | 208 | 220 | 227 | 237 | 251 | | | | | |
| F01154 | 165 | 171 | 186 | 198 | 212 | 220 | 235 | 244 | 258 | | | | | |
| F01155 | 155 | 165 | 175 | 184 | 193 | 209 | 218 | 223 | 226 | | | | | |
| F01156 | 157 | 168 | 185 | 197 | 206 | 218 | 225 | 233 | 242 | | | | | |
| F01157 | 148 | 161 | 171 | 185 | 191 | 194 | 200 | 199 | 212 | 208 | 216 | 221 | 229 | 230 |
| F01158 | 165 | 180 | 201 | 217 | 232 | 236 | 248 | 248 | 265 | 261 | 275 | 286 | 293 | 295 |
| F01159 | 156 | 171 | 184 | 193 | 206 | 210 | 220 | 222 | 234 | 232 | 243 | 251 | 257 | 256 |
| F01160 | 163 | 178 | 191 | 201 | 217 | 221 | 237 | 248 | 257 | 257 | 270 | 275 | 275 | 273 |
| F01161 | 161 | 172 | 184 | 193 | 201 | 204 | 216 | 222 | 238 | 238 | 244 | 250 | 253 | 253 |
| F01162 | 153 | 163 | 173 | 180 | 194 | 203 | 212 | 214 | 226 | 223 | 233 | 242 | 249 | 250 |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 | 6 |
| Mean | 159 | 170 | 183 | 194 | 205 | 212 | 223 | 229 | 241 | 237 | 247 | 254 | 259 | 260 |
| S.D. | 5 | 6 | 8 | 10 | 12 | 11 | 13 | 14 | 15 | 20 | 22 | 23 | 22 | 22 |

Appendix 4-2. Individual body weights (g) of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Days of administration | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 |
| F02251 | 158 | 165 | 182 | 202 | 212 | 221 | 236 | 245 | 251 |
| F02252 | 149 | 156 | 166 | 177 | 191 | 201 | 210 | 214 | 224 |
| F02253 | 170 | 180 | 190 | 211 | 224 | 241 | 256 | 259 | 264 |
| F02254 | 170 | 180 | 196 | 207 | 218 | 227 | 236 | 252 | 262 |
| F02255 | 159 | 169 | 184 | 198 | 208 | 220 | 232 | 233 | 243 |
| F02256 | 163 | 166 | 182 | 200 | 209 | 226 | 241 | 246 | 250 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 162 | 169 | 183 | 199 | 210 | 223 | 235 | 242 | 249 |
| S.D. | 8 | 9 | 10 | 12 | 11 | 13 | 15 | 16 | 15 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 4-3. Individual body weights (g) of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Days of administration | | | | | | | | | Days of recovery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 | 1 | 4 | 8 | 11 | 14 |
| F03351 | 165 | 176 | 185 | 206 | 211 | 223 | 236 | 240 | 247 | | | | | |
| F03352 | 154 | 168 | 183 | 199 | 211 | 227 | 236 | 248 | 252 | | | | | |
| F03353 | 158 | 173 | 183 | 197 | 213 | 218 | 230 | 245 | 254 | | | | | |
| F03354 | 162 | 177 | 187 | 202 | 213 | 221 | 233 | 235 | 244 | | | | | |
| F03355 | 172 | 186 | 195 | 215 | 228 | 239 | 255 | 267 | 277 | | | | | |
| F03356 | 154 | 161 | 168 | 177 | 186 | 191 | 201 | 211 | 219 | | | | | |
| F03357 | 161 | 169 | 180 | 191 | 202 | 202 | 216 | 225 | 231 | 237 | 242 | 254 | 254 | 259 |
| F03358 | 161 | 171 | 181 | 194 | 203 | 206 | 218 | 228 | 239 | 236 | 241 | 251 | 257 | 258 |
| F03359 | 160 | 170 | 179 | 193 | 201 | 211 | 218 | 223 | 233 | 231 | 237 | 248 | 253 | 258 |
| F03360 | 163 | 177 | 195 | 212 | 224 | 236 | 245 | 248 | 258 | 263 | 269 | 280 | 288 | 290 |
| F03361 | 160 | 167 | 178 | 197 | 207 | 217 | 229 | 228 | 228 | 236 | 240 | 247 | 256 | 268 |
| F03362 | 166 | 183 | 197 | 212 | 226 | 235 | 247 | 249 | 259 | 260 | 266 | 274 | 282 | 288 |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 | 6 |
| Mean | 161 | 173 | 184 | 200 | 210 | 219 | 230 | 237 | 245 | 244 | 249 | 259 | 265 | 270 |
| S.D. | 5 | 7 | 8 | 11 | 12 | 15 | 15 | 15 | 16 | 14 | 14 | 14 | 16 | 15 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 4-4. Individual body weights (g) of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Days of administration | | | | | | | | | Days of recovery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 4 | 8 | 11 | 15 | 18 | 22 | 25 | 28 | 1 | 4 | 8 | 11 | 14 |
| F04451 | 160 | 165 | 179 | 188 | 202 | 210 | 222 | 207 | 229 | | | | | |
| F04452 | 160 | 167 | 178 | 194 | 204 | 236 | 238 | 244 | 247 | | | | | |
| F04453 | 154 | 147 | 166 | 191 | 201 | 212 | 218 | 220 | 227 | | | | | |
| F04454 | 155 | Died on Day 2 of administration | | | | | | | | | | | | |
| F04455 | 165 | 175 | 188 | 199 | 214 | 233 | 245 | 248 | 246 | | | | | |
| F04456 | 171 | 158 | 191 | 205 | 230 | 250 | 267 | 268 | 276 | | | | | |
| F04457 | 159 | 162 | 185 | 198 | 216 | 229 | 238 | 247 | 255 | 257 | 257 | 261 | 264 | 270 |
| F04458 | 159 | 152 | 176 | 191 | 200 | 226 | 243 | 246 | 251 | 252 | 258 | 264 | 261 | 268 |
| F04459 | 157 | 168 | 181 | 201 | 219 | 221 | 230 | 234 | 241 | 236 | 238 | 245 | 251 | 255 |
| F04460 | 162 | 160 | 183 | 214 | 224 | 234 | 246 | 245 | 257 | 256 | 261 | 264 | 273 | 282 |
| F04461 | 173 | 178 | 200 | 214 | 231 | 246 | 253 | 263 | 263 | 266 | 266 | 270 | 276 | 284 |
| F04462 | 166 | 155 | 182 | 195 | 209 | 220 | 227 | 232 | 239 | 240 | 242 | 241 | 250 | 263 |
| Number of females | 12 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 6 | 6 | 6 | 6 | 6 |
| Mean | 162 | 162 | 183 | 199 | 214 | 229 | 239 | 241 | 248 | 251 | 254 | 258 | 263 | 270 |
| S.D. | 6 | 9 | 9 | 9 | 11 | 13 | 14 | 18 | 14 | 11 | 11 | 12 | 11 | 11 |
| Significance | NS | NS | NS | NS | NS | * | * | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 5-1. Individual food consumption (g/day) in male rats

Control group

| Male No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| M01101 | 20 | 23 | 25 | 26 | 24 | 25 | 25 | 24 | | | | |
| M01102 | 21 | 22 | 22 | 24 | 23 | 21 | 24 | 19 | | | | |
| M01103 | 20 | 21 | 24 | 23 | 28 | 23 | 27 | 26 | | | | |
| M01104 | 22 | 19 | 23 | 22 | 23 | 24 | 25 | 21 | | | | |
| M01105 | 23 | 22 | 19 | 25 | 27 | 23 | 23 | 22 | | | | |
| M01106 | 22 | 22 | 21 | 26 | 30 | 25 | 22 | 23 | | | | |
| M01107 | 20 | 20 | 26 | 20 | 28 | 25 | 21 | 22 | 24 | 27 | 29 | 28 |
| M01108 | 21 | 24 | 24 | 28 | 30 | 27 | 26 | 25 | 26 | 29 | 29 | 29 |
| M01109 | 21 | 25 | 23 | 23 | 25 | 22 | 24 | 26 | 25 | 30 | 29 | 27 |
| M01110 | 18 | 22 | 25 | 24 | 27 | 23 | 24 | 22 | 25 | 29 | 26 | 25 |
| M01111 | 23 | 20 | 26 | 26 | 27 | 27 | 27 | 28 | 27 | 26 | 29 | 30 |
| M01112 | 15 | 24 | 27 | 25 | 27 | 27 | 23 | 28 | 29 | 31 | 34 | 32 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 21 | 22 | 24 | 24 | 27 | 24 | 24 | 24 | 26 | 29 | 29 | 29 |
| S.D. | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 2 | 2 | 3 | 2 |

Appendix 5-2. Individual food consumption (g/day) in male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Days of administration | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 |
| M02201 | 25 | 26 | 24 | 24 | 25 | 25 | 28 | 26 |
| M02202 | 21 | 21 | 24 | 25 | 29 | 28 | 27 | 25 |
| M02203 | 21 | 21 | 25 | 24 | 25 | 25 | 25 | 22 |
| M02204 | 18 | 23 | 24 | 23 | 27 | 22 | 24 | 23 |
| M02205 | 25 | 24 | 24 | 28 | 28 | 26 | 28 | 22 |
| M02206 | 20 | 24 | 24 | 23 | 30 | 26 | 26 | 21 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 22 | 23 | 24 | 25 | 27 | 25 | 26 | 23 |
| S.D. | 3 | 2 | 0 | 2 | 2 | 2 | 2 | 2 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | STL | STL | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 5-3. Individual food consumption (g/day) in male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| M03301 | 23 | 20 | 25 | 23 | 29 | 26 | 27 | 25 | | | | |
| M03302 | 21 | 22 | 21 | 27 | 30 | 26 | 29 | 24 | | | | |
| M03303 | 22 | 21 | 21 | 23 | 28 | 27 | 26 | 24 | | | | |
| M03304 | 25 | 22 | 27 | 22 | 25 | 24 | 22 | 24 | | | | |
| M03305 | 21 | 23 | 22 | 20 | 29 | 25 | 25 | 24 | | | | |
| M03306 | 19 | 24 | 24 | 26 | 28 | 29 | 28 | 26 | | | | |
| M03307 | 24 | 25 | 21 | 24 | 26 | 24 | 25 | 27 | 24 | 27 | 29 | 24 |
| M03308 | 20 | 23 | 24 | 24 | 25 | 27 | 26 | 27 | 26 | 29 | 28 | 30 |
| M03309 | 24 | 20 | 24 | 23 | 26 | 26 | 28 | 28 | 28 | 29 | 23 | 29 |
| M03310 | 21 | 24 | 22 | 23 | 26 | 24 | 23 | 21 | 26 | 25 | 26 | 30 |
| M03311 | 23 | 19 | 26 | 26 | 29 | 25 | 26 | 25 | 27 | 30 | 30 | 31 |
| M03312 | 24 | 23 | 25 | 24 | 25 | 24 | 24 | 24 | 25 | 25 | 23 | 26 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 22 | 22 | 24 | 24 | 27 | 26 | 26 | 25 | 26 | 28 | 27 | 28 |
| S.D. | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 3 | 3 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | STL | STL | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 5-4. Individual food consumption (g/day) in male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| M04401 | 19 | 15 | 22 | 16 | 24 | 24 | 23 | 23 | | | | |
| M04402 | 17 | 20 | 27 | 26 | 30 | 31 | 30 | 29 | | | | |
| M04403 | 22 | 19 | 25 | 21 | 28 | 29 | 27 | 26 | | | | |
| M04404 | 21 | 11 | 26 | 25 | 30 | 29 | 29 | 31 | | | | |
| M04405 | 13 | 15 | 19 | 29 | 27 | 25 | 28 | 25 | | | | |
| M04406 | 19 | 16 | 24 | 27 | 26 | 32 | 29 | 28 | | | | |
| M04407 | 15 | 17 | 25 | 24 | 24 | 25 | 25 | 22 | 22 | 23 | 26 | 27 |
| M04408 | 19 | 13 | 20 | 27 | 27 | 28 | 31 | 29 | 28 | 24 | 29 | 33 |
| M04409 | 13 | 20 | 27 | 26 | 28 | 26 | 28 | 24 | 26 | 27 | 29 | 32 |
| M04410 | 19 | 13 | 24 | 28 | 26 | 30 | 26 | 25 | 27 | 28 | 29 | 27 |
| M04411 | 11 | 22 | 17 | 18 | 27 | 29 | 27 | 26 | 29 | 29 | 34 | 30 |
| M04412 | 17 | 10 | 22 | 24 | 21 | 25 | 26 | 25 | 23 | 22 | 23 | 27 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 17 | 16 | 23 | 24 | 27 | 28 | 27 | 26 | 26 | 26 | 28 | 29 |
| S.D. | 3 | 4 | 3 | 4 | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 3 |
| Significance | ** | ## | NS | NS | NS | ** | ** | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | STL | STL | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

Significantly different from the control group (##: $p<0.01$ by Steel's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 6-1. Individual food consumption (g/day) in female rats

Control group

| Female No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| F01151 | 14 | 17 | 16 | 19 | 20 | 20 | 16 | 15 | | | | |
| F01152 | 17 | 17 | 11 | 18 | 17 | 19 | 18 | 18 | | | | |
| F01153 | 14 | 15 | 16 | 13 | 16 | 19 | 17 | 18 | | | | |
| F01154 | 13 | 15 | 17 | 18 | 18 | 18 | 18 | 16 | | | | |
| F01155 | 15 | 16 | 17 | 17 | 15 | 14 | 14 | 16 | | | | |
| F01156 | 16 | 13 | 15 | 16 | 17 | 18 | 17 | 17 | | | | |
| F01157 | 16 | 10 | 8 | 14 | 15 | 17 | 15 | 14 | 16 | 11 | 13 | 19 |
| F01158 | 18 | 16 | 15 | 19 | 17 | 20 | 18 | 18 | 23 | 21 | 17 | 21 |
| F01159 | 11 | 17 | 11 | 20 | 16 | 16 | 15 | 14 | 19 | 20 | 16 | 21 |
| F01160 | 14 | 18 | 16 | 17 | 16 | 15 | 17 | 14 | 19 | 22 | 19 | 19 |
| F01161 | 12 | 14 | 15 | 17 | 18 | 16 | 17 | 16 | 17 | 22 | 20 | 21 |
| F01162 | 17 | 13 | 9 | 18 | 15 | 17 | 15 | 13 | 18 | 14 | 12 | 19 |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 15 | 15 | 14 | 17 | 17 | 17 | 16 | 16 | 19 | 18 | 16 | 20 |
| S.D. | 2 | 2 | 3 | 2 | 1 | 2 | 1 | 2 | 2 | 5 | 3 | 1 |

Appendix 6-2. Individual food consumption (g/day) in female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Days of administration | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 |
| F02251 | 17 | 16 | 16 | 12 | 13 | 18 | 16 | 17 |
| F02252 | 10 | 14 | 10 | 14 | 16 | 19 | 16 | 16 |
| F02253 | 19 | 21 | 19 | 16 | 16 | 21 | 21 | 22 |
| F02254 | 19 | 21 | 20 | 23 | 21 | 22 | 20 | 17 |
| F02255 | 10 | 14 | 16 | 20 | 18 | 20 | 20 | 20 |
| F02256 | 17 | 19 | 18 | 16 | 15 | 22 | 18 | 20 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 15 | 18 | 17 | 17 | 17 | 20 | 19 | 19 |
| S.D. | 4 | 3 | 4 | 4 | 3 | 2 | 2 | 2 |
| Significance | NS | NS | NS | NS | NS | * | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 6-3. Individual food consumption (g/day) in female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| F03351 | 15 | 18 | 16 | 18 | 20 | 20 | 20 | 16 | | | | |
| F03352 | 18 | 21 | 19 | 20 | 19 | 18 | 17 | 19 | | | | |
| F03353 | 20 | 17 | 16 | 19 | 19 | 18 | 16 | 14 | | | | |
| F03354 | 16 | 15 | 14 | 16 | 17 | 19 | 16 | 17 | | | | |
| F03355 | 17 | 18 | 19 | 21 | 17 | 22 | 19 | 17 | | | | |
| F03356 | 13 | 15 | 14 | 16 | 15 | 18 | 18 | 13 | | | | |
| F03357 | 14 | 15 | 16 | 19 | 15 | 17 | 14 | 15 | 18 | 23 | 19 | 21 |
| F03358 | 11 | 17 | 15 | 18 | 18 | 17 | 16 | 11 | 14 | 22 | 22 | 19 |
| F03359 | 15 | 14 | 13 | 16 | 17 | 20 | 16 | 17 | 21 | 15 | 14 | 22 |
| F03360 | 19 | 17 | 19 | 19 | 20 | 20 | 20 | 19 | 22 | 22 | 19 | 20 |
| F03361 | 19 | 19 | 19 | 14 | 13 | 19 | 18 | 17 | 21 | 21 | 19 | 19 |
| F03362 | 19 | 19 | 14 | 22 | 19 | 21 | 18 | 19 | 24 | 22 | 18 | 23 |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 16 | 17 | 16 | 18 | 17 | 19 | 17 | 16 | 20 | 21 | 19 | 21 |
| S.D. | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 4 | 3 | 3 | 2 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 6-4. Individual food consumption (g/day) in female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| F04451 | 11 | 18 | 13 | 18 | 21 | 15 | 23 | 11 | | | | |
| F04452 | 8 | 21 | 21 | 18 | 22 | 15 | 20 | 24 | | | | |
| F04453 | 8 | 17 | 15 | 18 | 19 | 15 | 17 | 13 | | | | |
| F04454 | Died on Day 2 of administration | | | | | | | | | | | |
| F04455 | 15 | 17 | 16 | 20 | 19 | 19 | 17 | 18 | | | | |
| F04456 | 15 | 10 | 17 | 20 | 21 | 22 | 22 | 18 | | | | |
| F04457 | 5 | 16 | 21 | 22 | 21 | 17 | 18 | 18 | 18 | 21 | 22 | 23 |
| F04458 | 7 | 9 | 9 | 21 | 23 | 13 | 22 | 16 | 25 | 23 | 24 | 21 |
| F04459 | 13 | 16 | 21 | 12 | 19 | 21 | 22 | 17 | 22 | 18 | 11 | 20 |
| F04460 | 5 | 15 | 21 | 18 | 21 | 20 | 21 | 19 | 24 | 17 | 19 | 24 |
| F04461 | 16 | 19 | 16 | 20 | 18 | 19 | 16 | 17 | 22 | 26 | 25 | 23 |
| F04462 | 3 | 15 | 15 | 19 | 16 | 15 | 14 | 12 | 20 | 19 | 23 | 17 |
| Number of females | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 6 | 6 | 6 | 6 |
| Mean | 10 | 16 | 17 | 19 | 20 | 17 | 19 | 17 | 22 | 21 | 21 | 21 |
| S.D. | 5 | 4 | 4 | 3 | 2 | 3 | 3 | 4 | 3 | 3 | 5 | 3 |
| Significance | ** | NS | NS | NS | ** | NS | ** | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 7-1. Individual water consumption (g/day) in male rats

Control group

| Male No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| M01101 | 31 | 38 | 40 | 45 | 40 | 43 | 44 | 41 | | | | |
| M01102 | 28 | 27 | 26 | 25 | 28 | 30 | 33 | 28 | | | | |
| M01103 | 28 | 30 | 30 | 30 | 38 | 41 | 38 | 38 | | | | |
| M01104 | 30 | 28 | 33 | 33 | 38 | 39 | 35 | 32 | | | | |
| M01105 | 29 | 26 | 32 | 35 | 36 | 38 | 29 | 27 | | | | |
| M01106 | 30 | 29 | 28 | 33 | 37 | 37 | 34 | 32 | | | | |
| M01107 | 33 | 34 | 33 | 29 | 30 | 31 | 29 | 33 | 30 | 30 | 32 | 31 |
| M01108 | 36 | 36 | 33 | 37 | 37 | 35 | 36 | 30 | 33 | 33 | 35 | 37 |
| M01109 | 32 | 34 | 29 | 30 | 33 | 33 | 35 | 40 | 33 | 37 | 32 | 33 |
| M01110 | 31 | 38 | 34 | 36 | 36 | 45 | 38 | 38 | 39 | 38 | 32 | 32 |
| M01111 | 33 | 31 | 31 | 35 | 40 | 43 | 39 | 46 | 36 | 42 | 44 | 41 |
| M01112 | 24 | 36 | 33 | 34 | 33 | 34 | 35 | 40 | 36 | 37 | 38 | 37 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 30 | 32 | 32 | 34 | 36 | 37 | 35 | 35 | 35 | 36 | 36 | 35 |
| S.D. | 3 | 4 | 4 | 5 | 4 | 5 | 4 | 6 | 3 | 4 | 5 | 4 |

Appendix 7-2. Individual water consumption (g/day) in male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Days of administration | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 |
| M02201 | 34 | 34 | 32 | 32 | 32 | 33 | 34 | 39 |
| M02202 | 35 | 28 | 39 | 38 | 37 | 38 | 35 | 43 |
| M02203 | 33 | 24 | 35 | 37 | 38 | 44 | 41 | 37 |
| M02204 | 25 | 33 | 30 | 35 | 41 | 31 | 35 | 37 |
| M02205 | 28 | 27 | 29 | 30 | 28 | 35 | 33 | 31 |
| M02206 | 28 | 31 | 31 | 29 | 38 | 35 | 33 | 35 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 31 | 30 | 33 | 34 | 36 | 36 | 35 | 37 |
| S.D. | 4 | 4 | 4 | 4 | 5 | 5 | 3 | 4 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 7-3. Individual water consumption (g/day) in male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| M03301 | 33 | 32 | 34 | 37 | 41 | 46 | 42 | 49 | | | | |
| M03302 | 28 | 30 | 31 | 36 | 41 | 38 | 41 | 33 | | | | |
| M03303 | 28 | 28 | 26 | 29 | 32 | 35 | 38 | 31 | | | | |
| M03304 | 33 | 25 | 28 | 29 | 29 | 31 | 32 | 38 | | | | |
| M03305 | 31 | 31 | 28 | 30 | 40 | 39 | 36 | 39 | | | | |
| M03306 | 28 | 35 | 32 | 37 | 41 | 46 | 43 | 42 | | | | |
| M03307 | 33 | 31 | 30 | 34 | 34 | 37 | 34 | 41 | 31 | 36 | 30 | 33 |
| M03308 | 26 | 27 | 28 | 28 | 28 | 35 | 32 | 35 | 31 | 36 | 31 | 38 |
| M03309 | 33 | 27 | 28 | 30 | 34 | 41 | 37 | 42 | 33 | 33 | 26 | 31 |
| M03310 | 31 | 35 | 28 | 34 | 35 | 38 | 36 | 37 | 38 | 35 | 32 | 35 |
| M03311 | 31 | 32 | 33 | 32 | 34 | 34 | 36 | 34 | 37 | 40 | 35 | 33 |
| M03312 | 31 | 34 | 41 | 39 | 41 | 42 | 41 | 42 | 40 | 36 | 38 | 36 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 31 | 31 | 31 | 33 | 36 | 39 | 37 | 39 | 35 | 36 | 32 | 34 |
| S.D. | 2 | 3 | 4 | 4 | 5 | 5 | 4 | 5 | 4 | 2 | 4 | 3 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 7-4. Individual water consumption (g/day) in male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| M04401 | 33 | 26 | 35 | 34 | 44 | 45 | 42 | 49 | | | | |
| M04402 | 28 | 33 | 42 | 42 | 49 | 52 | 52 | 51 | | | | |
| M04403 | 33 | 34 | 39 | 50 | 58 | 54 | 48 | 55 | | | | |
| M04404 | 38 | 28 | 37 | 41 | 58 | 67 | 61 | 67 | | | | |
| M04405 | 24 | 29 | 38 | 44 | 48 | 49 | 49 | 49 | | | | |
| M04406 | 29 | 30 | 42 | 43 | 58 | 55 | 54 | 55 | | | | |
| M04407 | 22 | 27 | 34 | 36 | 37 | 43 | 45 | 37 | 30 | 33 | 31 | 32 |
| M04408 | 30 | 25 | 40 | 50 | 42 | 65 | 59 | 58 | 41 | 42 | 38 | 40 |
| M04409 | 27 | 36 | 37 | 44 | 43 | 51 | 52 | 52 | 42 | 42 | 38 | 38 |
| M04410 | 26 | 29 | 41 | 45 | 44 | 54 | 43 | 48 | 37 | 36 | 31 | 31 |
| M04411 | 24 | 68 | 29 | 42 | 53 | 63 | 50 | 59 | 54 | 48 | 45 | 45 |
| M04412 | 25 | 18 | 37 | 49 | 43 | 47 | 53 | 51 | 40 | 32 | 29 | 37 |
| Number of males | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 28 | 32 | 38 | 43 | 48 | 54 | 51 | 53 | 41 | 39 | 35 | 37 |
| S.D. | 5 | 12 | 4 | 5 | 7 | 8 | 6 | 7 | 8 | 6 | 6 | 5 |
| Significance | NS | NS | ** | ** | ** | ** | ** | ** | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 8-1. Individual water consumption (g/day) in female rats

Control group

| Female No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| F01151 | 20 | 21 | 20 | 30 | 25 | 26 | 26 | 19 | | | | |
| F01152 | 23 | 25 | 12 | 25 | 21 | 25 | 25 | 23 | | | | |
| F01153 | 22 | 26 | 23 | 25 | 26 | 34 | 35 | 29 | | | | |
| F01154 | 20 | 25 | 24 | 31 | 26 | 29 | 24 | 21 | | | | |
| F01155 | 25 | 28 | 25 | 32 | 26 | 27 | 28 | 24 | | | | |
| F01156 | 26 | 22 | 20 | 29 | 27 | 30 | 30 | 23 | | | | |
| F01157 | 27 | 16 | 11 | 25 | 21 | 26 | 26 | 23 | 23 | 14 | 16 | 25 |
| F01158 | 27 | 21 | 16 | 26 | 20 | 27 | 27 | 25 | 28 | 23 | 20 | 28 |
| F01159 | 23 | 21 | 12 | 23 | 20 | 24 | 22 | 18 | 21 | 19 | 18 | 22 |
| F01160 | 29 | 28 | 21 | 31 | 25 | 23 | 29 | 17 | 29 | 28 | 25 | 30 |
| F01161 | 21 | 23 | 25 | 34 | 30 | 28 | 29 | 24 | 25 | 32 | 38 | 33 |
| F01162 | 30 | 21 | 17 | 28 | 22 | 25 | 28 | 22 | 30 | 18 | 15 | 26 |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 24 | 23 | 19 | 28 | 24 | 27 | 27 | 22 | 26 | 22 | 22 | 27 |
| S.D. | 3 | 3 | 5 | 3 | 3 | 3 | 3 | 3 | 4 | 7 | 9 | 4 |

Appendix 8-2. Individual water consumption (g/day) in female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Days of administration | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 |
| F02251 | 22 | 25 | 20 | 21 | 19 | 27 | 26 | 24 |
| F02252 | 19 | 19 | 13 | 27 | 20 | 28 | 26 | 24 |
| F02253 | 31 | 31 | 33 | 28 | 24 | 32 | 36 | 33 |
| F02254 | 25 | 28 | 27 | 32 | 34 | 36 | 33 | 21 |
| F02255 | 20 | 26 | 20 | 32 | 28 | 36 | 34 | 32 |
| F02256 | 28 | 27 | 26 | 27 | 24 | 25 | 25 | 27 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 24 | 26 | 23 | 28 | 25 | 31 | 30 | 27 |
| S.D. | 5 | 4 | 7 | 4 | 6 | 5 | 5 | 5 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | STL | DU | STL | STL | STL | STL | STL |

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 8-3. Individual water consumption (g/day) in female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| F03351 | 28 | 37 | 33 | 34 | 34 | 34 | 32 | 25 | | | | |
| F03352 | 35 | 33 | 32 | 36 | 40 | 32 | 33 | 32 | | | | |
| F03353 | 31 | 25 | 23 | 31 | 27 | 32 | 30 | 22 | | | | |
| F03354 | 30 | 21 | 21 | 25 | 23 | 27 | 27 | 26 | | | | |
| F03355 | 25 | 28 | 31 | 36 | 30 | 35 | 33 | 23 | | | | |
| F03356 | 20 | 25 | 22 | 26 | 20 | 24 | 26 | 19 | | | | |
| F03357 | 24 | 23 | 20 | 28 | 19 | 26 | 28 | 19 | 22 | 22 | 21 | 24 |
| F03358 | 20 | 26 | 22 | 27 | 26 | 28 | 26 | 16 | 17 | 25 | 25 | 27 |
| F03359 | 27 | 25 | 21 | 32 | 28 | 35 | 32 | 29 | 33 | 24 | 20 | 30 |
| F03360 | 28 | 26 | 24 | 30 | 32 | 32 | 37 | 30 | 36 | 40 | 31 | 31 |
| F03361 | 26 | 32 | 29 | 29 | 24 | 32 | 34 | 28 | 32 | 33 | 34 | 33 |
| F03362 | 33 | 25 | 20 | 29 | 25 | 30 | 29 | 24 | 29 | 27 | 19 | 23 |
| Number of females | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 6 | 6 | 6 | 6 |
| Mean | 27 | 27 | 25 | 30 | 27 | 31 | 31 | 24 | 28 | 29 | 25 | 28 |
| S.D. | 5 | 5 | 5 | 4 | 6 | 4 | 3 | 5 | 7 | 7 | 6 | 4 |
| Significance | NS | NS | * | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | STL | DU | STL | STL | STL | STL | STL | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 8-4. Individual water consumption (g/day) in female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Days of administration | | | | | | | | Days of recovery | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 5 | 9 | 12 | 16 | 19 | 23 | 26 | 2 | 5 | 9 | 12 |
| F04451 | 12 | 27 | 26 | 33 | 31 | 23 | 34 | 36 | | | | |
| F04452 | 16 | 34 | 34 | 34 | 40 | 27 | 38 | 37 | | | | |
| F04453 | 36 | 100 | 44 | 54 | 50 | 47 | 50 | 52 | | | | |
| F04454 | Died on Day 2 of administration | | | | | | | | | | | |
| F04455 | 26 | 33 | 31 | 38 | 33 | 33 | 36 | 32 | | | | |
| F04456 | 37 | 36 | 29 | 44 | 37 | 42 | 45 | 38 | | | | |
| F04457 | 9 | 22 | 28 | 33 | 34 | 29 | 32 | 28 | 31 | 33 | 32 | 29 |
| F04458 | 15 | 89 | 34 | 67 | 74 | 74 | 62 | 66 | 52 | 37 | 47 | 40 |
| F04459 | 28 | 58 | 43 | 32 | 41 | 50 | 41 | 32 | 38 | 29 | 22 | 39 |
| F04460 | 3 | 36 | 35 | 46 | 48 | 43 | 51 | 41 | 36 | 21 | 26 | 30 |
| F04461 | 38 | 71 | 42 | 51 | 40 | 47 | 37 | 47 | 45 | 33 | 37 | 36 |
| F04462 | 10 | 34 | 32 | 40 | 31 | 32 | 35 | 33 | 39 | 30 | 29 | 22 |
| Number of females | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 11 | 6 | 6 | 6 | 6 |
| Mean | 21 | 49 | 34 | 43 | 42 | 41 | 42 | 40 | 40 | 31 | 32 | 33 |
| S.D. | 13 | 27 | 6 | 11 | 12 | 14 | 9 | 11 | 7 | 5 | 9 | 7 |
| Significance | NS | ## | ** | ## | ## | # | ## | ## | ** | NS | NS | NS |
| Statistical method | STL | STL | DU | STL | STL | STL | STL | STL | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

Significantly different from the control group (#: $p<0.05$, ##: $p<0.01$ by Steel's test).

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 9-1. Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M01102 | M00001 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M01103 | M00026 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M01104 | M00046 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M01105 | M00047 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M01106 | M00011 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

Findings were graded as follows: (Continued)

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

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

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| M01102 | M00001 | 5 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| M01103 | M00026 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| M01104 | M00046 | 4 | 4 | 3 | 7 | 4 | 0 | 0 | 0 | 0 | 0 |
| M01105 | M00047 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M01106 | M00011 | 1 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.3 | 1.5 | 1.2 | 1.8 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| S.D. | | 2.3 | 1.4 | 1.2 | 2.6 | 1.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

(Continued)

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Palpebral closure: 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 9-1. (Continued) Individual FOB of male rats

Control group

| Male No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M01101 | M00010 | 1 | 1 | 1 | 1 | 1 |
| M01102 | M00001 | 1 | 1 | 1 | 1 | 1 |
| M01103 | M00026 | 1 | 1 | 1 | 1 | 1 |
| M01104 | M00046 | 1 | 1 | 1 | 1 | 1 |
| M01105 | M00047 | 1 | 1 | 1 | 1 | 1 |
| M01106 | M00011 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows:

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

Appendix 9-2. Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M02202 | M00017 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M02203 | M00020 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M02204 | M00044 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M02205 | M00019 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M02206 | M00028 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

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

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 0 | 2 | 9 | 0 | 0 | 0 | 0 | 0 | 0 |
| M02202 | M00017 | 4 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| M02203 | M00020 | 4 | 1 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| M02204 | M00044 | 3 | 8 | 1 | 11 | 2 | 0 | 0 | 0 | 0 | 0 |
| M02205 | M00019 | 3 | 4 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| M02206 | M00028 | 7 | 3 | 3 | 13 | 9 | 0 | 0 | 0 | 0 | 0 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 3.7 | 3.3 | 1.0 | 6.2 | 2.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| S.D. | | 2.0 | 2.8 | 1.3 | 5.5 | 3.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Significance | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | | DU | DU | DU | DU | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 9-2. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M02201 | M00023 | 1 | 1 | 1 | 1 | 1 |
| M02202 | M00017 | 1 | 1 | 1 | 1 | 1 |
| M02203 | M00020 | 1 | 1 | 1 | 1 | 1 |
| M02204 | M00044 | 1 | 1 | 1 | 1 | 1 |
| M02205 | M00019 | 1 | 1 | 1 | 1 | 1 |
| M02206 | M00028 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.
Findings were graded as follows:
Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 9-3. Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M03302 | M00048 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M03303 | M00042 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M03304 | M00014 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M03305 | M00051 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M03306 | M00043 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

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

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 6 | 4 | 1 | 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| M03302 | M00048 | 2 | 6 | 1 | 1 | 4 | 0 | 0 | 0 | 0 | 0 |
| M03303 | M00042 | 1 | 3 | 3 | 6 | 5 | 0 | 0 | 0 | 0 | 0 |
| M03304 | M00014 | 1 | 2 | 0 | 8 | 2 | 0 | 0 | 0 | 0 | 0 |
| M03305 | M00051 | 0 | 4 | 1 | 8 | 1 | 0 | 0 | 0 | 1 | 0 |
| M03306 | M00043 | 2 | 13 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 0 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 5.3 | 1.0 | 5.3 | 2.2 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| S.D. | | 2.1 | 4.0 | 1.1 | 2.7 | 1.9 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 |
| Significance | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | | DU | DU | DU | DU | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 9-3. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M03301 | M00008 | 1 | 1 | 1 | 1 | 1 |
| M03302 | M00048 | 1 | 1 | 1 | 1 | 1 |
| M03303 | M00042 | 1 | 1 | 1 | 1 | 1 |
| M03304 | M00014 | 1 | 1 | 1 | 1 | 1 |
| M03305 | M00051 | 1 | 1 | 1 | 1 | 1 |
| M03306 | M00043 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.
Findings were graded as follows:
Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 9-4. Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M04402 | M00035 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M04403 | M00027 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M04404 | M00004 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M04405 | M00025 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M04406 | M00030 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

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

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| M04402 | M00035 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 1 |
| M04403 | M00027 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| M04405 | M00025 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 | 1 |
| M04406 | M00030 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.3 | 1.3 | 1.7 | 1.3 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1-2 | 1-2 | 1-2 | 1-2 |
| Significance | | --- | --- | --- | --- | --- | --- | NS | NS | NS | NS |
| Statistical method | | UA | UA | UA | UA | UA | UA | STL | STL | STL | STL |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 4 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| M04402 | M00035 | 5 | 8 | 4 | 13 | 12 | 0 | 0 | 0 | 0 | 0 |
| M04403 | M00027 | 0 | 1 | 6 | 1 | 12 | 0 | 0 | 0 | 0 | 0 |
| M04404 | M00004 | 5 | 12 | 3 | 8 | 5 | 0 | 0 | 0 | 0 | 0 |
| M04405 | M00025 | 3 | 8 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| M04406 | M00030 | 12 | 3 | 0 | 6 | 0 | 0 | 0 | 0 | 0 | 0 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 4.8 | 5.7 | 2.5 | 5.5 | 5.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| S.D. | | 4.0 | 4.3 | 2.3 | 4.6 | 5.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Significance | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | | DU | DU | DU | DU | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 9-4. (Continued) Individual FOB of male rats

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| M04401 | M00003 | 1 | 1 | 1 | 1 | 1 |
| M04402 | M00035 | 1 | 1 | 1 | 1 | 1 |
| M04403 | M00027 | 1 | 1 | 1 | 1 | 1 |
| M04404 | M00004 | 1 | 1 | 1 | 1 | 1 |
| M04405 | M00025 | 1 | 1 | 1 | 1 | 1 |
| M04406 | M00030 | 1 | 1 | 1 | 1 | 1 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.
Findings were graded as follows:
Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 10-1. Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F01152 | F00039 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F01153 | F00047 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F01154 | F00033 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F01155 | F00034 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F01156 | F00049 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

Findings were graded as follows: (Continued)

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

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

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 4 | 5 | 8 | 6 | 8 | 0 | 0 | 0 | 0 | 0 |
| F01152 | F00039 | 2 | 9 | 3 | 7 | 9 | 0 | 0 | 0 | 0 | 0 |
| F01153 | F00047 | 7 | 8 | 8 | 5 | 4 | 0 | 0 | 0 | 0 | 0 |
| F01154 | F00033 | 6 | 9 | 16 | 15 | 1 | 0 | 0 | 0 | 0 | 0 |
| F01155 | F00034 | 4 | 17 | 11 | 9 | 4 | 0 | 0 | 0 | 0 | 0 |
| F01156 | F00049 | 3 | 12 | 5 | 13 | 8 | 0 | 0 | 0 | 0 | 0 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 4.3 | 10.0 | 8.5 | 9.2 | 5.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| S.D. | | 1.9 | 4.1 | 4.6 | 4.0 | 3.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

(Continued)

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Palpebral closure: 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows: (Continued)

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 10-1. (Continued) Individual FOB of female rats

Control group

| Female No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F01151 | F00024 | 1 | 1 | 1 | 1 | 1 |
| F01152 | F00039 | 1 | 1 | 1 | 1 | 1 |
| F01153 | F00047 | 1 | 1 | 1 | 1 | 1 |
| F01154 | F00033 | 1 | 1 | 1 | 1 | 1 |
| F01155 | F00034 | 1 | 1 | 1 | 1 | 1 |
| F01156 | F00049 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |

Findings were graded as follows:

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

Appendix 10-2. Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F02252 | F00021 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F02253 | F00019 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F02254 | F00036 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F02255 | F00017 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F02256 | F00030 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

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

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 5 | 11 | 12 | 3 | 6 | 0 | 0 | 0 | 0 | 0 |
| F02252 | F00021 | 6 | 5 | 6 | 6 | 10 | 0 | 0 | 0 | 0 | 0 |
| F02253 | F00019 | 0 | 1 | 5 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| F02254 | F00036 | 1 | 5 | 4 | 8 | 2 | 0 | 0 | 0 | 1 | 0 |
| F02255 | F00017 | 7 | 6 | 8 | 9 | 1 | 0 | 0 | 0 | 0 | 0 |
| F02256 | F00030 | 6 | 7 | 4 | 9 | 10 | 0 | 0 | 0 | 0 | 0 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 4.2 | 5.8 | 6.5 | 6.0 | 5.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| S.D. | | 2.9 | 3.3 | 3.1 | 3.3 | 4.3 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 |
| Significance | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 10-2. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F02251 | F00009 | 1 | 1 | 1 | 1 | 1 |
| F02252 | F00021 | 1 | 1 | 1 | 1 | 1 |
| F02253 | F00019 | 1 | 1 | 1 | 1 | 1 |
| F02254 | F00036 | 1 | 1 | 1 | 1 | 1 |
| F02255 | F00017 | 1 | 1 | 1 | 1 | 1 |
| F02256 | F00030 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.
Findings were graded as follows:
Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 10-3. Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F03352 | F00027 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F03353 | F00023 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F03354 | F00048 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F03355 | F00041 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F03356 | F00010 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

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

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 11 | 8 | 0 | 5 | 0 | 0 | 0 | 0 | 0 |
| F03352 | F00027 | 0 | 9 | 12 | 9 | 7 | 0 | 0 | 0 | 0 | 0 |
| F03353 | F00023 | 1 | 7 | 8 | 3 | 1 | 0 | 0 | 0 | 0 | 0 |
| F03354 | F00048 | 1 | 10 | 5 | 17 | 1 | 0 | 0 | 0 | 1 | 0 |
| F03355 | F00041 | 0 | 6 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| F03356 | F00010 | 2 | 4 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 0.8 | 7.8 | 6.2 | 5.3 | 2.3 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| S.D. | | 0.8 | 2.6 | 4.0 | 6.5 | 2.9 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 |
| Significance | | * | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

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

DU: Analysis by Dunnett's test.

NS: Not significantly different from the control group.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group. (Continued)

Findings were graded as follows:

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 10-3. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F03351 | F00038 | 1 | 1 | 1 | 1 | 1 |
| F03352 | F00027 | 1 | 1 | 1 | 1 | 1 |
| F03353 | F00023 | 1 | 1 | 1 | 1 | 1 |
| F03354 | F00048 | 1 | 1 | 1 | 1 | 1 |
| F03355 | F00041 | 1 | 1 | 1 | 1 | 1 |
| F03356 | F00010 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.
Findings were graded as follows:
Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Appendix 10-4. Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Posture | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 2 | & | | | | 1 | & | | | |
| F04455 | F00001 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration. (Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Biting behavior | | | | | Clonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 1 | & | | | | 1 | & | | | |
| F04455 | F00001 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration.

(Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Biting behavior 1: Not observed, 2: observed.

Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals in cages | | | | |
|---|---|---|---|---|---|---|
| | | Tonic convulsions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 1 | & | | | |
| F04455 | F00001 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration.

(Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

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

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Ease of removal from cage | | | | | Ease of handling | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F04452 | F00016 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F04453 | F00005 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F04454 | F00015 | 2 | & | | | | 2 | & | | | |
| F04455 | F00001 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| F04456 | F00042 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration. (Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

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

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

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Muscle tone | | | | | Fur conditions | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 2 | & | | | | 1 | & | | | |
| F04455 | F00001 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration.

(Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Muscle tone 1: Decreased, 2: normal, 3: increased.

Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Lacrimation | | | | | Salivation | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 3 |
| F04452 | F00016 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 3 |
| F04453 | F00005 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 1 | & | | | | 1 | & | | | |
| F04455 | F00001 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 |
| F04456 | F00042 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.2 | 1.6 | 1.6 | 1.8 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1-2 | 1-2 | 1-2 | 1-3 |
| Significance | | --- | --- | --- | --- | --- | --- | NS | NS | NS | NS |
| Statistical method | | UA | UA | UA | UA | UA | UA | STL | STL | STL | STL |

&: Died on Day 2 of administration.

(Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

Findings were graded as follows:

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Observation of animals on observer's palm | | | | |
|---|---|---|---|---|---|---|
| | | Respiration | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 1 | & | | | |
| F04455 | F00001 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration. (Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Frequency of rearing (during a 2-minute period) | | | | | Frequency of grooming (during a 2-minute period) | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 0 | 5 | 9 | 17 | 5 | 0 | 0 | 0 | 0 | 0 |
| F04452 | F00016 | 7 | 8 | 4 | 0 | 7 | 0 | 0 | 0 | 0 | 0 |
| F04453 | F00005 | 3 | 2 | 4 | 1 | 2 | 0 | 0 | 0 | 0 | 0 |
| F04454 | F00015 | 4 | & | | | | 0 | & | | | |
| F04455 | F00001 | 6 | 5 | 5 | 2 | 3 | 0 | 0 | 0 | 1 | 0 |
| F04456 | F00042 | 3 | 5 | 4 | 9 | 5 | 0 | 0 | 0 | 0 | 0 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 3.8 | 5.0 | 5.2 | 5.8 | 4.4 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |
| S.D. | | 2.5 | 2.1 | 2.2 | 7.2 | 1.9 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 |
| Significance | | NS | * | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

&: Died on Day 2 of administration.

(Continued)

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

DU: Analysis by Dunnett's test.

NS: Not significantly different from the control group.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gait | | | | | Palpebral closure | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 1 | & | | | | 1 | & | | | |
| F04455 | F00001 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration.

(Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

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

Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Open-field test | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Consciousness | | | | | Behavioral abnormalities | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 2 | & | | | | 1 | & | | | |
| F04455 | F00001 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 5 |
| Mean | | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration. (Continued)

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

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

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Appendix 10-4. (Continued) Individual FOB of female rats

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Open-field test | | | | |
|---|---|---|---|---|---|---|
| | | Righting reflex | | | | |
| | | Pre | Day 7 | Day 14 | Day 21 | Day 27 |
| F04451 | F00044 | 1 | 1 | 1 | 1 | 1 |
| F04452 | F00016 | 1 | 1 | 1 | 1 | 1 |
| F04453 | F00005 | 1 | 1 | 1 | 1 | 1 |
| F04454 | F00015 | 1 | & | | | |
| F04455 | F00001 | 1 | 1 | 1 | 1 | 1 |
| F04456 | F00042 | 1 | 1 | 1 | 1 | 1 |
| Number of females | | 6 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Range | | 1 | 1 | 1 | 1 | 1 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

&: Died on Day 2 of administration.

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

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

Appendix 11-1. Individual sensory response of male rats on termination of administration period

Control group

| Male No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| M01101 | M00010 | 1 | 2 | 2 | 2 | 3 |
| M01102 | M00001 | 1 | 2 | 2 | 2 | 3 |
| M01103 | M00026 | 1 | 2 | 2 | 2 | 3 |
| M01104 | M00046 | 1 | 2 | 2 | 2 | 3 |
| M01105 | M00047 | 1 | 2 | 2 | 2 | 3 |
| M01106 | M00011 | 1 | 2 | 2 | 2 | 3 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 11-2. Individual sensory response of male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| M02201 | M00023 | 1 | 2 | 2 | 2 | 3 |
| M02202 | M00017 | 1 | 2 | 2 | 2 | 3 |
| M02203 | M00020 | 1 | 2 | 2 | 2 | 3 |
| M02204 | M00044 | 1 | 2 | 2 | 2 | 3 |
| M02205 | M00019 | 1 | 2 | 2 | 2 | 3 |
| M02206 | M00028 | 1 | 2 | 2 | 2 | 3 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 11-3. Individual sensory response of male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| M03301 | M00008 | 1 | 2 | 2 | 2 | 3 |
| M03302 | M00048 | 1 | 2 | 2 | 2 | 3 |
| M03303 | M00042 | 1 | 2 | 2 | 2 | 3 |
| M03304 | M00014 | 1 | 2 | 2 | 2 | 3 |
| M03305 | M00051 | 1 | 2 | 2 | 2 | 3 |
| M03306 | M00043 | 1 | 2 | 2 | 2 | 3 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 11-4. Individual sensory response of male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| M04401 | M00003 | 1 | 2 | 2 | 2 | 3 |
| M04402 | M00035 | 1 | 2 | 2 | 2 | 3 |
| M04403 | M00027 | 1 | 2 | 2 | 2 | 3 |
| M04404 | M00004 | 1 | 2 | 2 | 2 | 3 |
| M04405 | M00025 | 1 | 2 | 2 | 2 | 3 |
| M04406 | M00030 | 1 | 2 | 2 | 2 | 3 |
| Number of males | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 12-1. Individual sensory response of female rats on termination of administration period

Control group

| Female No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| F01151 | F00024 | 1 | 2 | 2 | 2 | 3 |
| F01152 | F00039 | 1 | 2 | 2 | 2 | 3 |
| F01153 | F00047 | 1 | 2 | 2 | 2 | 3 |
| F01154 | F00033 | 1 | 2 | 2 | 2 | 3 |
| F01155 | F00034 | 1 | 2 | 2 | 2 | 3 |
| F01156 | F00049 | 1 | 2 | 2 | 2 | 3 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 12-2. Individual sensory response of female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| F02251 | F00009 | 1 | 2 | 2 | 2 | 3 |
| F02252 | F00021 | 1 | 2 | 2 | 2 | 3 |
| F02253 | F00019 | 1 | 2 | 2 | 2 | 3 |
| F02254 | F00036 | 1 | 2 | 2 | 2 | 3 |
| F02255 | F00017 | 1 | 2 | 2 | 2 | 3 |
| F02256 | F00030 | 1 | 2 | 2 | 2 | 3 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 12-3. Individual sensory response of female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| F03351 | F00038 | 1 | 2 | 2 | 2 | 3 |
| F03352 | F00027 | 1 | 2 | 2 | 2 | 3 |
| F03353 | F00023 | 1 | 2 | 2 | 2 | 3 |
| F03354 | F00048 | 1 | 2 | 2 | 2 | 3 |
| F03355 | F00041 | 1 | 2 | 2 | 2 | 3 |
| F03356 | F00010 | 1 | 2 | 2 | 2 | 3 |
| Number of females | | 6 | 6 | 6 | 6 | 6 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 12-4. Individual sensory response of female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Blind No. | Pupillary reflex | Approaching behavior | Response to touch | Auditory reflex | Pain reflex |
|---|---|---|---|---|---|---|
| F04451 | F00044 | 1 | 2 | 2 | 2 | 3 |
| F04452 | F00016 | 1 | 2 | 2 | 2 | 3 |
| F04453 | F00005 | 1 | 2 | 2 | 2 | 3 |
| F04454 | F00015 | Died on Day 2 of administration | | | | |
| F04455 | F00001 | 1 | 2 | 2 | 2 | 3 |
| F04456 | F00042 | 1 | 2 | 2 | 2 | 3 |
| Number of females | | 5 | 5 | 5 | 5 | 5 |
| Mean | | 1.0 | 2.0 | 2.0 | 2.0 | 3.0 |
| Range | | 1 | 2 | 2 | 2 | 3 |
| Significance | | --- | --- | --- | --- | --- |
| Statistical method | | UA | UA | UA | UA | UA |

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Findings were graded as follows:

Pupillary reflex: 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior: 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Response to touch: 1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing, 4: jumping at or biting at stimulus.

Auditory reflex: 1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex: 1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus, 3: quickly moving forward to escape from stimulus or biting at it immediately after looking back, 4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Appendix 13-1. Individual grip strength (g) of male rats on termination of administration period

Control group

| Male No. | Forelimb | Hindlimb |
|---|---|---|
| M01101 | 1650 | 475 |
| M01102 | 1572 | 393 |
| M01103 | 1432 | 422 |
| M01104 | 1319 | 341 |
| M01105 | 1208 | 378 |
| M01106 | 1258 | 385 |
| Number of males | 6 | 6 |
| Mean | 1407 | 399 |
| S.D. | 177 | 45 |

Appendix 13-2. Individual grip strength (g) of male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Forelimb | Hindlimb |
|---|---|---|
| M02201 | 1247 | 345 |
| M02202 | 1138 | 319 |
| M02203 | 1457 | 355 |
| M02204 | 1252 | 334 |
| M02205 | 1385 | 354 |
| M02206 | 1290 | 269 |
| Number of males | 6 | 6 |
| Mean | 1295 | 329 |
| S.D. | 112 | 33 |
| Significance | NS | * |
| Statistical method | DU | DU |

Significantly different from the control group (*: $p<0.05$ by Dunnett's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 13-3. Individual grip strength (g) of male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Forelimb | Hindlimb |
|---|---|---|
| M03301 | 1257 | 265 |
| M03302 | 1230 | 363 |
| M03303 | 1274 | 356 |
| M03304 | 1387 | 296 |
| M03305 | 1293 | 363 |
| M03306 | 1130 | 333 |
| Number of males | 6 | 6 |
| Mean | 1262 | 329 |
| S.D. | 84 | 41 |
| Significance | NS | * |
| Statistical method | DU | DU |

Significantly different from the control group (*: $p<0.05$ by Dunnett's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 13-4. Individual grip strength (g) of male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Forelimb | Hindlimb |
|---|---|---|
| M04401 | 1288 | 345 |
| M04402 | 1203 | 284 |
| M04403 | 945 | 326 |
| M04404 | 1405 | 266 |
| M04405 | 1153 | 300 |
| M04406 | 875 | 197 |
| Number of males | 6 | 6 |
| Mean | 1145 | 286 |
| S.D. | 202 | 52 |
| Significance | * | ** |
| Statistical method | DU | DU |

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).

DU: Analysis by Dunnett's test.

Appendix 14-1. Individual grip strength (g) of female rats on termination of administration period

Control group

| Female No. | Forelimb | Hindlimb |
|---|---|---|
| F01151 | 1179 | 262 |
| F01152 | 1058 | 258 |
| F01153 | 977 | 262 |
| F01154 | 1116 | 292 |
| F01155 | 1016 | 283 |
| F01156 | 973 | 273 |
| Number of females | 6 | 6 |
| Mean | 1053 | 272 |
| S.D. | 82 | 14 |

Appendix 14-2. Individual grip strength (g) of female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Forelimb | Hindlimb |
|---|---|---|
| F02251 | 1259 | 142 |
| F02252 | 896 | 287 |
| F02253 | 1188 | 298 |
| F02254 | 964 | 229 |
| F02255 | 1051 | 227 |
| F02256 | 1175 | 295 |
| Number of females | 6 | 6 |
| Mean | 1089 | 246 |
| S.D. | 142 | 60 |
| Significance | NS | NS |
| Statistical method | DU | STL |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 14-3. Individual grip strength (g) of female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Forelimb | Hindlimb |
|---|---|---|
| F03351 | 998 | 204 |
| F03352 | 728 | 293 |
| F03353 | 1024 | 304 |
| F03354 | 1194 | 258 |
| F03355 | 1129 | 258 |
| F03356 | 958 | 270 |
| Number of females | 6 | 6 |
| Mean | 1005 | 265 |
| S.D. | 162 | 35 |
| Significance | NS | NS |
| Statistical method | DU | STL |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 14-4. Individual grip strength (g) of female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Forelimb | Hindlimb |
|---|---|---|
| F04451 | 653 | 158 |
| F04452 | 942 | 230 |
| F04453 | 1069 | 265 |
| F04454 | Died on Day 2 of administration | |
| F04455 | 975 | 217 |
| F04456 | 1108 | 263 |
| Number of females | 5 | 5 |
| Mean | 949 | 227 |
| S.D. | 179 | 44 |
| Significance | NS | NS |
| Statistical method | DU | STL |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 15-1. Individual spontaneous motor activity of male rats on termination of administration priod

Control group

| Male No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| M01101 | 446 | 286 | 190 | 113 | 314 | 1 | 1350 | 48 | 31 | 21 | 10 | 31 | 1 | 142 |
| M01102 | 360 | 158 | 27 | 129 | 167 | 14 | 855 | 41 | 33 | 14 | 13 | 29 | 1 | 131 |
| M01103 | 161 | 45 | 4 | 0 | 0 | 0 | 210 | 23 | 7 | 7 | 0 | 0 | 0 | 37 |
| M01104 | 378 | 186 | 196 | 37 | 0 | 0 | 797 | 51 | 12 | 27 | 3 | 0 | 0 | 93 |
| M01105 | 154 | 37 | 56 | 0 | 0 | 0 | 247 | 32 | 20 | 16 | 0 | 0 | 0 | 68 |
| M01106 | 295 | 268 | 328 | 1 | 0 | 1 | 893 | 67 | 29 | 26 | 0 | 0 | 0 | 122 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 299 | 163 | 134 | 47 | 80 | 3 | 725 | 44 | 22 | 19 | 4 | 10 | 0 | 99 |
| S.D. | 120 | 106 | 126 | 60 | 133 | 6 | 432 | 15 | 11 | 8 | 6 | 16 | 1 | 41 |

Appendix 15-2. Individual spontaneous motor activity of male rats on termination of administration priod

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| M02201 | 440 | 259 | 211 | 209 | 129 | 107 | 1355 | 82 | 62 | 48 | 42 | 25 | 40 | 299 |
| M02202 | 376 | 255 | 233 | 158 | 158 | 140 | 1320 | 48 | 36 | 32 | 24 | 24 | 18 | 182 |
| M02203 | 583 | 470 | 186 | 39 | 182 | 16 | 1476 | 82 | 39 | 35 | 5 | 22 | 3 | 186 |
| M02204 | 145 | 103 | 0 | 30 | 0 | 0 | 278 | 18 | 11 | 0 | 2 | 0 | 0 | 31 |
| M02205 | 0 | 6 | 23 | 2 | 0 | 0 | 31 | 0 | 1 | 3 | 0 | 0 | 0 | 4 |
| M02206 | 296 | 86 | 0 | 0 | 267 | 0 | 649 | 38 | 11 | 0 | 0 | 17 | 0 | 66 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 307 | 197 | 109 | 73 | 123 | 44 | 852 | 45 | 27 | 20 | 12 | 15 | 10 | 128 |
| S.D. | 209 | 167 | 112 | 88 | 106 | 63 | 617 | 33 | 23 | 21 | 17 | 12 | 16 | 113 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | STL | DU | STL | DU | DU | DU | DU | STL | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 15-3. Individual spontaneous motor activity of male rats on termination of administration priod

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| M03301 | 316 | 212 | 92 | 0 | 0 | 72 | 692 | 61 | 26 | 20 | 3 | 0 | 19 | 129 |
| M03302 | 349 | 234 | 37 | 1339 | 1017 | 0 | 2976 | 70 | 31 | 4 | 0 | 0 | 0 | 105 |
| M03303 | 333 | 276 | 111 | 1 | 77 | 35 | 833 | 65 | 23 | 37 | 0 | 14 | 12 | 151 |
| M03304 | 271 | 241 | 78 | 39 | 0 | 0 | 629 | 66 | 61 | 39 | 15 | 4 | 0 | 185 |
| M03305 | 414 | 494 | 201 | 186 | 204 | 184 | 1683 | 75 | 82 | 22 | 19 | 21 | 21 | 240 |
| M03306 | 79 | 211 | 119 | 0 | 63 | 52 | 524 | 9 | 28 | 8 | 0 | 6 | 2 | 53 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 294 | 278 | 106 | 261 | 227 | 57 | 1223 | 58 | 42 | 22 | 6 | 8 | 9 | 144 |
| S.D. | 115 | 108 | 55 | 533 | 394 | 68 | 955 | 24 | 24 | 14 | 9 | 8 | 10 | 65 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | STL | DU | STL | DU | DU | DU | DU | STL | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 15-4. Individual spontaneous motor activity of male rats on termination of administration priod

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| M04401 | 426 | 344 | 220 | 209 | 26 | 336 | 1561 | 67 | 57 | 52 | 34 | 10 | 57 | 277 |
| M04402 | 382 | 142 | 1 | 0 | 0 | 0 | 525 | 63 | 26 | 3 | 0 | 0 | 0 | 92 |
| M04403 | 299 | 228 | 0 | 0 | 0 | 0 | 527 | 64 | 19 | 0 | 0 | 0 | 0 | 83 |
| M04404 | 445 | 278 | 190 | 143 | 0 | 0 | 1056 | 68 | 29 | 37 | 30 | 0 | 0 | 164 |
| M04405 | 580 | 509 | 433 | 118 | 0 | 0 | 1640 | 47 | 36 | 16 | 10 | 0 | 0 | 109 |
| M04406 | 433 | 193 | 80 | 0 | 0 | 0 | 706 | 70 | 28 | 5 | 0 | 0 | 0 | 103 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 428 | 282 | 154 | 78 | 4 | 56 | 1003 | 63 | 33 | 19 | 12 | 2 | 10 | 138 |
| S.D. | 92 | 131 | 165 | 91 | 11 | 137 | 503 | 8 | 13 | 21 | 16 | 4 | 23 | 74 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | STL | DU | STL | DU | DU | DU | DU | STL | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 16-1. Individual spontaneous motor activity of female rats on termination of administration priod

Control group

| Female No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| F01151 | 719 | 458 | 139 | 222 | 73 | 31 | 1642 | 81 | 56 | 17 | 21 | 6 | 8 | 189 |
| F01152 | 305 | 81 | 9 | 0 | 0 | 39 | 434 | 54 | 8 | 0 | 0 | 0 | 10 | 72 |
| F01153 | 6 | 306 | 1 | 0 | 0 | 0 | 313 | 14 | 48 | 2 | 0 | 0 | 0 | 64 |
| F01154 | 489 | 150 | 1 | 0 | 0 | 38 | 678 | 54 | 13 | 0 | 0 | 0 | 1 | 68 |
| F01155 | 215 | 249 | 119 | 0 | 0 | 0 | 583 | 22 | 20 | 6 | 0 | 0 | 0 | 48 |
| F01156 | 585 | 342 | 0 | 0 | 0 | 0 | 927 | 72 | 28 | 0 | 0 | 0 | 0 | 100 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 387 | 264 | 45 | 37 | 12 | 18 | 763 | 50 | 29 | 4 | 4 | 1 | 3 | 90 |
| S.D. | 261 | 136 | 66 | 91 | 30 | 20 | 480 | 27 | 19 | 7 | 9 | 2 | 5 | 51 |

Appendix 16-2. Individual spontaneous motor activity of female rats on termination of administration priod

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| F02251 | 324 | 174 | 266 | 260 | 0 | 0 | 1024 | 28 | 19 | 41 | 32 | 0 | 7 | 127 |
| F02252 | 808 | 319 | 87 | 0 | 182 | 58 | 1454 | 60 | 38 | 8 | 0 | 14 | 6 | 126 |
| F02253 | 126 | 98 | 142 | 32 | 0 | 0 | 398 | 18 | 14 | 39 | 3 | 0 | 0 | 74 |
| F02254 | 252 | 231 | 0 | 2 | 5 | 0 | 490 | 82 | 39 | 0 | 0 | 5 | 0 | 126 |
| F02255 | 218 | 152 | 0 | 0 | 0 | 0 | 370 | 24 | 16 | 0 | 0 | 0 | 0 | 40 |
| F02256 | 381 | 246 | 48 | 167 | 0 | 0 | 842 | 73 | 27 | 3 | 33 | 0 | 0 | 136 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 352 | 203 | 91 | 77 | 31 | 10 | 763 | 48 | 26 | 15 | 11 | 3 | 2 | 105 |
| S.D. | 240 | 78 | 102 | 111 | 74 | 24 | 428 | 28 | 11 | 19 | 16 | 6 | 3 | 39 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | DU | DU | STL | DU | STL | DU | DU | DU | STL | STL | STL | STL | DU |

NS: Not significantly different from the control group.
STL: Analysis by Steel's test.
DU: Analysis by Dunnett's test.

Appendix 16-3. Individual spontaneous motor activity of female rats on termination of administration priod

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| F03351 | 321 | 0 | 0 | 0 | 0 | 0 | 321 | 37 | 0 | 0 | 0 | 0 | 0 | 37 |
| F03352 | 346 | 136 | 0 | 209 | 0 | 0 | 691 | 44 | 21 | 0 | 15 | 0 | 0 | 80 |
| F03353 | 412 | 295 | 177 | 205 | 0 | 0 | 1089 | 66 | 37 | 54 | 39 | 0 | 0 | 196 |
| F03354 | 355 | 0 | 0 | 28 | 116 | 421 | 920 | 64 | 0 | 0 | 3 | 31 | 100 | 198 |
| F03355 | 425 | 276 | 108 | 430 | 239 | 0 | 1478 | 38 | 40 | 10 | 39 | 21 | 0 | 148 |
| F03356 | 566 | 284 | 279 | 0 | 0 | 0 | 1129 | 99 | 34 | 37 | 2 | 0 | 0 | 172 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 404 | 165 | 94 | 145 | 59 | 70 | 938 | 58 | 22 | 17 | 16 | 9 | 17 | 139 |
| S.D. | 89 | 140 | 116 | 170 | 100 | 172 | 398 | 24 | 18 | 23 | 18 | 14 | 41 | 66 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | DU | DU | STL | DU | STL | DU | DU | DU | STL | STL | STL | STL | DU |

NS: Not significantly different from the control group.
STL: Analysis by Steel's test.
DU: Analysis by Dunnett's test.

Appendix 16-4. Individual spontaneous motor activity of female rats on termination of administration priod

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Ambulatory counts | | | | | | | Vertical counts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Minutes after administration | | | | | | | Minutes after administration | | | | | | |
| | 70 | 80 | 90 | 100 | 110 | 120 | Total | 70 | 80 | 90 | 100 | 110 | 120 | Total |
| F04451 | 239 | 162 | 80 | 42 | 0 | 3 | 526 | 56 | 26 | 7 | 7 | 0 | 0 | 96 |
| F04452 | 59 | 343 | 66 | 0 | 180 | 215 | 863 | 8 | 31 | 2 | 0 | 15 | 33 | 89 |
| F04453 | 28 | 0 | 252 | 51 | 0 | 0 | 331 | 1 | 0 | 12 | 0 | 0 | 0 | 13 |
| F04454 | Died on Day 2 of administration | | | | | | | | | | | | | |
| F04455 | 158 | 91 | 68 | 0 | 0 | 0 | 317 | 37 | 14 | 12 | 0 | 0 | 0 | 63 |
| F04456 | 52 | 0 | 17 | 3 | 0 | 0 | 72 | 3 | 0 | 0 | 0 | 0 | 0 | 3 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 107 | 119 | 97 | 19 | 36 | 44 | 422 | 21 | 14 | 7 | 1 | 3 | 7 | 53 |
| S.D. | 89 | 142 | 90 | 25 | 80 | 96 | 295 | 24 | 14 | 6 | 3 | 7 | 15 | 43 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | DU | DU | STL | DU | STL | DU | DU | DU | STL | STL | STL | STL | DU |

NS: Not significantly different from the control group.
STL: Analysis by Steel's test.
DU: Analysis by Dunnett's test.

Appendix 17-1. Individual urinary findings in male rats on termination of administration period

Control group

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M01101 | 18.9 | 1.035 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M01102 | 6.6 | 1.068 | Light yellow | 8.5 | + | - | + | - | - | 1.0 | ± | ± | ± | - | + |
| M01103 | 10.0 | 1.056 | Light yellow | 8.5 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| M01104 | 9.7 | 1.052 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M01105 | 9.8 | 1.064 | Light yellow | 7.5 | ± | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M01106 | 9.8 | 1.060 | Light yellow | 8.5 | ± | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 10.8 | 1.056 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 4.2 | 0.012 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.

Appendix 17-2. Individual urinary findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M02201 | 6.8 | 1.072 | Light yellow | 8.5 | + | - | + | - | +++ | 0.1 | ± | + | ± | - | + |
| M02202 | 13.1 | 1.050 | Light yellow | 8.5 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| M02203 | 14.1 | 1.044 | Light yellow | ≧9.0 | + | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M02204 | 11.0 | 1.048 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M02205 | 8.9 | 1.068 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M02206 | 7.3 | 1.062 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 10.2 | 1.057 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 3.0 | 0.012 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 17-3. Individual urinary findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M03301 | 12.4 | 1.052 | Light yellow | ≧9.0 | + | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M03302 | 15.4 | 1.048 | Light yellow | 8.5 | + | - | + | - | - | 1.0 | ± | ± | ± | - | + |
| M03303 | 9.9 | 1.066 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M03304 | 8.1 | 1.068 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M03305 | 21.0 | 1.030 | Light yellow | 8.5 | ± | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M03306 | 16.4 | 1.042 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 13.9 | 1.051 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 4.7 | 0.014 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 17-4. Individual urinary findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M04401 | 11.4 | 1.056 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M04402 | 16.3 | 1.054 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M04403 | 20.7 | 1.042 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M04404 | 25.2 | 1.040 | Light yellow | 8.0 | ± | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M04405 | 20.3 | 1.044 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M04406 | 17.9 | 1.041 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 18.6 | 1.046 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 4.7 | 0.007 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | * | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
Significantly different from the control group (*: $p<0.05$ by Dunnett's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 18-1. Individual urinary findings in female rats on termination of administration period

Control group

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F01151 | 7.3 | 1.056 | Light yellow | 8.5 | ± | - | ± | - | - | 1.0 | ± | ± | ± | - | - |
| F01152 | 6.3 | 1.054 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F01153 | 9.9 | 1.045 | Light yellow | ≧9.0 | - | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| F01154 | 11.6 | 1.033 | Light yellow | ≧9.0 | + | - | ± | - | - | 1.0 | ± | ± | ± | - | + |
| F01155 | 10.1 | 1.046 | Light yellow | 8.0 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F01156 | 10.0 | 1.050 | Light yellow | 8.0 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 9.2 | 1.047 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 2.0 | 0.008 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.

Appendix 18-2. Individual urinary findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F02251 | 4.6 | 1.070 | Light yellow | 8.5 | ± | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| F02252 | 6.8 | 1.056 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| F02253 | 5.5 | 1.068 | Light yellow | 8.0 | ± | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| F02254 | 8.8 | 1.058 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F02255 | 8.6 | 1.037 | Light yellow | 8.0 | - | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| F02256 | 5.5 | 1.052 | Light yellow | 7.5 | ± | - | + | - | - | 1.0 | ± | ± | ± | - | + |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 6.6 | 1.057 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 1.7 | 0.012 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | STL | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
STL: Analysis by Steel's test.
DU: Analysis by Dunnett's test.

Appendix 18-3. Individual urinary findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F03351 | 9.0 | 1.052 | Light yellow | 8.5 | - | - | ± | - | ± | 0.1 | ± | ± | ± | - | + |
| F03352 | 12.1 | 1.037 | Light yellow | 8.0 | - | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| F03353 | 10.8 | 1.046 | Light yellow | 8.0 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F03354 | 8.1 | 1.054 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F03355 | 14.8 | 1.045 | Light yellow | 8.5 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| F03356 | 9.1 | 1.050 | Light yellow | 8.5 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 10.7 | 1.047 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 2.5 | 0.006 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | STL | UA | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
STL: Analysis by Steel's test.
UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Appendix 18-4. Individual urinary findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F04451 | 13.7 | 1.046 | Light yellow | 8.5 | - | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| F04452 | 5.4 | 1.056 | Light yellow | 8.5 | - | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| F04453 | 6.4 | 1.058 | Light yellow | 8.0 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| F04454 | Died on Day 2 of administration | | | | | | | | | | | | | | |
| F04455 | 13.0 | 1.042 | Light yellow | 8.5 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F04456 | 21.1 | 1.036 | Light yellow | 8.0 | - | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 11.9 | 1.048 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 6.4 | 0.009 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | STL | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
STL: Analysis by Steel's test.
DU: Analysis by Dunnett's test.

Appendix 19-1. Individual urinary findings in male rats on termination of recovery period

Control group

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M01107 | 14.8 | 1.030 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| M01108 | 16.6 | 1.028 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M01109 | 14.1 | 1.032 | Light yellow | 8.5 | ++ | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M01110 | 9.8 | 1.036 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| M01111 | 16.2 | 1.029 | Light yellow | 8.5 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| M01112 | 28.9 | 1.019 | Light yellow | 8.5 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 16.7 | 1.029 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 6.4 | 0.006 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.

Appendix 19-2. Individual urinary findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M03307 | 14.6 | 1.029 | Light yellow | ≧9.0 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| M03308 | 14.4 | 1.028 | Light yellow | 8.5 | + | - | + | - | - | 0.1 | ± | ± | ± | - | - |
| M03309 | 11.8 | 1.035 | Light yellow | 8.5 | + | - | + | + | - | 0.1 | ± | ± | ± | - | + |
| M03310 | 24.3 | 1.048 | Light yellow | 8.5 | + | - | ± | - | + | 0.1 | ± | ± | ± | - | + |
| M03311 | 6.6 | 1.032 | Light yellow | 8.5 | ++ | - | + | - | - | 0.1 | ± | ± | ± | - | + |
| M03312 | 24.3 | 1.016 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 16.0 | 1.031 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 7.0 | 0.010 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 19-3. Individual urinary findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| M04407 | 10.8 | 1.033 | Light yellow | 8.5 | + | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| M04408 | 17.6 | 1.026 | Light yellow | 8.5 | + | - | ± | - | ± | 0.1 | ± | ± | ± | - | + |
| M04409 | 10.3 | 1.037 | Light yellow | ≧9.0 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| M04410 | 12.1 | 1.034 | Light yellow | 8.5 | + | - | ± | - | + | 0.1 | ± | ± | ± | - | + |
| M04411 | 26.3 | 1.020 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| M04412 | 9.6 | 1.039 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 14.5 | 1.032 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 6.5 | 0.007 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 20-1. Individual urinary findings in female rats on termination of recovery period

Control group

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F01157 | 9.9 | 1.045 | Light yellow | 7.0 | + | - | ± | - | - | 1.0 | ± | ± | ± | - | + |
| F01158 | 10.5 | 1.054 | Light yellow | 8.0 | ± | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| F01159 | 7.4 | 1.070 | Light yellow | 6.0 | ± | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| F01160 | 9.4 | 1.049 | Light yellow | 8.5 | ± | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| F01161 | 11.6 | 1.038 | Light yellow | 8.5 | - | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| F01162 | 7.2 | 1.062 | Light yellow | 7.5 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | - |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 9.3 | 1.053 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 1.7 | 0.012 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.

Appendix 20-2. Individual urinary findings in female rats on termination of recovery period.

1,8-dichlorooctane group at 200 mg/kg

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F03357 | 7.4 | 1.042 | Light yellow | 8.5 | ± | - | ± | - | - | 1.0 | ± | ± | ± | - | + |
| F03358 | 9.0 | 1.034 | Light yellow | 8.5 | - | - | - | - | ± | 0.1 | ± | ± | ± | - | - |
| F03359 | 14.4 | 1.046 | Light yellow | 7.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F03360 | 19.2 | 1.036 | Light yellow | 8.5 | ± | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| F03361 | 12.9 | 1.044 | Light yellow | 8.0 | - | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| F03362 | 6.3 | 1.066 | Light yellow | 7.0 | + | - | ± | - | - | 0.1 | ± | ± | ± | - | + |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 11.5 | 1.045 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 4.9 | 0.011 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 20-3. Individual urinary findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | UV mL | S.G. | Color | pH | Protein | Glucose | Ketone body | Bilirubin | Occult blood | Urobilinogen E.U./dL | Urinary sediments | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Epithelial cells | Erythrocytes | Leukocytes | Casts | Crystals |
| F04457 | 12.6 | 1.035 | Light yellow | 8.5 | - | - | - | - | - | 0.1 | ± | ± | ± | - | - |
| F04458 | 14.8 | 1.037 | Light yellow | 8.5 | - | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| F04459 | 14.0 | 1.033 | Light yellow | 8.5 | - | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| F04460 | 7.5 | 1.046 | Light yellow | 8.5 | - | - | - | - | ± | 0.1 | ± | ± | ± | - | + |
| F04461 | 13.2 | 1.047 | Light yellow | 8.0 | - | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| F04462 | 9.0 | 1.056 | Light yellow | 8.5 | - | - | - | - | - | 0.1 | ± | ± | ± | - | + |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 11.9 | 1.042 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.D. | 2.9 | 0.009 | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Significance | NS | NS | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Statistical method | DU | DU | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |

Protein: -; negative, ±; trace, +; 30 mg/dL, ++; 100 mg/dL, +++; ≧300 mg/dL.
Glucose: -; negative, +; 100 mg/dL, ++; 250 mg/dL, +++; 500 mg/dL, ++++; ≧1000 mg/dL.
Ketone body: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Bilirubin: -; negative, +; slight, ++; moderate, +++; marked.
Occult blood: -; negative, ±; trace, +; slight, ++; moderate, +++; marked.
Epithelial cells: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; ≧201 cells/100 fields.
Erythrocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Leukocytes: ±; 0-20 cells/100 fields, +; 21-100 cells/100 fields, ++; 101-200 cells/100 fields, +++; 201-500 cells/100 fields ++++; ≧501 cells/100 fields.
Casts: -; not observed, +; observed.
Crystals: -; not observed, +; observed.
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 21-1. Individual hematological findings in male rats on termination of administration period

Control group

| Male No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| M01101 | 810 | 15.7 | 44.7 | 55.2 | 19.4 | 35.1 | 127.7 | 3.75 | 27.5 a) | 29.0 | 231.3 |
| M01102 | 798 | 14.8 | 42.0 | 52.6 | 18.5 | 35.2 | 131.3 | 2.73 | 26.3 a) | 28.0 | 180.9 |
| M01103 | 736 | 14.7 | 41.8 | 56.8 | 20.0 | 35.2 | 109.6 | 2.84 | 21.5 | 26.0 | 217.4 |
| M01104 | 860 | 15.9 | 44.7 | 52.0 | 18.5 | 35.6 | 132.0 | 3.10 | 29.4 a) | 26.5 | 209.0 |
| M01105 | 820 | 14.4 | 40.6 | 49.5 | 17.6 | 35.5 | 127.7 | 2.19 | 38.8 a) | 27.8 | 187.2 |
| M01106 | 750 | 15.7 | 44.8 | 59.7 | 20.9 | 35.0 | 115.6 | 3.37 | 19.5 | 25.2 | 226.5 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 796 | 15.2 | 43.1 | 54.3 | 19.2 | 35.3 | 124.0 | 3.00 | 27.2 | 27.1 | 208.7 |
| S.D. | 46 | 0.6 | 1.9 | 3.7 | 1.2 | 0.2 | 9.2 | 0.54 | 6.8 | 1.4 | 20.7 |

a): Obtained in the scheduled measurement (1st measurement); the value, which is abnormally higher than that in other animals, was confirmed to be correct in the 2nd measurement.

(Continued)

Appendix 21-1. (Continued) Individual hematological findings in male rats on termination of administration period

Control group

| Male No. | WBC $10^2/\mu L$ | LYMPH % | NEUT % | EO % | BASO % | MONO % |
|---|---|---|---|---|---|---|
| M01101 | 78.8 | 83.8 | 13.4 | 1.0 | 0.0 | 1.8 |
| M01102 | 69.4 | 81.4 | 14.6 | 1.4 | 0.0 | 2.6 |
| M01103 | 51.2 | 74.0 | 23.3 | 0.4 | 0.0 | 2.3 |
| M01104 | 73.5 | 75.4 | 20.3 | 1.6 | 0.0 | 2.7 |
| M01105 | 73.4 | 77.2 | 18.3 | 1.2 | 0.0 | 3.3 |
| M01106 | 118.9 | 80.8 | 16.4 | 1.3 | 0.0 | 1.5 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 77.5 | 78.8 | 17.7 | 1.2 | 0.0 | 2.4 |
| S.D. | 22.4 | 3.8 | 3.7 | 0.4 | 0.0 | 0.7 |

Appendix 21-2. Individual hematological findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | RBC | Hemoglobin | Hematocrit | MCV | MCH | MCHC | Platelet | Reticulocyte | PT | APTT | Fibrinogen |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $10^4/\mu L$ | g/dL | % | fL | pg | g/dL | $10^4/\mu L$ | % | sec. | sec. | mg/dL |
| M02201 | 805 | 16.0 | 45.8 | 56.9 | 19.9 | 34.9 | 103.4 | 3.84 | 15.7 | 21.3 | 228.9 |
| M02202 | 742 | 14.4 | 41.1 | 55.4 | 19.4 | 35.0 | 107.8 | 3.20 | 18.6 | 22.5 | 199.3 |
| M02203 | 812 | 15.3 | 42.9 | 52.8 | 18.8 | 35.7 | 119.0 | 2.49 | 18.4 | 23.2 | 176.5 |
| M02204 | 777 | 14.6 | 41.7 | 53.7 | 18.8 | 35.0 | 124.3 | 3.04 | 26.1 a) | 29.5 | 207.0 |
| M02205 | 767 | 15.3 | 43.6 | 56.8 | 19.9 | 35.1 | 108.8 | 2.49 | 22.0 | 26.5 | 205.0 |
| M02206 | 846 | 16.2 | 45.4 | 53.7 | 19.1 | 35.7 | 130.0 | 3.49 | 19.2 | 20.3 | 205.0 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 792 | 15.3 | 43.4 | 54.9 | 19.3 | 35.2 | 115.6 | 3.09 | 20.0 | 23.9 | 203.6 |
| S.D. | 37 | 0.7 | 1.9 | 1.7 | 0.5 | 0.4 | 10.5 | 0.54 | 3.6 | 3.5 | 16.8 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | STL | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

a): Obtained in the scheduled measurement (1st measurement); the value, which is abnormally higher than that in other animals, was confirmed to be correct in the 2nd measurement.

Appendix 21-2. (Continued) Individual hematological findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| M02201 | 75.6 | 80.8 | 15.8 | 0.8 | 0.0 | 2.6 |
| M02202 | 84.3 | 68.0 | 27.4 | 1.5 | 0.0 | 3.1 |
| M02203 | 83.9 | 88.1 | 7.8 | 0.8 | 0.0 | 3.3 |
| M02204 | 58.5 | 83.8 | 12.4 | 1.7 | 0.0 | 2.1 |
| M02205 | 59.0 | 76.9 | 19.0 | 1.4 | 0.0 | 2.7 |
| M02206 | 58.9 | 80.6 | 16.0 | 0.7 | 0.0 | 2.7 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 70.0 | 79.7 | 16.4 | 1.2 | 0.0 | 2.8 |
| S.D. | 12.7 | 6.8 | 6.6 | 0.4 | 0.0 | 0.4 |
| Significance | NS | NS | NS | --- | NS | NS |
| Statistical method | DU | DU | STL | UA | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Appendix 21-3. Individual hematological findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | RBC | Hemoglobin | Hematocrit | MCV | MCH | MCHC | Platelet | Reticulocyte | PT | APTT | Fibrinogen |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $10^4/\mu L$ | g/dL | % | fL | pg | g/dL | $10^4/\mu L$ | % | sec. | sec. | mg/dL |
| M03301 | 834 | 15.8 | 44.9 | 53.8 | 18.9 | 35.2 | 115.7 | 2.85 | 17.6 | 19.6 | 217.4 |
| M03302 | 793 | 15.2 | 43.1 | 54.4 | 19.2 | 35.3 | 90.4 | 2.84 | 20.5 | 24.8 | 207.0 |
| M03303 | 759 | 15.1 | 43.0 | 56.7 | 19.9 | 35.1 | 111.1 | 3.18 | 18.0 | 21.5 | 190.5 |
| M03304 | 830 | 15.1 | 43.3 | 52.2 | 18.2 | 34.9 | 124.8 | 2.80 | 16.8 | 21.0 | 190.5 |
| M03305 | 841 | 15.9 | 45.1 | 53.6 | 18.9 | 35.3 | 111.2 | 2.94 | 17.7 | 22.6 | 195.7 |
| M03306 | 830 | 16.3 | 45.9 | 55.3 | 19.6 | 35.5 | 133.2 | 2.95 | 17.8 | 22.2 | 217.4 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 815 | 15.6 | 44.2 | 54.3 | 19.1 | 35.2 | 114.4 | 2.93 | 18.1 | 22.0 | 203.1 |
| S.D. | 32 | 0.5 | 1.2 | 1.5 | 0.6 | 0.2 | 14.6 | 0.14 | 1.3 | 1.7 | 12.6 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | # | ** | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | STL | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test). (Continued)

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 21-3. (Continued) Individual hematological findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| M03301 | 49.8 | 84.1 | 12.9 | 0.6 | 0.0 | 2.4 |
| M03302 | 64.2 | 85.5 | 11.4 | 1.1 | 0.0 | 2.0 |
| M03303 | 57.5 | 80.5 | 15.9 | 1.0 | 0.0 | 2.6 |
| M03304 | 34.2 | 81.3 | 13.7 | 1.5 | 0.0 | 3.5 |
| M03305 | 68.3 | 71.9 | 23.4 | 0.7 | 0.0 | 4.0 |
| M03306 | 57.3 | 90.6 | 6.8 | 0.5 | 0.0 | 2.1 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 55.2 | 82.3 | 14.0 | 0.9 | 0.0 | 2.8 |
| S.D. | 12.1 | 6.2 | 5.5 | 0.4 | 0.0 | 0.8 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 21-4. Individual hematological findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | RBC | Hemoglobin | Hematocrit | MCV | MCH | MCHC | Platelet | Reticulocyte | PT | APTT | Fibrinogen |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $10^4/\mu L$ | g/dL | % | fL | pg | g/dL | $10^4/\mu L$ | % | sec. | sec. | mg/dL |
| M04401 | 804 | 14.9 | 43.7 | 54.4 | 18.5 | 34.1 | 112.3 | 2.78 | 17.8 | 18.9 | 184.0 |
| M04402 | 759 | 15.2 | 43.6 | 57.4 | 20.0 | 34.9 | 97.5 | 2.74 | 16.4 | 18.7 | 221.8 |
| M04403 | 777 | 15.7 | 44.9 | 57.8 | 20.2 | 35.0 | 142.4 | 3.60 | 16.0 | 20.2 | 247.2 |
| M04404 | 805 | 14.8 | 42.3 | 52.5 | 18.4 | 35.0 | 111.8 | 2.65 | 16.2 | 19.7 | 215.2 |
| M04405 | 783 | 14.7 | 43.0 | 54.9 | 18.8 | 34.2 | 124.7 | 2.69 | 17.4 | 23.3 | 197.5 |
| M04406 | 777 | 16.1 | 45.4 | 58.4 | 20.7 | 35.5 | 102.2 | 3.56 | 27.8 a) | 24.1 | 219.6 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 784 | 15.2 | 43.8 | 55.9 | 19.4 | 34.8 | 115.2 | 3.00 | 18.6 | 20.8 | 214.2 |
| S.D. | 18 | 0.6 | 1.2 | 2.3 | 1.0 | 0.5 | 16.3 | 0.45 | 4.6 | 2.3 | 21.8 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | ** | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | STL | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

a): Obtained in the scheduled measurement (1st measurement); the value, which is abnormally higher than that in other animals, was confirmed to be correct in the 2nd measurement.

Appendix 21-4. (Continued) Individual hematological findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| M04401 | 65.5 | 86.1 | 8.8 | 0.8 | 0.0 | 4.3 |
| M04402 | 55.6 | 84.0 | 10.8 | 0.9 | 0.0 | 4.3 |
| M04403 | 64.1 | 81.7 | 13.1 | 0.8 | 0.0 | 4.4 |
| M04404 | 53.2 | 85.2 | 11.2 | 1.1 | 0.2 | 2.3 |
| M04405 | 57.6 | 83.2 | 11.8 | 1.2 | 0.0 | 3.8 |
| M04406 | 102.7 | 87.9 | 9.5 | 0.6 | 0.0 | 2.0 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 66.5 | 84.7 | 10.9 | 0.9 | 0.0 | 3.5 |
| S.D. | 18.4 | 2.2 | 1.6 | 0.2 | 0.1 | 1.1 |
| Significance | NS | NS | # | NS | NS | * |
| Statistical method | DU | DU | STL | DU | DU | DU |

Significantly different from the control group (*: $p<0.05$ by Dunnett's test).
Significantly different from the control group (#: $p<0.05$ by Steel's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 22-1. Individual hematological findings in female rats on termination of administration period

Control group

| Female No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F01151 | 770 | 14.3 | 40.0 | 51.9 | 18.6 | 35.8 | 129.0 | 2.80 | 14.8 | 17.3 | 166.0 |
| F01152 | 785 | 14.0 | 38.8 | 49.4 | 17.8 | 36.1 | 107.6 | 2.52 | 14.9 | 18.5 | 172.8 |
| F01153 | 741 | 14.7 | 40.1 | 54.1 | 19.8 | 36.7 | 117.1 | 2.82 | 15.8 | 16.3 | 191.4 |
| F01154 | 683 | 13.2 | 37.7 | 55.2 | 19.3 | 35.0 | 98.1 | 3.66 | 14.9 | 17.2 | 184.8 |
| F01155 | 741 | 14.6 | 40.0 | 54.0 | 19.7 | 36.5 | 118.4 | 2.16 | 16.1 | 17.3 | 172.8 |
| F01156 | 833 | 15.6 | 43.1 | 51.7 | 18.7 | 36.2 | 111.7 | 2.33 | 14.1 | 18.6 | 195.0 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 759 | 14.4 | 40.0 | 52.7 | 19.0 | 36.1 | 113.7 | 2.72 | 15.1 | 17.5 | 180.5 |
| S.D. | 50 | 0.8 | 1.8 | 2.1 | 0.8 | 0.6 | 10.5 | 0.53 | 0.7 | 0.9 | 11.6 |

(Continued)

Appendix 22-1. (Continued) Individual hematological findings in female rats on termination of administration period

Control group

| Female No. | WBC $10^2/\mu L$ | LYMPH % | NEUT % | EO % | BASO % | MONO % |
|---|---|---|---|---|---|---|
| F01151 | 58.1 | 86.1 | 11.5 | 0.9 | 0.0 | 1.5 |
| F01152 | 70.2 | 69.8 | 25.5 | 1.1 | 0.0 | 3.6 |
| F01153 | 37.8 | 81.2 | 14.3 | 2.1 | 0.0 | 2.4 |
| F01154 | 39.6 | 78.0 | 17.2 | 1.8 | 0.0 | 3.0 |
| F01155 | 36.5 | 78.9 | 16.7 | 1.9 | 0.0 | 2.5 |
| F01156 | 103.1 | 83.1 | 12.4 | 1.9 | 0.1 | 2.5 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 57.6 | 79.5 | 16.3 | 1.6 | 0.0 | 2.6 |
| S.D. | 26.0 | 5.6 | 5.1 | 0.5 | 0.0 | 0.7 |

Appendix 22-2. Individual hematological findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F02251 | 738 | 14.5 | 40.8 | 55.3 | 19.6 | 35.5 | 125.5 | 3.21 | 16.4 | 17.2 | 195.0 |
| F02252 | 776 | 14.6 | 41.2 | 53.1 | 18.8 | 35.4 | 115.1 | 2.84 | 14.7 | 17.2 | 175.6 |
| F02253 | 749 | 13.9 | 38.4 | 51.3 | 18.6 | 36.2 | 120.7 | 3.47 | 15.2 | 16.3 | 183.2 |
| F02254 | 787 | 14.1 | 39.5 | 50.2 | 17.9 | 35.7 | 129.6 | 3.29 | 16.1 | 16.2 | 188.1 |
| F02255 | 758 | 14.5 | 40.8 | 53.8 | 19.1 | 35.5 | 117.3 | 2.68 | 15.1 | 17.5 | 162.2 |
| F02256 | 791 | 15.2 | 42.2 | 53.4 | 19.2 | 36.0 | 115.5 | 2.57 | 15.7 | 17.8 | 171.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 767 | 14.5 | 40.5 | 52.9 | 18.9 | 35.7 | 120.6 | 3.01 | 15.5 | 17.0 | 179.3 |
| S.D. | 21 | 0.5 | 1.3 | 1.8 | 0.6 | 0.3 | 5.9 | 0.36 | 0.6 | 0.6 | 11.9 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 22-2. (Continued) Individual hematological findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| F02251 | 81.9 | 85.1 | 11.0 | 1.0 | 0.1 | 2.8 |
| F02252 | 59.9 | 88.6 | 7.9 | 1.7 | 0.0 | 1.8 |
| F02253 | 64.6 | 85.9 | 9.9 | 2.5 | 0.0 | 1.7 |
| F02254 | 47.7 | 71.7 | 25.6 | 1.0 | 0.0 | 1.7 |
| F02255 | 35.3 | 73.7 | 21.8 | 3.1 | 0.0 | 1.4 |
| F02256 | 67.5 | 85.8 | 11.1 | 1.0 | 0.0 | 2.1 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 59.5 | 81.8 | 14.6 | 1.7 | 0.0 | 1.9 |
| S.D. | 16.2 | 7.2 | 7.3 | 0.9 | 0.0 | 0.5 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 22-3. Individual hematological findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F03351 | 748 | 14.7 | 41.0 | 54.8 | 19.7 | 35.9 | 129.2 | 2.68 | 17.4 | 18.6 | 157.4 |
| F03352 | 767 | 15.0 | 41.5 | 54.1 | 19.6 | 36.1 | 119.5 | 2.36 | 17.2 | 17.5 | 147.6 |
| F03353 | 732 | 14.1 | 39.7 | 54.2 | 19.3 | 35.5 | 116.6 | 3.18 | 17.8 | 16.7 | 180.1 |
| F03354 | 785 | 14.9 | 42.1 | 53.6 | 19.0 | 35.4 | 118.1 | 2.69 | 16.6 | 17.4 | 171.4 |
| F03355 | 741 | 13.9 | 39.5 | 53.3 | 18.8 | 35.2 | 116.5 | 2.94 | 16.4 | 15.7 | 198.6 |
| F03356 | 795 | 15.1 | 41.7 | 52.5 | 19.0 | 36.2 | 113.4 | 2.98 | 17.5 | 17.8 | 152.9 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 761 | 14.6 | 40.9 | 53.8 | 19.2 | 35.7 | 118.9 | 2.81 | 17.2 | 17.3 | 168.0 |
| S.D. | 25 | 0.5 | 1.1 | 0.8 | 0.4 | 0.4 | 5.4 | 0.29 | 0.5 | 1.0 | 19.2 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | ** | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 22-3. (Continued) Individual hematological findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| F03351 | 55.5 | 75.0 | 17.4 | 2.2 | 0.0 | 5.4 |
| F03352 | 37.1 | 79.8 | 12.9 | 3.0 | 0.0 | 4.3 |
| F03353 | 34.0 | 76.8 | 19.1 | 1.2 | 0.0 | 2.9 |
| F03354 | 41.1 | 80.5 | 15.1 | 1.7 | 0.0 | 2.7 |
| F03355 | 47.1 | 85.6 | 10.8 | 1.5 | 0.0 | 2.1 |
| F03356 | 59.1 | 83.2 | 11.7 | 1.4 | 0.0 | 3.7 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 45.7 | 80.2 | 14.5 | 1.8 | 0.0 | 3.5 |
| S.D. | 10.1 | 3.9 | 3.3 | 0.7 | 0.0 | 1.2 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 22-4. Individual hematological findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F04451 | 722 | 13.2 | 38.0 | 52.6 | 18.3 | 34.7 | 114.6 | 2.34 | 15.1 | 16.2 | 181.6 |
| F04452 | 779 | 14.8 | 42.0 | 53.9 | 19.0 | 35.2 | 132.1 | 2.95 | 14.7 | 17.9 | 198.6 |
| F04453 | 730 | 13.9 | 39.9 | 54.7 | 19.0 | 34.8 | 115.7 | 2.44 | 16.3 | 13.9 | 189.7 |
| F04454 | Died on Day 2 of administration | | | | | | | | | | |
| F04455 | 701 | 13.1 | 38.3 | 54.6 | 18.7 | 34.2 | 94.0 | 3.42 | 16.8 | 15.9 | 171.4 |
| F04456 | 753 | 14.3 | 40.8 | 54.2 | 19.0 | 35.0 | 115.8 | 2.73 | 16.9 | 16.5 | 198.6 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 737 | 13.9 | 39.8 | 54.0 | 18.8 | 34.8 | 114.4 | 2.78 | 16.0 | 16.1 | 188.0 |
| S.D. | 30 | 0.7 | 1.7 | 0.8 | 0.3 | 0.4 | 13.5 | 0.43 | 1.0 | 1.4 | 11.7 |
| Significance | NS | NS | NS | NS | NS | ** | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 22-4. (Continued) Individual hematological findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| F04451 | 43.0 | 87.0 | 8.5 | 1.2 | 0.0 | 3.3 |
| F04452 | 34.6 | 85.3 | 8.9 | 2.3 | 0.0 | 3.5 |
| F04453 | 33.9 | 84.7 | 9.4 | 0.9 | 0.0 | 5.0 |
| F04454 | Died on Day 2 of administration | | | | | |
| F04455 | 71.3 | 88.5 | 7.3 | 1.4 | 0.0 | 2.8 |
| F04456 | 38.6 | 80.3 | 14.8 | 1.8 | 0.0 | 3.1 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 44.3 | 85.2 | 9.8 | 1.5 | 0.0 | 3.5 |
| S.D. | 15.5 | 3.1 | 2.9 | 0.5 | 0.0 | 0.9 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 23-1. Individual hematological findings in male rats on termination of recovery period

Control group

| Male No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| M01107 | 876 | 15.7 | 43.6 | 49.8 | 17.9 | 36.0 | 120.9 | 2.96 | 17.8 | 21.2 | 214.0 |
| M01108 | 860 | 15.5 | 42.2 | 49.1 | 18.0 | 36.7 | 131.9 | 2.99 | 20.4 | 23.2 | 190.5 |
| M01109 | 882 | 15.7 | 43.1 | 48.9 | 17.8 | 36.4 | 128.3 | 3.51 | 22.7 | 25.1 | 195.8 |
| M01110 | 868 | 15.8 | 43.7 | 50.3 | 18.2 | 36.2 | 115.6 | 2.67 | 17.5 | 21.7 | 209.7 |
| M01111 | 786 | 15.6 | 44.3 | 56.4 | 19.8 | 35.2 | 110.1 | 3.41 | 15.8 | 21.3 | 216.2 |
| M01112 | 854 | 15.4 | 42.8 | 50.1 | 18.0 | 36.0 | 119.0 | 4.02 | 21.2 | 26.1 | 228.1 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 854 | 15.6 | 43.3 | 50.8 | 18.3 | 36.1 | 121.0 | 3.26 | 19.2 | 23.1 | 209.1 |
| S.D. | 35 | 0.1 | 0.7 | 2.8 | 0.8 | 0.5 | 8.1 | 0.48 | 2.6 | 2.1 | 13.8 |

(Continued)

Appendix 23-1. (Continued) Individual hematological findings in male rats on termination of recovery period

Control group

| Male No. | WBC $10^2/\mu L$ | LYMPH % | NEUT % | EO % | BASO % | MONO % |
|---|---|---|---|---|---|---|
| M01107 | 90.5 | 79.3 | 15.5 | 2.4 | 0.0 | 2.8 |
| M01108 | 88.8 | 80.0 | 17.0 | 1.7 | 0.1 | 1.2 |
| M01109 | 66.0 | 79.7 | 16.2 | 1.5 | 0.2 | 2.4 |
| M01110 | 67.3 | 74.4 | 22.0 | 1.5 | 0.0 | 2.1 |
| M01111 | 46.1 | 71.6 | 23.1 | 2.0 | 0.0 | 3.3 |
| M01112 | 56.9 | 78.9 | 16.0 | 1.8 | 0.0 | 3.3 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 69.3 | 77.3 | 18.3 | 1.8 | 0.1 | 2.5 |
| S.D. | 17.5 | 3.5 | 3.3 | 0.3 | 0.1 | 0.8 |

Appendix 23-2. Individual hematological findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | RBC | Hemoglobin | Hematocrit | MCV | MCH | MCHC | Platelet | Reticulocyte | PT | APTT | Fibrinogen |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $10^4/\mu L$ | g/dL | % | fL | pg | g/dL | $10^4/\mu L$ | % | sec. | sec. | mg/dL |
| M03307 | 860 | 15.6 | 42.8 | 49.8 | 18.1 | 36.4 | 127.2 | 2.86 | 17.7 | 21.2 | 197.7 |
| M03308 | 853 | 15.2 | 42.2 | 49.5 | 17.8 | 36.0 | 116.4 | 3.02 | 21.9 | 26.0 | 183.7 |
| M03309 | 832 | 15.1 | 42.8 | 51.4 | 18.1 | 35.3 | 107.0 | 3.94 | 18.7 | 21.5 | 201.5 |
| M03310 | 859 | 15.7 | 43.8 | 51.0 | 18.3 | 35.8 | 130.4 | 2.46 | 18.9 | 20.6 | 218.5 |
| M03311 | 839 | 15.8 | 43.7 | 52.1 | 18.8 | 36.2 | 127.8 | 3.68 | 23.0 | 25.2 | 209.7 |
| M03312 | 884 | 16.0 | 45.0 | 50.9 | 18.1 | 35.6 | 98.4 | 2.49 | 24.0 | 24.5 | 199.6 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 855 | 15.6 | 43.4 | 50.8 | 18.2 | 35.9 | 117.9 | 3.08 | 20.7 | 23.2 | 201.8 |
| S.D. | 18 | 0.4 | 1.0 | 1.0 | 0.3 | 0.4 | 13.0 | 0.61 | 2.6 | 2.3 | 11.8 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 23-2. (Continued) Individual hematological findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| M03307 | 82.4 | 91.3 | 6.3 | 0.8 | 0.0 | 1.6 |
| M03308 | 115.2 | 88.7 | 8.2 | 1.1 | 0.1 | 1.9 |
| M03309 | 89.3 | 80.7 | 15.9 | 1.5 | 0.0 | 1.9 |
| M03310 | 52.2 | 77.8 | 17.8 | 2.1 | 0.0 | 2.3 |
| M03311 | 67.8 | 82.3 | 12.4 | 2.8 | 0.0 | 2.5 |
| M03312 | 36.0 | 77.2 | 18.1 | 2.5 | 0.0 | 2.2 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 73.8 | 83.0 | 13.1 | 1.8 | 0.0 | 2.1 |
| S.D. | 28.1 | 5.8 | 5.0 | 0.8 | 0.0 | 0.3 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 23-3. Individual hematological findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | RBC | Hemoglobin | Hematocrit | MCV | MCH | MCHC | Platelet | Reticulocyte | PT | APTT | Fibrinogen |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $10^4/\mu L$ | g/dL | % | fL | pg | g/dL | $10^4/\mu L$ | % | sec. | sec. | mg/dL |
| M04407 | 820 | 14.4 | 39.7 | 48.4 | 17.6 | 36.3 | 115.0 | 3.46 | 15.8 | 21.9 | 180.5 |
| M04408 | 827 | 15.3 | 42.3 | 51.1 | 18.5 | 36.2 | 116.8 | 2.75 | 14.9 | 20.5 | 192.2 |
| M04409 | 862 | 15.0 | 42.2 | 49.0 | 17.4 | 35.5 | 118.1 | 3.32 | 18.0 | 21.6 | 216.2 |
| M04410 | 796 | 14.3 | 40.3 | 50.6 | 18.0 | 35.5 | 114.0 | 3.39 | 15.5 | 19.1 | 211.8 |
| M04411 | 893 | 15.5 | 43.2 | 48.4 | 17.4 | 35.9 | 118.4 | 3.08 | 18.5 | 23.5 | 207.6 |
| M04412 | 879 | 15.4 | 43.4 | 49.4 | 17.5 | 35.5 | 125.6 | 2.64 | 28.4 | 26.0 | 192.2 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 846 | 15.0 | 41.9 | 49.5 | 17.7 | 35.8 | 118.0 | 3.11 | 18.5 | 22.1 | 200.1 |
| S.D. | 38 | 0.5 | 1.5 | 1.1 | 0.4 | 0.4 | 4.1 | 0.35 | 5.0 | 2.4 | 13.9 |
| Significance | NS | * | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 23-3. (Continued) Individual hematological findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| M04407 | 66.3 | 81.7 | 13.3 | 0.9 | 0.0 | 4.1 |
| M04408 | 41.8 | 84.9 | 12.4 | 1.0 | 0.0 | 1.7 |
| M04409 | 66.2 | 84.0 | 12.8 | 1.4 | 0.0 | 1.8 |
| M04410 | 57.5 | 71.1 | 21.9 | 3.3 | 0.0 | 3.7 |
| M04411 | 72.9 | 76.8 | 17.7 | 1.4 | 0.1 | 4.0 |
| M04412 | 48.2 | 82.6 | 12.4 | 2.5 | 0.0 | 2.5 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 58.8 | 80.2 | 15.1 | 1.8 | 0.0 | 3.0 |
| S.D. | 11.9 | 5.3 | 3.9 | 0.9 | 0.0 | 1.1 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 24-1. Individual hematological findings in female rats on termination of recovery period

Control group

| Female No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F01157 | 758 | 14.0 | 38.4 | 50.7 | 18.5 | 36.5 | 143.1 | 3.24 | 15.0 | 17.8 | 191.6 |
| F01158 | 787 | 14.6 | 40.2 | 51.1 | 18.6 | 36.3 | 107.6 | 2.92 | 15.1 | 17.0 | 166.2 |
| F01159 | 802 | 14.7 | 40.1 | 50.0 | 18.3 | 36.7 | 132.1 | 3.22 | 15.3 | 18.5 | 168.8 |
| F01160 | 832 | 14.5 | 40.0 | 48.1 | 17.4 | 36.3 | 112.1 | 2.56 | 15.2 | 17.3 | 158.7 |
| F01161 | 726 | 13.7 | 38.0 | 52.3 | 18.9 | 36.1 | 135.4 | 3.54 | 13.9 | 17.1 | 175.8 |
| F01162 | 852 | 15.1 | 41.7 | 48.9 | 17.7 | 36.2 | 121.7 | 2.51 | 15.8 | 18.3 | 189.9 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 793 | 14.4 | 39.7 | 50.2 | 18.2 | 36.4 | 125.3 | 3.00 | 15.1 | 17.7 | 175.2 |
| S.D. | 47 | 0.5 | 1.3 | 1.5 | 0.6 | 0.2 | 13.9 | 0.41 | 0.6 | 0.6 | 13.3 |

(Continued)

Appendix 24-1. (Continued) Individual hematological findings in female rats on termination of recovery period

Control group

| Female No. | WBC $10^2/\mu L$ | LYMPH % | NEUT % | EO % | BASO % | MONO % |
|---|---|---|---|---|---|---|
| F01157 | 75.8 | 77.8 | 18.9 | 1.5 | 0.0 | 1.8 |
| F01158 | 43.9 | 71.8 | 22.7 | 1.6 | 0.0 | 3.9 |
| F01159 | 49.3 | 79.9 | 16.5 | 2.0 | 0.0 | 1.6 |
| F01160 | 41.8 | 85.2 | 9.3 | 3.6 | 0.0 | 1.9 |
| F01161 | 54.2 | 88.0 | 8.3 | 1.7 | 0.0 | 2.0 |
| F01162 | 25.2 | 72.2 | 18.2 | 4.8 | 0.0 | 4.8 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 48.4 | 79.2 | 15.7 | 2.5 | 0.0 | 2.7 |
| S.D. | 16.7 | 6.6 | 5.7 | 1.4 | 0.0 | 1.3 |

Appendix 24-2. Individual hematological findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | RBC $10^4/\mu L$ | Hemoglobin g/dL | Hematocrit % | MCV fL | MCH pg | MCHC g/dL | Platelet $10^4/\mu L$ | Reticulocyte % | PT sec. | APTT sec. | Fibrinogen mg/dL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F03357 | 749 | 13.9 | 37.5 | 50.1 | 18.6 | 37.1 | 98.0 | 2.76 | 15.9 | 17.4 | 177.3 |
| F03358 | 827 | 15.3 | 42.1 | 50.9 | 18.5 | 36.3 | 83.2 | 3.18 | 14.7 | 17.7 | 175.8 |
| F03359 | 762 | 14.3 | 39.8 | 52.2 | 18.8 | 35.9 | 112.8 | 2.67 | 15.1 | 17.3 | 163.6 |
| F03360 | 798 | 15.2 | 41.7 | 52.3 | 19.0 | 36.5 | 135.4 | 2.73 | 15.9 | 16.9 | 185.0 |
| F03361 | 768 | 14.3 | 39.8 | 51.8 | 18.6 | 35.9 | 103.6 | 3.51 | 15.2 | 17.8 | 170.2 |
| F03362 | 854 | 15.6 | 42.9 | 50.2 | 18.3 | 36.4 | 105.6 | 2.55 | 15.5 | 17.4 | 161.1 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 793 | 14.8 | 40.6 | 51.3 | 18.6 | 36.4 | 106.4 | 2.90 | 15.4 | 17.4 | 172.2 |
| S.D. | 41 | 0.7 | 2.0 | 1.0 | 0.2 | 0.4 | 17.3 | 0.37 | 0.5 | 0.3 | 9.0 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 24-2. (Continued) Individual hematological findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| F03357 | 52.7 | 82.2 | 12.9 | 1.5 | 0.0 | 3.4 |
| F03358 | 59.7 | 85.3 | 10.7 | 1.7 | 0.0 | 2.3 |
| F03359 | 53.0 | 85.5 | 10.2 | 2.6 | 0.0 | 1.7 |
| F03360 | 59.4 | 79.5 | 16.5 | 1.3 | 0.0 | 2.7 |
| F03361 | 42.2 | 78.2 | 17.7 | 2.4 | 0.0 | 1.7 |
| F03362 | 26.3 | 74.1 | 19.1 | 3.4 | 0.0 | 3.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 48.9 | 80.8 | 14.5 | 2.2 | 0.0 | 2.5 |
| S.D. | 12.8 | 4.4 | 3.8 | 0.8 | 0.0 | 0.8 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 24-3. Individual hematological findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | RBC | Hemoglobin | Hematocrit | MCV | MCH | MCHC | Platelet | Reticulocyte | PT | APTT | Fibrinogen |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | $10^4/\mu L$ | g/dL | % | fL | pg | g/dL | $10^4/\mu L$ | % | sec. | sec. | mg/dL |
| F04457 | 793 | 15.0 | 41.1 | 51.8 | 18.9 | 36.5 | 144.5 | 1.91 | 15.2 | 19.7 | 168.8 |
| F04458 | 729 | 13.9 | 38.8 | 53.2 | 19.1 | 35.8 | 132.8 | 4.64 | 14.0 | 17.8 | 198.8 |
| F04459 | 762 | 14.0 | 39.6 | 52.0 | 18.4 | 35.4 | 115.4 | 2.48 | 15.2 | 16.9 | 202.6 |
| F04460 | 789 | 14.1 | 39.9 | 50.6 | 17.9 | 35.3 | 144.7 | 2.62 | 15.4 | 17.4 | 208.5 |
| F04461 | 803 | 14.6 | 40.7 | 50.7 | 18.2 | 35.9 | 125.7 | 3.04 | 15.0 | 17.8 | 191.6 |
| F04462 | 758 | 13.9 | 39.0 | 51.5 | 18.3 | 35.6 | 110.1 | 2.95 | 14.3 | 17.4 | 208.5 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 772 | 14.3 | 39.9 | 51.6 | 18.5 | 35.8 | 128.9 | 2.94 | 14.9 | 17.8 | 196.5 |
| S.D. | 28 | 0.5 | 0.9 | 1.0 | 0.5 | 0.4 | 14.5 | 0.92 | 0.6 | 1.0 | 15.0 |
| Significance | NS | NS | NS | NS | NS | * | NS | NS | NS | NS | * |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 24-3. (Continued) Individual hematological findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | WBC | LYMPH | NEUT | EO | BASO | MONO |
|---|---|---|---|---|---|---|
| | $10^2/\mu L$ | % | % | % | % | % |
| F04457 | 54.0 | 83.7 | 10.6 | 2.4 | 0.0 | 3.3 |
| F04458 | 45.8 | 86.7 | 9.6 | 2.4 | 0.0 | 1.3 |
| F04459 | 48.2 | 88.8 | 8.0 | 1.5 | 0.0 | 1.7 |
| F04460 | 75.8 | 77.4 | 18.7 | 1.2 | 0.1 | 2.6 |
| F04461 | 37.4 | 74.1 | 20.8 | 1.9 | 0.0 | 3.2 |
| F04462 | 36.9 | 78.0 | 16.8 | 1.9 | 0.0 | 3.3 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 49.7 | 81.5 | 14.1 | 1.9 | 0.0 | 2.6 |
| S.D. | 14.4 | 5.8 | 5.3 | 0.5 | 0.0 | 0.9 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 25-1. Individual blood chemical findings in male rats on termination of administration period

Control group

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M01101 | 74.9 | 28.8 | 534.2 | 0.28 | 5.51 | 2.97 | 1.17 |
| M01102 | 71.8 | 23.3 | 487.8 | 0.82 | 5.13 | 2.75 | 1.16 |
| M01103 | 84.6 | 24.5 | 639.8 | 0.36 | 5.40 | 2.76 | 1.05 |
| M01104 | 69.0 | 17.3 | 565.9 | 0.73 | 5.28 | 2.82 | 1.15 |
| M01105 | 94.2 | 56.6 | 641.9 | 1.37 | 5.62 | 3.19 | 1.31 |
| M01106 | 62.2 | 19.6 | 460.6 | 0.58 | 5.33 | 2.74 | 1.06 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 76.1 | 28.4 | 555.0 | 0.69 | 5.38 | 2.87 | 1.15 |
| S.D. | 11.5 | 14.4 | 75.8 | 0.39 | 0.17 | 0.18 | 0.09 |

(Continued)

Appendix 25-1. (Continued) Individual blood chemical findings in male rats on termination of administration period

Control group

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M01101 | 0.12 | 14.1 | 0.24 | 102.5 | 43.7 | 49.7 |
| M01102 | 0.09 | 13.6 | 0.25 | 118.7 | 60.2 | 51.7 |
| M01103 | 0.11 | 12.5 | 0.26 | 115.4 | 52.8 | 36.5 |
| M01104 | 0.11 | 14.7 | 0.26 | 105.4 | 50.9 | 35.8 |
| M01105 | 0.11 | 27.0 | 0.28 | 116.8 | 35.1 | 18.2 |
| M01106 | 0.10 | 10.6 | 0.22 | 109.1 | 41.3 | 20.2 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.11 | 15.4 | 0.25 | 111.3 | 47.3 | 35.4 |
| S.D. | 0.01 | 5.9 | 0.02 | 6.6 | 9.0 | 14.1 |

(Continued)

Appendix 25-1. (Continued) Individual blood chemical findings in male rats on termination of administration period

Control group

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M01101 | 144.7 | 4.00 | 105.4 | 9.8 | 7.7 |
| M01102 | 144.8 | 4.17 | 104.6 | 9.2 | 8.4 |
| M01103 | 144.3 | 3.98 | 105.2 | 9.7 | 8.2 |
| M01104 | 145.2 | 4.13 | 104.6 | 9.6 | 8.4 |
| M01105 | 142.9 | 4.62 | 103.7 | 9.4 | 9.2 |
| M01106 | 143.1 | 3.93 | 104.5 | 10.0 | 7.3 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 144.2 | 4.14 | 104.7 | 9.6 | 8.2 |
| S.D. | 1.0 | 0.25 | 0.6 | 0.3 | 0.7 |

Appendix 25-2. Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M02201 | 90.7 | 32.7 | 498.8 | 0.92 | 5.50 | 2.96 | 1.17 |
| M02202 | 93.6 | 29.5 | 593.4 | 0.59 | 5.19 | 2.70 | 1.08 |
| M02203 | 112.9 | 36.0 | 391.9 | 0.80 | 5.00 | 2.58 | 1.06 |
| M02204 | 61.7 | 20.1 | 460.5 | 0.86 | 5.41 | 2.80 | 1.07 |
| M02205 | 68.2 | 24.1 | 641.8 | 0.52 | 4.92 | 2.79 | 1.31 |
| M02206 | 71.8 | 22.2 | 435.9 | 0.62 | 5.33 | 2.83 | 1.13 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 83.2 | 27.4 | 503.7 | 0.72 | 5.23 | 2.78 | 1.14 |
| S.D. | 19.3 | 6.3 | 96.0 | 0.16 | 0.23 | 0.13 | 0.09 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-2. (Continued) Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M02201 | 0.12 | 21.5 | 0.27 | 123.1 | 43.4 | 17.7 |
| M02202 | 0.09 | 17.2 | 0.23 | 112.6 | 45.6 | 18.4 |
| M02203 | 0.09 | 18.7 | 0.18 | 124.1 | 27.3 | 14.7 |
| M02204 | 0.10 | 12.4 | 0.21 | 101.9 | 64.1 | 25.9 |
| M02205 | 0.11 | 16.8 | 0.25 | 119.9 | 31.6 | 22.9 |
| M02206 | 0.09 | 13.7 | 0.20 | 106.0 | 42.0 | 10.4 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.10 | 16.7 | 0.22 | 114.6 | 42.3 | 18.3 |
| S.D. | 0.01 | 3.3 | 0.03 | 9.3 | 12.9 | 5.6 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 25-2. (Continued) Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M02201 | 144.9 | 4.24 | 104.9 | 9.0 | 9.2 |
| M02202 | 144.2 | 4.12 | 105.9 | 9.3 | 8.3 |
| M02203 | 142.7 | 4.42 | 106.2 | 9.2 | 8.3 |
| M02204 | 145.1 | 4.39 | 105.9 | 9.4 | 8.4 |
| M02205 | 144.9 | 4.14 | 105.8 | 9.4 | 8.5 |
| M02206 | 145.6 | 4.42 | 106.0 | 9.4 | 8.1 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 144.6 | 4.29 | 105.8 | 9.3 | 8.5 |
| S.D. | 1.0 | 0.14 | 0.5 | 0.2 | 0.4 |
| Significance | NS | NS | # | NS | NS |
| Statistical method | DU | DU | STL | DU | DU |

Significantly different from the control group (#: $p<0.05$ by Steel's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 25-3. Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M03301 | 82.0 | 28.6 | 522.9 | 0.83 | 5.50 | 2.92 | 1.13 |
| M03302 | 83.6 | 24.0 | 709.5 | 0.72 | 5.25 | 2.80 | 1.14 |
| M03303 | 78.1 | 21.8 | 419.7 | 0.87 | 5.32 | 2.84 | 1.14 |
| M03304 | 98.4 | 21.9 | 502.7 | 0.38 | 5.06 | 2.82 | 1.26 |
| M03305 | 90.0 | 26.8 | 383.5 | 0.75 | 5.47 | 2.98 | 1.19 |
| M03306 | 107.7 | 30.0 | 757.8 | 0.99 | 5.84 | 3.08 | 1.11 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 90.0 | 25.5 | 549.4 | 0.76 | 5.41 | 2.91 | 1.16 |
| S.D. | 11.2 | 3.5 | 152.5 | 0.21 | 0.27 | 0.11 | 0.05 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-3. (Continued) Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M03301 | 0.13 | 21.2 | 0.24 | 115.6 | 49.1 | 18.5 |
| M03302 | 0.11 | 19.6 | 0.24 | 114.6 | 57.8 | 24.6 |
| M03303 | 0.10 | 22.5 | 0.22 | 132.4 | 38.4 | 25.3 |
| M03304 | 0.11 | 21.8 | 0.21 | 107.3 | 28.7 | 18.2 |
| M03305 | 0.13 | 19.7 | 0.23 | 114.4 | 50.5 | 28.7 |
| M03306 | 0.12 | 16.5 | 0.18 | 145.6 | 40.9 | 41.2 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.12 | 20.2 | 0.22 | 121.7 | 44.2 | 26.1 |
| S.D. | 0.01 | 2.2 | 0.02 | 14.4 | 10.3 | 8.5 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-3. (Continued) Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M03301 | 142.6 | 4.48 | 104.9 | 9.0 | 8.0 |
| M03302 | 143.2 | 4.08 | 105.1 | 9.1 | 8.5 |
| M03303 | 144.1 | 4.34 | 105.3 | 9.3 | 8.9 |
| M03304 | 143.5 | 4.72 | 105.3 | 9.1 | 8.8 |
| M03305 | 142.7 | 4.63 | 105.4 | 9.5 | 8.4 |
| M03306 | 144.5 | 4.60 | 103.8 | 9.8 | 8.9 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 143.4 | 4.48 | 105.0 | 9.3 | 8.6 |
| S.D. | 0.8 | 0.23 | 0.6 | 0.3 | 0.4 |
| Significance | NS | * | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU |

Significantly different from the control group (*: $p<0.05$ by Dunnett's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 25-4. Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M04401 | 93.9 | 26.7 | 531.1 | 0.95 | 5.54 | 3.12 | 1.29 |
| M04402 | 83.1 | 26.9 | 575.7 | 1.58 | 5.57 | 2.94 | 1.12 |
| M04403 | 64.6 | 28.9 | 512.3 | 1.37 | 6.22 | 3.28 | 1.11 |
| M04404 | 88.8 | 30.4 | 890.6 | 0.80 | 4.88 | 2.64 | 1.18 |
| M04405 | 97.9 | 74.3 | 472.4 | 1.10 | 5.89 | 3.08 | 1.10 |
| M04406 | 78.3 | 32.8 | 502.9 | 0.79 | 5.63 | 3.06 | 1.19 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 84.4 | 36.7 | 580.8 | 1.10 | 5.62 | 3.02 | 1.17 |
| S.D. | 12.0 | 18.6 | 155.6 | 0.32 | 0.44 | 0.22 | 0.07 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 25-4. (Continued) Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M04401 | 0.12 | 15.7 | 0.22 | 112.7 | 26.9 | 12.2 |
| M04402 | 0.12 | 21.8 | 0.22 | 114.1 | 46.7 | 23.3 |
| M04403 | 0.12 | 19.6 | 0.23 | 103.3 | 78.2 | 116.3 a) |
| M04404 | 0.10 | 11.5 | 0.20 | 108.0 | 29.5 | 19.8 |
| M04405 | 0.13 | 17.0 | 0.23 | 103.5 | 44.9 | 22.9 |
| M04406 | 0.12 | 19.6 | 0.19 | 126.0 | 58.7 | 22.8 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.12 | 17.5 | 0.22 | 111.3 | 47.5 | 36.2 |
| S.D. | 0.01 | 3.7 | 0.02 | 8.5 | 19.1 | 39.5 |
| Significance | NS | NS | * | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

a): Obtained in the scheduled measurement (1st measurement); the value, which is abnormally higher than that in other animals, was confirmed to be correct in the 2nd measurement.

Appendix 25-4. (Continued) Individual blood chemical findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M04401 | 143.2 | 4.63 | 105.7 | 9.2 | 8.5 |
| M04402 | 144.1 | 4.57 | 102.6 | 9.3 | 8.9 |
| M04403 | 142.8 | 4.70 | 101.9 | 10.3 | 8.6 |
| M04404 | 144.5 | 4.31 | 105.4 | 9.1 | 8.7 |
| M04405 | 144.3 | 4.46 | 105.1 | 9.8 | 7.9 |
| M04406 | 143.4 | 4.27 | 103.2 | 9.9 | 8.2 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 143.7 | 4.49 | 104.0 | 9.6 | 8.5 |
| S.D. | 0.7 | 0.17 | 1.6 | 0.5 | 0.4 |
| Significance | NS | * | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU |

Significantly different from the control group (*: $p<0.05$ by Dunnett's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 26-1. Individual blood chemical findings in female rats on termination of administration period

Control group

| Female No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| F01151 | 89.4 | 21.4 | 236.0 | 0.54 | 5.57 | 3.27 | 1.42 |
| F01152 | 92.9 | 23.9 | 453.7 | 0.92 | 5.47 | 2.96 | 1.18 |
| F01153 | 72.5 | 20.0 | 214.6 | 1.01 | 5.55 | 3.10 | 1.27 |
| F01154 | 60.3 | 24.5 | 383.7 | 0.57 | 5.25 | 2.88 | 1.22 |
| F01155 | 67.0 | 21.4 | 203.2 | 0.88 | 5.25 | 3.00 | 1.33 |
| F01156 | 85.3 | 24.1 | 344.8 | 0.96 | 5.70 | 3.02 | 1.12 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 77.9 | 22.6 | 306.0 | 0.81 | 5.47 | 3.04 | 1.26 |
| S.D. | 13.2 | 1.9 | 103.1 | 0.20 | 0.18 | 0.13 | 0.11 |

(Continued)

Appendix 26-1. (Continued) Individual blood chemical findings in female rats on termination of administration period

Control group

| Female No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| F01151 | 0.10 | 14.2 | 0.27 | 115.6 | 60.5 | 29.6 |
| F01152 | 0.12 | 16.6 | 0.29 | 118.3 | 49.6 | 25.9 |
| F01153 | 0.12 | 15.2 | 0.28 | 109.7 | 65.9 | 48.8 |
| F01154 | 0.13 | 12.0 | 0.26 | 119.6 | 71.7 | 21.9 |
| F01155 | 0.11 | 17.6 | 0.26 | 112.9 | 60.0 | 12.5 |
| F01156 | 0.10 | 15.8 | 0.28 | 92.1 | 72.1 | 22.8 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.11 | 15.2 | 0.27 | 111.4 | 63.3 | 26.9 |
| S.D. | 0.01 | 2.0 | 0.01 | 10.1 | 8.5 | 12.1 |

(Continued)

Appendix 26-1. (Continued) Individual blood chemical findings in female rats on termination of administration period

Control group

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F01151 | 144.1 | 4.15 | 106.5 | 9.7 | 6.6 |
| F01152 | 142.5 | 3.94 | 105.9 | 9.7 | 6.6 |
| F01153 | 142.2 | 4.13 | 105.5 | 9.7 | 6.5 |
| F01154 | 144.2 | 4.04 | 107.2 | 9.5 | 6.6 |
| F01155 | 144.1 | 4.08 | 105.9 | 9.6 | 7.5 |
| F01156 | 143.7 | 4.35 | 105.4 | 9.8 | 7.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 |
| Mean | 143.5 | 4.12 | 106.1 | 9.7 | 6.9 |
| S.D. | 0.9 | 0.14 | 0.7 | 0.1 | 0.5 |

Appendix 26-2. Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | AST IU/L | ALT IU/L | ALP IU/L | γ-GTP IU/L | Total protein g/dL | Albumin g/dL | A/G |
|---|---|---|---|---|---|---|---|
| F02251 | 116.0 | 23.1 | 319.8 | 1.64 | 5.54 | 2.95 | 1.14 |
| F02252 | 84.6 | 23.8 | 419.0 | 1.32 | 5.15 | 2.82 | 1.21 |
| F02253 | 77.5 | 22.7 | 335.9 | 0.91 | 5.45 | 3.02 | 1.24 |
| F02254 | 78.1 | 23.0 | 360.2 | 0.53 | 5.71 | 3.24 | 1.31 |
| F02255 | 66.8 | 17.5 | 285.4 | 0.49 | 5.46 | 3.14 | 1.35 |
| F02256 | 102.5 | 20.6 | 334.2 | 1.31 | 5.91 | 3.23 | 1.21 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 87.6 | 21.8 | 342.4 | 1.03 | 5.54 | 3.07 | 1.24 |
| S.D. | 18.2 | 2.4 | 44.8 | 0.47 | 0.26 | 0.17 | 0.08 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 26-2. (Continued) Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Total bilirubin | Urea nitrogen | Creatinine | Glucose | Total cholesterol | Triglyceride |
|---|---|---|---|---|---|---|
| | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL |
| F02251 | 0.11 | 21.8 | 0.32 | 105.7 | 81.1 | 13.3 |
| F02252 | 0.10 | 19.1 | 0.29 | 110.1 | 53.7 | 20.7 |
| F02253 | 0.11 | 24.5 | 0.31 | 114.8 | 60.3 | 17.6 |
| F02254 | 0.09 | 17.6 | 0.24 | 114.3 | 47.8 | 21.1 |
| F02255 | 0.09 | 16.3 | 0.25 | 111.1 | 64.1 | 29.5 |
| F02256 | 0.11 | 18.8 | 0.23 | 107.4 | 39.8 | 8.0 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.10 | 19.7 | 0.27 | 110.6 | 57.8 | 18.4 |
| S.D. | 0.01 | 3.0 | 0.04 | 3.6 | 14.4 | 7.4 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-2. (Continued) Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F02251 | 141.7 | 4.52 | 107.5 | 9.3 | 7.0 |
| F02252 | 141.9 | 4.31 | 107.6 | 9.1 | 6.6 |
| F02253 | 142.2 | 4.36 | 107.2 | 9.4 | 7.9 |
| F02254 | 144.0 | 4.24 | 109.5 | 9.2 | 6.6 |
| F02255 | 142.9 | 4.53 | 106.9 | 9.4 | 8.1 |
| F02256 | 143.2 | 4.31 | 105.4 | 9.5 | 7.3 |
| Number of females | 6 | 6 | 6 | 6 | 6 |
| Mean | 142.7 | 4.38 | 107.4 | 9.3 | 7.3 |
| S.D. | 0.9 | 0.12 | 1.3 | 0.1 | 0.6 |
| Significance | NS | ** | NS | ** | NS |
| Statistical method | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 26-3. Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| F03351 | 71.9 | 20.7 | 386.2 | 0.88 | 5.59 | 3.37 | 1.51 |
| F03352 | 73.0 | 24.2 | 370.9 | 0.80 | 5.55 | 3.31 | 1.48 |
| F03353 | 79.6 | 23.6 | 347.4 | 0.72 | 5.46 | 3.21 | 1.42 |
| F03354 | 73.2 | 20.4 | 349.7 | 1.06 | 5.53 | 3.26 | 1.44 |
| F03355 | 78.7 | 25.0 | 427.8 | 1.29 | 5.49 | 3.15 | 1.34 |
| F03356 | 75.9 | 26.1 | 432.8 | 1.53 | 5.94 | 3.42 | 1.36 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 75.4 | 23.3 | 385.8 | 1.05 | 5.59 | 3.29 | 1.43 |
| S.D. | 3.2 | 2.3 | 37.3 | 0.31 | 0.18 | 0.10 | 0.07 |
| Significance | NS | NS | NS | NS | NS | * | ** |
| Statistical method | STL | STL | DU | DU | DU | DU | DU |

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 26-3. (Continued) Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Total bilirubin | Urea nitrogen | Creatinine | Glucose | Total cholesterol | Triglyceride |
|---|---|---|---|---|---|---|
| | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL |
| F03351 | 0.11 | 18.9 | 0.25 | 105.2 | 45.4 | 28.5 |
| F03352 | 0.10 | 28.8 | 0.28 | 119.4 | 34.6 | 15.7 |
| F03353 | 0.10 | 21.3 | 0.24 | 104.9 | 54.5 | 17.9 |
| F03354 | 0.09 | 19.4 | 0.27 | 104.2 | 41.2 | 21.4 |
| F03355 | 0.11 | 20.5 | 0.29 | 108.3 | 57.5 | 58.4 |
| F03356 | 0.12 | 17.4 | 0.24 | 115.3 | 52.1 | 24.5 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.11 | 21.1 | 0.26 | 109.6 | 47.6 | 27.7 |
| S.D. | 0.01 | 4.0 | 0.02 | 6.3 | 8.7 | 15.7 |
| Significance | NS | * | NS | NS | * | NS |
| Statistical method | DU | DU | STL | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-3. (Continued) Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F03351 | 142.5 | 4.19 | 106.1 | 9.3 | 7.3 |
| F03352 | 140.9 | 4.25 | 106.5 | 9.5 | 7.9 |
| F03353 | 143.2 | 4.35 | 107.6 | 9.4 | 7.3 |
| F03354 | 143.1 | 4.47 | 108.0 | 9.4 | 7.6 |
| F03355 | 145.1 | 4.45 | 109.2 | 9.6 | 8.3 |
| F03356 | 143.7 | 4.33 | 107.4 | 9.5 | 7.2 |
| Number of females | 6 | 6 | 6 | 6 | 6 |
| Mean | 143.1 | 4.34 | 107.5 | 9.5 | 7.6 |
| S.D. | 1.4 | 0.11 | 1.1 | 0.1 | 0.4 |
| Significance | NS | * | NS | * | * |
| Statistical method | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 26-4. Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| F04451 | 62.6 | 28.3 | 261.1 | 0.66 | 5.48 | 3.04 | 1.25 |
| F04452 | 67.6 | 20.2 | 447.3 | 1.47 | 6.05 | 3.40 | 1.28 |
| F04453 | 60.2 | 40.8 | 263.8 | 1.36 | 5.77 | 3.28 | 1.31 |
| F04454 | Died on Day 2 of administration | | | | | | |
| F04455 | 77.8 | 33.7 | 410.3 | 1.28 | 5.37 | 2.98 | 1.25 |
| F04456 | 55.4 | 29.3 | 356.1 | 1.41 | 5.44 | 3.02 | 1.25 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 64.7 | 30.5 | 347.7 | 1.24 | 5.62 | 3.14 | 1.27 |
| S.D. | 8.5 | 7.6 | 84.3 | 0.33 | 0.28 | 0.19 | 0.03 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | STL | STL | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 26-4. (Continued) Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Total bilirubin | Urea nitrogen | Creatinine | Glucose | Total cholesterol | Triglyceride |
|---|---|---|---|---|---|---|
| | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL |
| F04451 | 0.11 | 12.4 | 0.23 | 94.7 | 79.2 | 26.5 |
| F04452 | 0.11 | 18.6 | 0.25 | 96.7 | 87.8 | 23.9 |
| F04453 | 0.11 | 19.6 | 0.24 | 112.7 | 86.4 | 28.2 |
| F04454 | Died on Day 2 of administration | | | | | |
| F04455 | 0.11 | 19.6 | 0.26 | 108.1 | 80.9 | 21.1 |
| F04456 | 0.12 | 21.6 | 0.24 | 106.4 | 78.3 | 53.3 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 0.11 | 18.4 | 0.24 | 103.7 | 82.5 | 30.6 |
| S.D. | 0.00 | 3.5 | 0.01 | 7.7 | 4.3 | 13.0 |
| Significance | NS | NS | # | NS | * | NS |
| Statistical method | DU | DU | STL | DU | DU | DU |

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

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 26-4. (Continued) Individual blood chemical findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F04451 | 143.8 | 4.28 | 104.2 | 9.6 | 8.1 |
| F04452 | 141.4 | 4.35 | 106.4 | 9.2 | 8.2 |
| F04453 | 143.0 | 4.42 | 105.2 | 9.4 | 8.0 |
| F04454 | Died on Day 2 of administration | | | | |
| F04455 | 143.8 | 4.66 | 108.9 | 9.4 | 8.4 |
| F04456 | 142.0 | 4.18 | 106.3 | 9.3 | 7.6 |
| Number of females | 5 | 5 | 5 | 5 | 5 |
| Mean | 142.8 | 4.38 | 106.2 | 9.4 | 8.1 |
| S.D. | 1.1 | 0.18 | 1.8 | 0.1 | 0.3 |
| Significance | NS | * | NS | ** | ** |
| Statistical method | DU | DU | DU | DU | DU |

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test).
NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 27-1. Individual blood chemical findings in male rats on termination of recovery period

Control group

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M01107 | 90.6 | 27.6 | 452.6 | 0.54 | 5.53 | 2.91 | 1.11 |
| M01108 | 78.9 | 24.9 | 299.8 | 0.55 | 5.86 | 2.89 | 0.98 |
| M01109 | 74.4 | 21.5 | 373.3 | 0.70 | 5.46 | 2.75 | 1.02 |
| M01110 | 108.6 | 33.3 | 711.0 | 0.80 | 5.56 | 2.95 | 1.13 |
| M01111 | 74.3 | 26.0 | 446.6 | 0.81 | 5.47 | 2.88 | 1.11 |
| M01112 | 66.2 | 32.1 | 441.2 | 0.67 | 5.80 | 2.75 | 0.90 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 82.2 | 27.6 | 454.1 | 0.68 | 5.61 | 2.86 | 1.04 |
| S.D. | 15.2 | 4.5 | 139.0 | 0.12 | 0.17 | 0.08 | 0.09 |

(Continued)

Appendix 27-1. (Continued) Individual blood chemical findings in male rats on termination of recovery period

Control group

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M01107 | 0.13 | 16.4 | 0.25 | 142.8 | 80.7 | 66.4 |
| M01108 | 0.11 | 18.7 | 0.31 | 128.7 | 51.2 | 41.4 |
| M01109 | 0.11 | 15.3 | 0.25 | 115.1 | 54.8 | 57.5 |
| M01110 | 0.10 | 14.4 | 0.24 | 137.1 | 46.1 | 35.1 |
| M01111 | 0.14 | 14.3 | 0.26 | 121.8 | 66.4 | 31.6 |
| M01112 | 0.11 | 15.3 | 0.24 | 167.1 | 73.3 | 38.3 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.12 | 15.7 | 0.26 | 135.4 | 62.1 | 45.1 |
| S.D. | 0.02 | 1.6 | 0.03 | 18.5 | 13.5 | 13.8 |

(Continued)

Appendix 27-1. (Continued) Individual blood chemical findings in male rats on termination of recovery period

Control group

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M01107 | 142.3 | 4.28 | 104.2 | 9.3 | 7.0 |
| M01108 | 143.1 | 4.38 | 104.1 | 9.5 | 6.8 |
| M01109 | 142.9 | 4.28 | 102.6 | 9.4 | 6.9 |
| M01110 | 144.8 | 4.25 | 103.7 | 9.2 | 7.5 |
| M01111 | 145.4 | 4.17 | 104.4 | 9.7 | 6.2 |
| M01112 | 145.4 | 4.02 | 101.2 | 10.0 | 7.6 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 144.0 | 4.23 | 103.4 | 9.5 | 7.0 |
| S.D. | 1.4 | 0.12 | 1.2 | 0.3 | 0.5 |

Appendix 27-2. Individual blood chemical findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M03307 | 73.2 | 32.6 | 438.1 | 0.82 | 5.62 | 2.75 | 0.96 |
| M03308 | 71.7 | 29.3 | 637.9 | 1.05 | 5.52 | 2.95 | 1.15 |
| M03309 | 85.5 | 31.0 | 462.6 | 0.93 | 5.53 | 2.58 | 0.88 |
| M03310 | 82.3 | 25.6 | 404.5 | 0.81 | 6.04 | 2.99 | 0.98 |
| M03311 | 101.6 | 28.3 | 451.7 | 0.51 | 5.85 | 2.88 | 0.97 |
| M03312 | 73.9 | 30.0 | 471.7 | 0.46 | 5.49 | 2.90 | 1.12 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 81.4 | 29.5 | 477.8 | 0.76 | 5.68 | 2.84 | 1.01 |
| S.D. | 11.3 | 2.4 | 81.9 | 0.23 | 0.22 | 0.15 | 0.10 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 27-2. (Continued) Individual blood chemical findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M03307 | 0.13 | 15.8 | 0.25 | 158.5 | 68.6 | 41.9 |
| M03308 | 0.10 | 18.2 | 0.27 | 135.1 | 48.6 | 29.9 |
| M03309 | 0.10 | 13.7 | 0.22 | 122.1 | 62.4 | 33.1 |
| M03310 | 0.14 | 15.6 | 0.25 | 114.6 | 54.4 | 39.4 |
| M03311 | 0.12 | 13.7 | 0.22 | 116.3 | 55.4 | 61.8 |
| M03312 | 0.12 | 17.6 | 0.21 | 125.1 | 44.8 | 18.7 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.12 | 15.8 | 0.24 | 128.6 | 55.7 | 37.5 |
| S.D. | 0.02 | 1.9 | 0.02 | 16.4 | 8.7 | 14.5 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

Appendix 27-2. (Continued) Individual blood chemical findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M03307 | 142.0 | 3.94 | 103.2 | 9.6 | 7.4 |
| M03308 | 143.7 | 4.10 | 104.8 | 9.6 | 7.9 |
| M03309 | 145.1 | 4.54 | 105.1 | 9.1 | 7.5 |
| M03310 | 144.4 | 4.15 | 104.0 | 9.9 | 6.4 |
| M03311 | 143.7 | 4.42 | 102.1 | 9.5 | 6.9 |
| M03312 | 145.5 | 4.24 | 103.7 | 9.1 | 7.8 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 144.1 | 4.23 | 103.8 | 9.5 | 7.3 |
| S.D. | 1.2 | 0.22 | 1.1 | 0.3 | 0.6 |
| Significance | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 27-3. Individual blood chemical findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| M04407 | 83.1 | 28.7 | 328.3 | 0.66 | 5.16 | 2.72 | 1.11 |
| M04408 | 67.1 | 25.3 | 354.8 | 0.49 | 5.45 | 2.80 | 1.06 |
| M04409 | 73.5 | 32.0 | 379.7 | 0.52 | 5.66 | 2.80 | 0.98 |
| M04410 | 65.6 | 23.2 | 403.9 | 0.55 | 5.91 | 2.90 | 0.96 |
| M04411 | 72.8 | 24.7 | 370.8 | 0.70 | 5.53 | 2.86 | 1.07 |
| M04412 | 60.1 | 27.9 | 350.9 | 0.62 | 5.58 | 2.89 | 1.07 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 70.4 | 27.0 | 364.7 | 0.59 | 5.55 | 2.83 | 1.04 |
| S.D. | 8.0 | 3.2 | 26.1 | 0.08 | 0.25 | 0.07 | 0.06 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 27-3. (Continued) Individual blood chemical findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| M04407 | 0.11 | 14.3 | 0.23 | 111.4 | 71.7 | 43.8 |
| M04408 | 0.10 | 16.8 | 0.31 | 141.5 | 96.1 | 42.4 |
| M04409 | 0.12 | 14.3 | 0.23 | 112.5 | 53.7 | 67.8 |
| M04410 | 0.11 | 14.5 | 0.23 | 125.5 | 93.3 | 76.6 |
| M04411 | 0.11 | 15.8 | 0.28 | 102.7 | 61.2 | 48.1 |
| M04412 | 0.09 | 18.7 | 0.23 | 122.4 | 56.9 | 38.2 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.11 | 15.7 | 0.25 | 119.3 | 72.2 | 52.8 |
| S.D. | 0.01 | 1.8 | 0.03 | 13.6 | 18.5 | 15.6 |
| Significance | NS | --- | NS | NS | NS | NS |
| Statistical method | DU | UA | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

UA: Unable to be analyzed because the value in the treated group was the same as the value in the control group.

Appendix 27-3. (Continued) Individual blood chemical findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| M04407 | 143.9 | 4.07 | 105.1 | 9.5 | 7.1 |
| M04408 | 143.7 | 3.94 | 102.0 | 9.5 | 7.6 |
| M04409 | 143.9 | 4.51 | 103.2 | 9.7 | 8.2 |
| M04410 | 145.7 | 4.18 | 101.8 | 10.0 | 7.2 |
| M04411 | 146.0 | 4.37 | 102.5 | 9.6 | 8.5 |
| M04412 | 145.8 | 4.05 | 103.0 | 10.0 | 8.8 |
| Number of males | 6 | 6 | 6 | 6 | 6 |
| Mean | 144.8 | 4.19 | 102.9 | 9.7 | 7.9 |
| S.D. | 1.1 | 0.22 | 1.2 | 0.2 | 0.7 |
| Significance | NS | NS | NS | NS | * |
| Statistical method | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 28-1. Individual blood chemical findings in female rats on termination of recovery period

Control group

| Female No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| F01157 | 80.7 | 22.9 | 228.5 | 0.42 | 5.80 | 3.20 | 1.23 |
| F01158 | 97.2 | 26.3 | 236.5 | 0.79 | 6.00 | 3.21 | 1.15 |
| F01159 | 73.0 | 22.7 | 207.9 | 0.67 | 6.43 | 3.62 | 1.29 |
| F01160 | 70.4 | 26.0 | 253.6 | 0.69 | 5.66 | 3.05 | 1.17 |
| F01161 | 98.1 | 26.8 | 177.1 | 0.48 | 6.09 | 3.23 | 1.13 |
| F01162 | 94.8 | 20.0 | 384.1 | 1.03 | 5.32 | 2.82 | 1.13 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 85.7 | 24.1 | 248.0 | 0.68 | 5.88 | 3.19 | 1.18 |
| S.D. | 12.6 | 2.7 | 71.7 | 0.22 | 0.38 | 0.26 | 0.06 |

(Continued)

Appendix 28-1. (Continued) Individual blood chemical findings in female rats on termination of recovery period

Control group

| Female No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| F01157 | 0.19 | 17.7 | 0.32 | 115.5 | 74.3 | 12.1 |
| F01158 | 0.17 | 17.7 | 0.29 | 129.8 | 48.9 | 20.6 |
| F01159 | 0.10 | 16.5 | 0.29 | 122.2 | 73.3 | 28.2 |
| F01160 | 0.13 | 21.0 | 0.35 | 118.4 | 57.7 | 10.9 |
| F01161 | 0.13 | 14.9 | 0.28 | 103.5 | 95.1 | 21.1 |
| F01162 | 0.15 | 17.8 | 0.33 | 114.6 | 59.4 | 19.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.15 | 17.6 | 0.31 | 117.3 | 68.1 | 18.7 |
| S.D. | 0.03 | 2.0 | 0.03 | 8.7 | 16.4 | 6.4 |

(Continued)

Appendix 28-1. (Continued) Individual blood chemical findings in female rats on termination of recovery period

Control group

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F01157 | 141.2 | 3.81 | 105.8 | 9.5 | 5.3 |
| F01158 | 141.3 | 3.94 | 104.3 | 9.5 | 5.7 |
| F01159 | 140.2 | 4.36 | 104.4 | 9.8 | 5.7 |
| F01160 | 142.1 | 3.45 | 104.5 | 9.6 | 5.7 |
| F01161 | 142.7 | 4.36 | 107.1 | 9.7 | 6.1 |
| F01162 | 142.0 | 4.01 | 104.3 | 9.3 | 6.7 |
| Number of females | 6 | 6 | 6 | 6 | 6 |
| Mean | 141.6 | 3.99 | 105.1 | 9.6 | 5.9 |
| S.D. | 0.9 | 0.35 | 1.2 | 0.2 | 0.5 |

Appendix 28-2. Individual blood chemical findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| F03357 | 60.9 | 26.1 | 237.1 | 0.57 | 5.73 | 3.13 | 1.20 |
| F03358 | 73.5 | 21.5 | 130.2 | 0.52 | 6.37 | 3.56 | 1.27 |
| F03359 | 63.9 | 22.9 | 253.1 | 0.51 | 5.63 | 3.25 | 1.36 |
| F03360 | 78.9 | 22.2 | 208.6 | 0.49 | 6.61 | 3.57 | 1.17 |
| F03361 | 74.4 | 16.7 | 332.3 | 0.59 | 5.78 | 3.16 | 1.21 |
| F03362 | 78.0 | 21.6 | 264.4 | 0.40 | 5.72 | 3.12 | 1.20 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 71.6 | 21.8 | 237.6 | 0.51 | 5.97 | 3.30 | 1.24 |
| S.D. | 7.5 | 3.0 | 66.8 | 0.07 | 0.41 | 0.21 | 0.07 |
| Significance | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group. (Continued)

DU: Analysis by Dunnett's test.

Appendix 28-2. (Continued) Individual blood chemical findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Total bilirubin mg/dL | Urea nitrogen mg/dL | Creatinine mg/dL | Glucose mg/dL | Total cholesterol mg/dL | Triglyceride mg/dL |
|---|---|---|---|---|---|---|
| F03357 | 0.15 | 21.1 | 0.26 | 124.2 | 61.5 | 24.3 |
| F03358 | 0.13 | 18.5 | 0.26 | 126.9 | 91.4 | 28.3 |
| F03359 | 0.11 | 15.6 | 0.25 | 150.2 | 69.9 | 33.4 |
| F03360 | 0.15 | 19.4 | 0.26 | 131.0 | 76.6 | 49.2 |
| F03361 | 0.13 | 16.9 | 0.26 | 115.0 | 57.5 | 17.6 |
| F03362 | 0.11 | 15.6 | 0.28 | 124.8 | 51.5 | 21.7 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.13 | 17.9 | 0.26 | 128.7 | 68.1 | 29.1 |
| S.D. | 0.02 | 2.2 | 0.01 | 11.8 | 14.5 | 11.3 |
| Significance | NS | NS | ## | NS | NS | NS |
| Statistical method | DU | DU | STL | DU | DU | DU |

Significantly different from the control group (##: $p<0.01$ by Steel's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 28-2. (Continued) Individual blood chemical findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F03357 | 139.7 | 4.02 | 102.9 | 9.3 | 5.8 |
| F03358 | 141.3 | 4.00 | 103.5 | 10.2 | 6.2 |
| F03359 | 141.3 | 3.81 | 105.4 | 9.6 | 5.5 |
| F03360 | 142.9 | 4.05 | 107.8 | 10.2 | 4.8 |
| F03361 | 142.8 | 4.02 | 105.0 | 9.6 | 6.5 |
| F03362 | 142.4 | 4.31 | 106.1 | 9.5 | 6.3 |
| Number of females | 6 | 6 | 6 | 6 | 6 |
| Mean | 141.7 | 4.04 | 105.1 | 9.7 | 5.9 |
| S.D. | 1.2 | 0.16 | 1.8 | 0.4 | 0.6 |
| Significance | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 28-3. Individual blood chemical findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | AST | ALT | ALP | γ-GTP | Total protein | Albumin | A/G |
|---|---|---|---|---|---|---|---|
| | IU/L | IU/L | IU/L | IU/L | g/dL | g/dL | |
| F04457 | 78.7 | 20.1 | 207.1 | 1.10 | 6.61 | 3.34 | 1.02 |
| F04458 | 89.5 | 22.0 | 192.6 | 1.37 | 5.66 | 3.03 | 1.15 |
| F04459 | 58.8 | 20.7 | 225.2 | 1.09 | 5.97 | 3.21 | 1.16 |
| F04460 | 96.9 | 24.8 | 286.7 | 1.37 | 5.86 | 2.84 | 0.94 |
| F04461 | 64.9 | 21.6 | 349.6 | 1.00 | 5.80 | 3.10 | 1.15 |
| F04462 | 67.9 | 16.7 | 270.9 | 0.86 | 6.06 | 3.10 | 1.05 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 76.1 | 21.0 | 255.4 | 1.13 | 5.99 | 3.10 | 1.08 |
| S.D. | 14.9 | 2.7 | 58.8 | 0.20 | 0.33 | 0.17 | 0.09 |
| Significance | NS | NS | NS | ** | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 28-3. (Continued) Individual blood chemical findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Total bilirubin | Urea nitrogen | Creatinine | Glucose | Total cholesterol | Triglyceride |
|---|---|---|---|---|---|---|
| | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL | mg/dL |
| F04457 | 0.18 | 16.3 | 0.26 | 117.8 | 110.9 | 33.8 |
| F04458 | 0.12 | 13.0 | 0.27 | 136.0 | 89.8 | 41.4 |
| F04459 | 0.13 | 15.8 | 0.23 | 112.3 | 84.7 | 29.8 |
| F04460 | 0.10 | 19.9 | 0.34 | 93.9 | 97.6 | 31.0 |
| F04461 | 0.17 | 15.0 | 0.28 | 115.1 | 106.5 | 55.7 |
| F04462 | 0.15 | 18.1 | 0.34 | 110.2 | 114.7 | 34.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 0.14 | 16.4 | 0.29 | 114.2 | 100.7 | 37.7 |
| S.D. | 0.03 | 2.4 | 0.04 | 13.6 | 12.0 | 9.7 |
| Significance | NS | NS | NS | NS | ** | ** |
| Statistical method | DU | DU | STL | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 28-3. (Continued) Individual blood chemical findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Na | K | Cl | Ca | Inorganic phosphate |
|---|---|---|---|---|---|
| | mEq/L | mEq/L | mEq/L | mg/dL | mg/dL |
| F04457 | 140.1 | 4.10 | 101.1 | 10.0 | 6.5 |
| F04458 | 141.2 | 4.05 | 103.5 | 9.4 | 6.3 |
| F04459 | 142.5 | 4.18 | 105.4 | 9.8 | 6.5 |
| F04460 | 142.6 | 4.30 | 106.7 | 9.4 | 7.1 |
| F04461 | 143.5 | 4.16 | 105.8 | 9.7 | 6.2 |
| F04462 | 142.6 | 4.07 | 106.3 | 9.6 | 6.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 |
| Mean | 142.1 | 4.14 | 104.8 | 9.7 | 6.5 |
| S.D. | 1.2 | 0.09 | 2.1 | 0.2 | 0.3 |
| Significance | NS | NS | NS | NS | NS |
| Statistical method | DU | STL | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.
STL: Analysis by Steel's test.

Appendix 29. Individual necropsy findings in a dead female rat

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Findings | |
|---|---|---|
| F04454 | Stomach | Red dot |
| | Stomach | Erosion |
| | Other organs and tissues | Normal |

Appendix 30-1. Individual necropsy findings in male rats on termination of administration period

Control group

| Male No. | Findings | |
|---|---|---|
| M01101 | All organs and tissues | Normal |
| M01102 | All organs and tissues | Normal |
| M01103 | All organs and tissues | Normal |
| M01104 | All organs and tissues | Normal |
| M01105 | All organs and tissues | Normal |
| M01106 | All organs and tissues | Normal |

Appendix 30-2. Individual necropsy findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Findings | |
|---|---|---|
| M02201 | All organs and tissues | Normal |
| M02202 | All organs and tissues | Normal |
| M02203 | All organs and tissues | Normal |
| M02204 | All organs and tissues | Normal |
| M02205 | All organs and tissues | Normal |
| M02206 | All organs and tissues | Normal |

Appendix 30-3. Individual necropsy findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | | Findings |
|---|---|---|
| M03301 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M03302 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M03303 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M03304 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M03305 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M03306 | Liver | Discoloration |
| | Other organs and tissues | Normal |

Appendix 30-4. Individual necropsy findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Findings | |
|---|---|---|
| M04401 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M04402 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M04403 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M04404 | All organs and tissues | Normal |
| M04405 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M04406 | All organs and tissues | Normal |

Appendix 31-1. Individual necropsy findings in female rats on termination of administration period

Control group

| Female No. | Findings | |
|---|---|---|
| F01151 | All organs and tissues | Normal |
| F01152 | All organs and tissues | Normal |
| F01153 | All organs and tissues | Normal |
| F01154 | All organs and tissues | Normal |
| F01155 | All organs and tissues | Normal |
| F01156 | All organs and tissues | Normal |

Appendix 31-2. Individual necropsy findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Findings | |
|---|---|---|
| F02251 | All organs and tissues | Normal |
| F02252 | All organs and tissues | Normal |
| F02253 | All organs and tissues | Normal |
| F02254 | All organs and tissues | Normal |
| F02255 | All organs and tissues | Normal |
| F02256 | All organs and tissues | Normal |

Appendix 31-3. Individual necropsy findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Findings | |
|---|---|---|
| F03351 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| F03352 | All organs and tissues | Normal |
| F03353 | All organs and tissues | Normal |
| F03354 | All organs and tissues | Normal |
| F03355 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| F03356 | All organs and tissues | Normal |

Appendix 31-4. Individual necropsy findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Findings | |
|---|---|---|
| F04451 | All organs and tissues | Normal |
| F04452 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| F04453 | All organs and tissues | Normal |
| F04455 | All organs and tissues | Normal |
| F04456 | Liver | Discoloration |
| | Other organs and tissues | Normal |

Appendix 32-1.Individual necropsy findings in male rats on termination of recovery period

Control group

| Male No. | Findings | |
|---|---|---|
| M01107 | All organs and tissues | Normal |
| M01108 | All organs and tissues | Normal |
| M01109 | All organs and tissues | Normal |
| M01110 | All organs and tissues | Normal |
| M01111 | All organs and tissues | Normal |
| M01112 | All organs and tissues | Normal |

Appendix 32-2. Individual necropsy findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Findings | |
|---|---|---|
| M03307 | Liver | Discoloration |
| | Other organs and tissues | Normal |
| M03308 | All organs and tissues | Normal |
| M03309 | All organs and tissues | Normal |
| M03310 | All organs and tissues | Normal |
| M03311 | All organs and tissues | Normal |
| M03312 | All organs and tissues | Normal |

Appendix 32-3. Individual necropsy findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Findings | |
|---|---|---|
| M04407 | All organs and tissues | Normal |
| M04408 | All organs and tissues | Normal |
| M04409 | All organs and tissues | Normal |
| M04410 | All organs and tissues | Normal |
| M04411 | All organs and tissues | Normal |
| M04412 | All organs and tissues | Normal |

Appendix 33-1. Individual necropsy findings in female rats on termination of recovery period

Control group

| Female No. | | Findings |
|---|---|---|
| F01157 | All organs and tissues | Normal |
| F01158 | All organs and tissues | Normal |
| F01159 | All organs and tissues | Normal |
| F01160 | All organs and tissues | Normal |
| F01161 | All organs and tissues | Normal |
| F01162 | All organs and tissues | Normal |

Appendix 33-2. Individual necropsy findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Findings | |
|---|---|---|
| F03357 | All organs and tissues | Normal |
| F03358 | All organs and tissues | Normal |
| F03359 | All organs and tissues | Normal |
| F03360 | All organs and tissues | Normal |
| F03361 | All organs and tissues | Normal |
| F03362 | All organs and tissues | Normal |

Appendix 33-3. Individual necropsy findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Findings | |
|---|---|---|
| F04457 | All organs and tissues | Normal |
| F04458 | All organs and tissues | Normal |
| F04459 | All organs and tissues | Normal |
| F04460 | All organs and tissues | Normal |
| F04461 | All organs and tissues | Normal |
| F04462 | All organs and tissues | Normal |

Appendix 34. Individual organ weights of a dead female rat

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F04454 | 149 | 1.61 | 1.08 | 10.2 | 6.8 | 318 | 213 | 19.0 | 12.8 | 521 | 350 | 0.70 | 0.47 | 6.80 | 4.56 | 356 | 239 |
| Number of females | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Mean | 149 | 1.61 | 1.08 | 10.2 | 6.8 | 318 | 213 | 19.0 | 12.8 | 521 | 350 | 0.70 | 0.47 | 6.80 | 4.56 | 356 | 239 |

(Continued)

Appendix 34. (Continued) Individual organ weights of a dead female rat

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F04454 | 1.88 | 1.26 | 54.0 | 36.2 | 58.5 | 39.3 |
| Number of females | 1 | 1 | 1 | 1 | 1 | 1 |
| Mean | 1.88 | 1.26 | 54.0 | 36.2 | 58.5 | 39.3 |

Appendix 35-1. Individual organ weights of male rats on termination of administration period

Control group

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M01101 | 346 | 1.93 | 0.56 | 13.9 | 4.0 | 540 | 156 | 12.2 | 3.5 | 542 | 157 | 1.23 | 0.36 | 10.02 | 2.90 | 498 | 144 |
| M01102 | 356 | 2.02 | 0.57 | 18.2 | 5.1 | 617 | 173 | 16.1 | 4.5 | 444 | 125 | 1.14 | 0.32 | 10.01 | 2.81 | 649 | 182 |
| M01103 | 371 | 2.10 | 0.57 | 14.6 | 3.9 | 732 | 197 | 25.7 | 6.9 | 418 | 113 | 1.26 | 0.34 | 11.20 | 3.02 | 642 | 173 |
| M01104 | 361 | 2.07 | 0.57 | 13.2 | 3.7 | 663 | 184 | 16.2 | 4.5 | 428 | 119 | 1.22 | 0.34 | 10.58 | 2.93 | 594 | 165 |
| M01105 | 341 | 2.08 | 0.61 | 10.5 | 3.1 | 668 | 196 | 25.7 | 7.5 | 367 | 108 | 1.37 | 0.40 | 9.65 | 2.83 | 733 | 215 |
| M01106 | 371 | 1.97 | 0.53 | 14.8 | 4.0 | 611 | 165 | 22.4 | 6.0 | 660 | 178 | 1.28 | 0.35 | 10.42 | 2.81 | 654 | 176 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 358 | 2.03 | 0.57 | 14.2 | 4.0 | 639 | 179 | 19.7 | 5.5 | 477 | 133 | 1.25 | 0.35 | 10.31 | 2.88 | 628 | 176 |
| S.D. | 13 | 0.07 | 0.03 | 2.5 | 0.7 | 65 | 17 | 5.7 | 1.6 | 107 | 28 | 0.08 | 0.03 | 0.55 | 0.08 | 78 | 23 |

(Continued)

Appendix 35-1. (Continued) Individual organ weights of male rats on termination of administration period

Control group

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M01101 | 2.26 | 0.65 | 60.0 | 17.3 | 2.87 | 0.83 | 780 | 225 |
| M01102 | 2.32 | 0.65 | 79.3 | 22.3 | 2.95 | 0.83 | 867 | 244 |
| M01103 | 2.49 | 0.67 | 68.8 | 18.5 | 3.10 | 0.84 | 822 | 222 |
| M01104 | 2.39 | 0.66 | 72.9 | 20.2 | 3.06 | 0.85 | 909 | 252 |
| M01105 | 2.91 | 0.85 | 50.3 | 14.8 | 3.00 | 0.88 | 783 | 230 |
| M01106 | 2.53 | 0.68 | 58.3 | 15.7 | 2.90 | 0.78 | 687 | 185 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 2.48 | 0.69 | 64.9 | 18.1 | 2.98 | 0.84 | 808 | 226 |
| S.D. | 0.23 | 0.08 | 10.7 | 2.8 | 0.09 | 0.03 | 77 | 23 |

Appendix 35-2. Individual organ weights of male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M02201 | 336 | 1.90 | 0.57 | 13.1 | 3.9 | 619 | 184 | 15.5 | 4.6 | 519 | 154 | 1.18 | 0.35 | 9.64 | 2.87 | 509 | 151 |
| M02202 | 348 | 2.04 | 0.59 | 12.5 | 3.6 | 586 | 168 | 22.7 | 6.5 | 454 | 130 | 1.20 | 0.34 | 10.34 | 2.97 | 603 | 173 |
| M02203 | 327 | 2.10 | 0.64 | 17.2 | 5.3 | 614 | 188 | 26.1 | 8.0 | 646 | 198 | 1.11 | 0.34 | 11.12 | 3.40 | 737 | 225 |
| M02204 | 346 | 2.07 | 0.60 | 14.2 | 4.1 | 636 | 184 | 23.6 | 6.8 | 597 | 173 | 1.19 | 0.34 | 11.94 | 3.45 | 611 | 177 |
| M02205 | 353 | 1.98 | 0.56 | 12.8 | 3.6 | 514 | 146 | 21.0 | 5.9 | 555 | 157 | 1.06 | 0.30 | 10.50 | 2.97 | 488 | 138 |
| M02206 | 365 | 2.09 | 0.57 | 13.1 | 3.6 | 651 | 178 | 27.0 | 7.4 | 696 | 191 | 1.23 | 0.34 | 10.80 | 2.96 | 543 | 149 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 346 | 2.03 | 0.59 | 13.8 | 4.0 | 603 | 175 | 22.7 | 6.5 | 578 | 167 | 1.16 | 0.34 | 10.72 | 3.10 | 582 | 169 |
| S.D. | 13 | 0.08 | 0.03 | 1.8 | 0.7 | 49 | 16 | 4.1 | 1.2 | 88 | 25 | 0.06 | 0.02 | 0.78 | 0.25 | 91 | 31 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

(Continued)

Appendix 35-2. (Continued) Individual organ weights of male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M02201 | 2.36 | 0.70 | 59.9 | 17.8 | 3.09 | 0.92 | 871 | 259 |
| M02202 | 2.51 | 0.72 | 47.9 | 13.8 | 3.20 | 0.92 | 861 | 247 |
| M02203 | 2.86 | 0.87 | 55.8 | 17.1 | 3.21 | 0.98 | 857 | 262 |
| M02204 | 2.90 | 0.84 | 56.1 | 16.2 | 3.46 | 1.00 | 916 | 265 |
| M02205 | 2.79 | 0.79 | 65.2 | 18.5 | 3.25 | 0.92 | 806 | 228 |
| M02206 | 2.80 | 0.77 | 59.9 | 16.4 | 3.35 | 0.92 | 929 | 255 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 2.70 | 0.78 | 57.5 | 16.6 | 3.26 | 0.94 | 873 | 253 |
| S.D. | 0.22 | 0.07 | 5.8 | 1.6 | 0.13 | 0.04 | 44 | 14 |
| Significance | NS | NS | NS | NS | NS | ## | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL | DU | DU |

Significantly different from the control group (##: $p<0.01$ by Steel's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 35-3. Individual organ weights of male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M03301 | 334 | 2.04 | 0.61 | 13.5 | 4.0 | 576 | 172 | 18.4 | 5.5 | 417 | 125 | 1.08 | 0.32 | 12.10 | 3.62 | 591 | 177 |
| M03302 | 368 | 1.98 | 0.54 | 13.6 | 3.7 | 627 | 170 | 16.3 | 4.4 | 606 | 165 | 1.11 | 0.30 | 13.54 | 3.68 | 560 | 152 |
| M03303 | 348 | 1.94 | 0.56 | 14.5 | 4.2 | 492 | 141 | 18.4 | 5.3 | 482 | 139 | 1.18 | 0.34 | 12.48 | 3.59 | 562 | 161 |
| M03304 | 327 | 1.91 | 0.58 | 10.1 | 3.1 | 524 | 160 | 19.0 | 5.8 | 486 | 149 | 1.12 | 0.34 | 13.33 | 4.08 | 423 | 129 |
| M03305 | 326 | 2.11 | 0.65 | 17.2 | 5.3 | 559 | 171 | 15.4 | 4.7 | 633 | 194 | 1.23 | 0.38 | 13.91 | 4.27 | 724 | 222 |
| M03306 | 353 | 1.96 | 0.56 | 13.7 | 3.9 | 570 | 161 | 21.8 | 6.2 | 565 | 160 | 1.21 | 0.34 | 14.24 | 4.03 | 551 | 156 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 343 | 1.99 | 0.58 | 13.8 | 4.0 | 558 | 163 | 18.2 | 5.3 | 532 | 155 | 1.16 | 0.34 | 13.27 | 3.88 | 569 | 166 |
| S.D. | 17 | 0.07 | 0.04 | 2.3 | 0.7 | 46 | 12 | 2.2 | 0.7 | 83 | 24 | 0.06 | 0.03 | 0.83 | 0.29 | 96 | 31 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | ** | ** | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: p<0.01 by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 35-3. (Continued) Individual organ weights of male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M03301 | 2.67 | 0.80 | 51.0 | 15.3 | 2.99 | 0.90 | 820 | 246 |
| M03302 | 2.86 | 0.78 | 46.2 | 12.6 | 3.07 | 0.83 | 842 | 229 |
| M03303 | 2.80 | 0.80 | 53.2 | 15.3 | 2.83 | 0.81 | 835 | 240 |
| M03304 | 3.11 | 0.95 | 51.6 | 15.8 | 3.01 | 0.92 | 923 | 282 |
| M03305 | 2.62 | 0.80 | 50.8 | 15.6 | 3.39 | 1.04 | 859 | 263 |
| M03306 | 2.81 | 0.80 | 69.1 | 19.6 | 3.06 | 0.87 | 812 | 230 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 2.81 | 0.82 | 53.7 | 15.7 | 3.06 | 0.90 | 849 | 248 |
| S.D. | 0.17 | 0.06 | 7.9 | 2.2 | 0.18 | 0.08 | 40 | 21 |
| Significance | * | * | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 35-4. Individual organ weights of male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M04401 | 295 | 1.99 | 0.67 | 11.0 | 3.7 | 549 | 186 | 15.4 | 5.2 | 469 | 159 | 1.16 | 0.39 | 14.49 | 4.91 | 447 | 152 |
| M04402 | 369 | 1.99 | 0.54 | 20.8 | 5.6 | 639 | 173 | 22.8 | 6.2 | 417 | 113 | 1.30 | 0.35 | 18.52 | 5.02 | 470 | 127 |
| M04403 | 358 | 1.98 | 0.55 | 15.7 | 4.4 | 501 | 140 | 20.6 | 5.8 | 454 | 127 | 1.21 | 0.34 | 17.35 | 4.85 | 545 | 152 |
| M04404 | 364 | 1.95 | 0.54 | 13.1 | 3.6 | 618 | 170 | 18.3 | 5.0 | 456 | 125 | 1.07 | 0.29 | 16.47 | 4.52 | 593 | 163 |
| M04405 | 324 | 1.94 | 0.60 | 16.3 | 5.0 | 495 | 153 | 18.0 | 5.6 | 405 | 125 | 1.15 | 0.35 | 15.50 | 4.78 | 551 | 170 |
| M04406 | 323 | 1.86 | 0.58 | 11.8 | 3.7 | 562 | 174 | 20.2 | 6.3 | 383 | 119 | 1.12 | 0.35 | 15.02 | 4.65 | 789 | 244 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 339 | 1.95 | 0.58 | 14.8 | 4.3 | 561 | 166 | 19.2 | 5.7 | 431 | 128 | 1.17 | 0.35 | 16.23 | 4.79 | 566 | 168 |
| S.D. | 29 | 0.05 | 0.05 | 3.6 | 0.8 | 59 | 17 | 2.6 | 0.5 | 34 | 16 | 0.08 | 0.03 | 1.52 | 0.18 | 122 | 40 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | ** | ** | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: p<0.01 by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 35-4. (Continued) Individual organ weights of male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M04401 | 3.28 | 1.11 | 57.1 | 19.4 | 3.33 | 1.13 | 800 | 271 |
| M04402 | 3.37 | 0.91 | 74.1 | 20.1 | 3.49 | 0.95 | 857 | 232 |
| M04403 | 3.02 | 0.84 | 63.9 | 17.8 | 2.98 | 0.83 | 804 | 225 |
| M04404 | 3.07 | 0.84 | 48.4 | 13.3 | 3.23 | 0.89 | 814 | 224 |
| M04405 | 2.94 | 0.91 | 60.0 | 18.5 | 3.26 | 1.01 | 748 | 231 |
| M04406 | 3.27 | 1.01 | 60.6 | 18.8 | 3.86 | 1.20 | 903 | 280 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 3.16 | 0.94 | 60.7 | 18.0 | 3.36 | 1.00 | 821 | 244 |
| S.D. | 0.17 | 0.11 | 8.4 | 2.4 | 0.30 | 0.14 | 53 | 25 |
| Significance | ** | ** | NS | NS | ** | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | STL | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 36-1. Individual organ weights of female rats on termination of administration period

Control group

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F01151 | 225 | 1.88 | 0.84 | 18.1 | 8.0 | 401 | 178 | 15.4 | 6.8 | 624 | 277 | 0.86 | 0.38 | 6.79 | 3.02 | 465 | 207 |
| F01152 | 220 | 1.80 | 0.82 | 25.5 | 11.6 | 378 | 172 | 17.3 | 7.9 | 468 | 213 | 0.84 | 0.38 | 6.61 | 3.00 | 488 | 222 |
| F01153 | 229 | 1.92 | 0.84 | 16.8 | 7.3 | 440 | 192 | 20.3 | 8.9 | 390 | 170 | 0.77 | 0.34 | 7.62 | 3.33 | 531 | 232 |
| F01154 | 242 | 1.96 | 0.81 | 14.6 | 6.0 | 438 | 181 | 23.6 | 9.8 | 498 | 206 | 0.94 | 0.39 | 7.70 | 3.18 | 782 | 323 |
| F01155 | 213 | 1.73 | 0.81 | 12.9 | 6.1 | 402 | 189 | 16.6 | 7.8 | 367 | 172 | 0.75 | 0.35 | 6.40 | 3.00 | 455 | 214 |
| F01156 | 225 | 1.74 | 0.77 | 13.3 | 5.9 | 400 | 178 | 17.3 | 7.7 | 490 | 218 | 0.74 | 0.33 | 6.68 | 2.97 | 561 | 249 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 226 | 1.84 | 0.82 | 16.9 | 7.5 | 410 | 182 | 18.4 | 8.2 | 473 | 209 | 0.82 | 0.36 | 6.97 | 3.08 | 547 | 241 |
| S.D. | 10 | 0.10 | 0.03 | 4.7 | 2.2 | 24 | 8 | 3.0 | 1.0 | 92 | 39 | 0.08 | 0.02 | 0.55 | 0.14 | 122 | 43 |

(Continued)

Appendix 36-1. (Continued) Individual organ weights of female rats on termination of administration period

Control group

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F01151 | 1.78 | 0.79 | 79.6 | 35.4 | 79.0 | 35.1 |
| F01152 | 1.68 | 0.76 | 79.7 | 36.2 | 88.3 | 40.1 |
| F01153 | 1.83 | 0.80 | 75.0 | 32.8 | 94.7 | 41.4 |
| F01154 | 1.94 | 0.80 | 58.5 | 24.2 | 80.0 | 33.1 |
| F01155 | 1.56 | 0.73 | 62.3 | 29.2 | 74.2 | 34.8 |
| F01156 | 1.58 | 0.70 | 74.2 | 33.0 | 77.3 | 34.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 1.73 | 0.76 | 71.6 | 31.8 | 82.3 | 36.5 |
| S.D. | 0.15 | 0.04 | 9.0 | 4.5 | 7.7 | 3.4 |

Appendix 36-2. Individual organ weights of female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F02251 | 236 | 1.84 | 0.78 | 15.4 | 6.5 | 476 | 202 | 16.3 | 6.9 | 422 | 179 | 0.97 | 0.41 | 7.78 | 3.30 | 540 | 229 |
| F02252 | 210 | 1.80 | 0.86 | 14.3 | 6.8 | 343 | 163 | 17.4 | 8.3 | 482 | 230 | 0.75 | 0.36 | 7.03 | 3.35 | 441 | 210 |
| F02253 | 247 | 1.91 | 0.77 | 15.1 | 6.1 | 415 | 168 | 20.7 | 8.4 | 591 | 239 | 0.95 | 0.38 | 8.68 | 3.51 | 493 | 200 |
| F02254 | 242 | 1.88 | 0.78 | 15.5 | 6.4 | 406 | 168 | 19.8 | 8.2 | 448 | 185 | 0.89 | 0.37 | 8.46 | 3.50 | 421 | 174 |
| F02255 | 230 | 1.86 | 0.81 | 13.4 | 5.8 | 412 | 179 | 24.6 | 10.7 | 502 | 218 | 0.79 | 0.34 | 7.93 | 3.45 | 429 | 187 |
| F02256 | 239 | 1.77 | 0.74 | 14.3 | 6.0 | 350 | 146 | 15.1 | 6.3 | 411 | 172 | 0.89 | 0.37 | 8.03 | 3.36 | 498 | 208 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 234 | 1.84 | 0.79 | 14.7 | 6.3 | 400 | 171 | 19.0 | 8.1 | 476 | 204 | 0.87 | 0.37 | 7.99 | 3.41 | 470 | 201 |
| S.D. | 13 | 0.05 | 0.04 | 0.8 | 0.4 | 49 | 19 | 3.5 | 1.5 | 66 | 29 | 0.09 | 0.02 | 0.58 | 0.09 | 47 | 19 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | * | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 36-2. (Continued) Individual organ weights of female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F02251 | 1.81 | 0.77 | 69.5 | 29.4 | 88.3 | 37.4 |
| F02252 | 1.59 | 0.76 | 56.2 | 26.8 | 71.5 | 34.0 |
| F02253 | 1.84 | 0.74 | 82.6 | 33.4 | 97.5 | 39.5 |
| F02254 | 1.85 | 0.76 | 73.1 | 30.2 | 86.0 | 35.5 |
| F02255 | 1.82 | 0.79 | 70.4 | 30.6 | 85.8 | 37.3 |
| F02256 | 1.78 | 0.74 | 62.3 | 26.1 | 97.2 | 40.7 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 1.78 | 0.76 | 69.0 | 29.4 | 87.7 | 37.4 |
| S.D. | 0.10 | 0.02 | 9.1 | 2.7 | 9.5 | 2.5 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 36-3. Individual organ weights of female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F03351 | 229 | 1.84 | 0.80 | 22.2 | 9.7 | 389 | 170 | 17.3 | 7.6 | 385 | 168 | 0.77 | 0.34 | 8.98 | 3.92 | 395 | 172 |
| F03352 | 231 | 1.81 | 0.78 | 11.5 | 5.0 | 377 | 163 | 17.4 | 7.5 | 402 | 174 | 0.80 | 0.35 | 8.80 | 3.81 | 421 | 182 |
| F03353 | 229 | 1.90 | 0.83 | 16.3 | 7.1 | 405 | 177 | 16.6 | 7.2 | 390 | 170 | 0.77 | 0.34 | 8.50 | 3.71 | 503 | 220 |
| F03354 | 224 | 1.70 | 0.76 | 13.2 | 5.9 | 430 | 192 | 16.5 | 7.4 | 502 | 224 | 0.87 | 0.39 | 9.39 | 4.19 | 508 | 227 |
| F03355 | 253 | 1.86 | 0.74 | 14.5 | 5.7 | 432 | 171 | 19.1 | 7.5 | 494 | 195 | 0.91 | 0.36 | 10.82 | 4.28 | 450 | 178 |
| F03356 | 206 | 1.89 | 0.92 | 12.4 | 6.0 | 384 | 186 | 16.1 | 7.8 | 337 | 164 | 0.67 | 0.33 | 7.94 | 3.85 | 340 | 165 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 229 | 1.83 | 0.81 | 15.0 | 6.6 | 403 | 177 | 17.2 | 7.5 | 418 | 183 | 0.80 | 0.35 | 9.07 | 3.96 | 436 | 191 |
| S.D. | 15 | 0.07 | 0.06 | 3.9 | 1.7 | 24 | 11 | 1.1 | 0.2 | 66 | 23 | 0.08 | 0.02 | 0.98 | 0.23 | 65 | 26 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | ** | ** | NS | * |
| Statistical method | DU | DU | DU | STL | STL | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 36-3. (Continued) Individual organ weights of female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F03351 | 1.92 | 0.84 | 63.5 | 27.7 | 75.8 | 33.1 |
| F03352 | 1.79 | 0.77 | 53.8 | 23.3 | 73.8 | 31.9 |
| F03353 | 2.01 | 0.88 | 66.4 | 29.0 | 99.6 | 43.5 |
| F03354 | 1.91 | 0.85 | 64.5 | 28.8 | 92.2 | 41.2 |
| F03355 | 1.91 | 0.75 | 73.2 | 28.9 | 79.9 | 31.6 |
| F03356 | 1.72 | 0.83 | 61.9 | 30.0 | 67.7 | 32.9 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 1.88 | 0.82 | 63.9 | 28.0 | 81.5 | 35.7 |
| S.D. | 0.10 | 0.05 | 6.3 | 2.4 | 12.1 | 5.2 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 36-4. Individual organ weights of female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F04451 | 208 | 1.90 | 0.91 | 13.5 | 6.5 | 392 | 188 | 23.9 | 11.5 | 288 | 138 | 0.79 | 0.38 | 10.35 | 4.98 | 470 | 226 |
| F04452 | 221 | 1.92 | 0.87 | 18.7 | 8.5 | 363 | 164 | 22.8 | 10.3 | 508 | 230 | 0.78 | 0.35 | 10.28 | 4.65 | 398 | 180 |
| F04453 | 206 | 1.80 | 0.87 | 15.3 | 7.4 | 314 | 152 | 20.2 | 9.8 | 281 | 136 | 0.79 | 0.38 | 10.75 | 5.22 | 291 | 141 |
| F04454 | Died on Day 2 of administration | | | | | | | | | | | | | | | | |
| F04455 | 231 | 1.86 | 0.81 | 17.1 | 7.4 | 432 | 187 | 22.8 | 9.9 | 420 | 182 | 0.94 | 0.41 | 10.36 | 4.48 | 564 | 244 |
| F04456 | 245 | 1.87 | 0.76 | 15.0 | 6.1 | 412 | 168 | 17.3 | 7.1 | 542 | 221 | 0.85 | 0.35 | 12.28 | 5.01 | 517 | 211 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 222 | 1.87 | 0.84 | 15.9 | 7.2 | 383 | 172 | 21.4 | 9.7 | 408 | 181 | 0.83 | 0.37 | 10.80 | 4.87 | 448 | 200 |
| S.D. | 16 | 0.05 | 0.06 | 2.0 | 0.9 | 46 | 15 | 2.7 | 1.6 | 121 | 44 | 0.07 | 0.03 | 0.85 | 0.30 | 107 | 41 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | ** | ** | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: p<0.01 by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

STL: Analysis by Steel's test.

DU: Analysis by Dunnett's test.

Appendix 36-4. (Continued) Individual organ weights of female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F04451 | 2.07 | 1.00 | 79.2 | 38.1 | 97.3 | 46.8 |
| F04452 | 1.90 | 0.86 | 67.7 | 30.6 | 80.3 | 36.3 |
| F04453 | 1.90 | 0.92 | 67.8 | 32.9 | 100.4 | 48.7 |
| F04454 | Died on Day 2 of administration | | | | | |
| F04455 | 2.14 | 0.93 | 81.4 | 35.2 | 81.0 | 35.1 |
| F04456 | 2.20 | 0.90 | 55.6 | 22.7 | 70.8 | 28.9 |
| Number of females | 5 | 5 | 5 | 5 | 5 | 5 |
| Mean | 2.04 | 0.92 | 70.3 | 31.9 | 86.0 | 39.2 |
| S.D. | 0.14 | 0.05 | 10.4 | 5.8 | 12.5 | 8.4 |
| Significance | ** | ** | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (**: $p<0.01$ by Dunnett's test).

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 37-1. Individual organ weights of male rats on termination of recovery period

Control group

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M01107 | 390 | 1.87 | 0.48 | 13.9 | 3.6 | 622 | 159 | 18.0 | 4.6 | 478 | 123 | 1.28 | 0.33 | 11.81 | 3.03 | 724 | 186 |
| M01108 | 444 | 2.11 | 0.48 | 16.6 | 3.7 | 675 | 152 | 25.4 | 5.7 | 662 | 149 | 1.37 | 0.31 | 12.90 | 2.91 | 663 | 149 |
| M01109 | 433 | 2.06 | 0.48 | 19.0 | 4.4 | 647 | 149 | 23.7 | 5.5 | 454 | 105 | 1.46 | 0.34 | 14.10 | 3.26 | 616 | 142 |
| M01110 | 383 | 2.04 | 0.53 | 14.5 | 3.8 | 627 | 164 | 25.9 | 6.8 | 330 | 86 | 1.29 | 0.34 | 9.39 | 2.45 | 595 | 155 |
| M01111 | 406 | 2.04 | 0.50 | 10.2 | 2.5 | 686 | 169 | 20.6 | 5.1 | 613 | 151 | 1.47 | 0.36 | 10.84 | 2.67 | 725 | 179 |
| M01112 | 455 | 2.16 | 0.47 | 20.8 | 4.6 | 764 | 168 | 22.7 | 5.0 | 423 | 93 | 1.62 | 0.36 | 13.80 | 3.03 | 878 | 193 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 419 | 2.05 | 0.49 | 15.8 | 3.8 | 670 | 160 | 22.7 | 5.5 | 493 | 118 | 1.42 | 0.34 | 12.14 | 2.89 | 700 | 167 |
| S.D. | 30 | 0.10 | 0.02 | 3.8 | 0.7 | 53 | 8 | 3.0 | 0.8 | 123 | 28 | 0.13 | 0.02 | 1.82 | 0.29 | 102 | 21 |

(Continued)

Appendix 37-1. (Continued) Individual organ weights of male rats on termination of recovery period

Control group

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M01107 | 2.61 | 0.67 | 64.7 | 16.6 | 3.13 | 0.80 | 1106 | 284 |
| M01108 | 2.91 | 0.66 | 57.9 | 13.0 | 3.80 | 0.86 | 1157 | 261 |
| M01109 | 3.02 | 0.70 | 63.3 | 14.6 | 3.12 | 0.72 | 1028 | 237 |
| M01110 | 2.68 | 0.70 | 45.6 | 11.9 | 3.29 | 0.86 | 1071 | 280 |
| M01111 | 2.60 | 0.64 | 56.4 | 13.9 | 3.46 | 0.85 | 1120 | 276 |
| M01112 | 3.46 | 0.76 | 72.8 | 16.0 | 3.66 | 0.80 | 1252 | 275 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 2.88 | 0.69 | 60.1 | 14.3 | 3.41 | 0.82 | 1122 | 269 |
| S.D. | 0.33 | 0.04 | 9.2 | 1.8 | 0.28 | 0.05 | 77 | 17 |

Appendix 37-2. Individual organ weights of male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M03307 | 406 | 1.97 | 0.49 | 15.8 | 3.9 | 647 | 159 | 24.3 | 6.0 | 345 | 85 | 1.35 | 0.33 | 12.77 | 3.15 | 595 | 147 |
| M03308 | 394 | 2.07 | 0.53 | 12.8 | 3.2 | 571 | 145 | 23.1 | 5.9 | 425 | 108 | 1.60 | 0.41 | 11.41 | 2.90 | 656 | 166 |
| M03309 | 419 | 2.16 | 0.52 | 15.3 | 3.7 | 603 | 144 | 29.5 | 7.0 | 613 | 146 | 1.61 | 0.38 | 11.45 | 2.73 | 680 | 162 |
| M03310 | 378 | 2.04 | 0.54 | 13.4 | 3.5 | 608 | 161 | 23.9 | 6.3 | 545 | 144 | 1.17 | 0.31 | 11.32 | 2.99 | 692 | 183 |
| M03311 | 417 | 2.07 | 0.50 | 14.6 | 3.5 | 651 | 156 | 23.2 | 5.6 | 456 | 109 | 1.64 | 0.39 | 12.45 | 2.99 | 775 | 186 |
| M03312 | 379 | 2.07 | 0.55 | 15.3 | 4.0 | 711 | 188 | 21.2 | 5.6 | 433 | 114 | 1.45 | 0.38 | 10.52 | 2.78 | 663 | 175 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 399 | 2.06 | 0.52 | 14.5 | 3.6 | 632 | 159 | 24.2 | 6.1 | 470 | 118 | 1.47 | 0.37 | 11.65 | 2.92 | 677 | 170 |
| S.D. | 18 | 0.06 | 0.02 | 1.2 | 0.3 | 49 | 16 | 2.8 | 0.5 | 95 | 23 | 0.18 | 0.04 | 0.82 | 0.15 | 59 | 15 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 37-2. (Continued) Individual organ weights of male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M03307 | 2.86 | 0.70 | 46.2 | 11.4 | 3.07 | 0.76 | 1033 | 254 |
| M03308 | 3.02 | 0.77 | 60.0 | 15.2 | 3.19 | 0.81 | 1160 | 294 |
| M03309 | 3.24 | 0.77 | 63.8 | 15.2 | 3.25 | 0.78 | 1132 | 270 |
| M03310 | 2.70 | 0.71 | 47.0 | 12.4 | 3.17 | 0.84 | 1103 | 292 |
| M03311 | 3.09 | 0.74 | 66.1 | 15.9 | 3.39 | 0.81 | 1123 | 269 |
| M03312 | 2.98 | 0.79 | 52.4 | 13.8 | 3.53 | 0.93 | 1161 | 306 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 2.98 | 0.75 | 55.9 | 14.0 | 3.27 | 0.82 | 1119 | 281 |
| S.D. | 0.19 | 0.04 | 8.6 | 1.8 | 0.17 | 0.06 | 48 | 20 |
| Significance | NS | * | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 37-3. Individual organ weights of male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| M04407 | 356 | 1.99 | 0.56 | 14.3 | 4.0 | 558 | 157 | 19.5 | 5.5 | 404 | 113 | 1.26 | 0.35 | 10.01 | 2.81 | 707 | 199 |
| M04408 | 430 | 2.09 | 0.49 | 14.0 | 3.3 | 765 | 178 | 20.9 | 4.9 | 475 | 110 | 1.24 | 0.29 | 12.12 | 2.82 | 767 | 178 |
| M04409 | 376 | 2.01 | 0.53 | 11.5 | 3.1 | 632 | 168 | 23.5 | 6.3 | 436 | 116 | 1.54 | 0.41 | 11.77 | 3.13 | 609 | 162 |
| M04410 | 418 | 1.89 | 0.45 | 12.7 | 3.0 | 554 | 133 | 21.7 | 5.2 | 658 | 157 | 1.57 | 0.38 | 12.95 | 3.10 | 689 | 165 |
| M04411 | 417 | 2.13 | 0.51 | 14.1 | 3.4 | 624 | 150 | 25.5 | 6.1 | 659 | 158 | 1.40 | 0.34 | 11.53 | 2.76 | 751 | 180 |
| M04412 | 344 | 2.02 | 0.59 | 16.4 | 4.8 | 582 | 169 | 22.1 | 6.4 | 362 | 105 | 1.19 | 0.35 | 11.44 | 3.33 | 614 | 178 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 390 | 2.02 | 0.52 | 13.8 | 3.6 | 619 | 159 | 22.2 | 5.7 | 499 | 127 | 1.37 | 0.35 | 11.64 | 2.99 | 690 | 177 |
| S.D. | 36 | 0.08 | 0.05 | 1.7 | 0.7 | 79 | 16 | 2.1 | 0.6 | 129 | 24 | 0.16 | 0.04 | 0.97 | 0.23 | 67 | 13 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

(Continued)

Appendix 37-3. (Continued) Individual organ weights of male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Kidneys | | Adrenals | | Testes | | Epididymides | |
|---|---|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (g) | (g%) | (mg) | (mg%) |
| M04407 | 2.78 | 0.78 | 58.3 | 16.4 | 3.13 | 0.88 | 1030 | 289 |
| M04408 | 3.03 | 0.70 | 64.0 | 14.9 | 3.60 | 0.84 | 1216 | 283 |
| M04409 | 2.97 | 0.79 | 59.2 | 15.7 | 3.14 | 0.84 | 1084 | 288 |
| M04410 | 3.11 | 0.74 | 42.9 | 10.3 | 2.88 | 0.69 | 1056 | 253 |
| M04411 | 2.94 | 0.71 | 76.7 | 18.4 | 3.41 | 0.82 | 1122 | 269 |
| M04412 | 2.72 | 0.79 | 63.3 | 18.4 | 3.52 | 1.02 | 1002 | 291 |
| Number of males | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 2.93 | 0.75 | 60.7 | 15.7 | 3.28 | 0.85 | 1085 | 279 |
| S.D. | 0.15 | 0.04 | 10.9 | 3.0 | 0.28 | 0.11 | 77 | 15 |
| Significance | NS | * | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU | DU | DU |

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

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

Appendix 38-1. Individual organ weights of female rats on termination of recovery period

Control group

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F01157 | 215 | 1.92 | 0.89 | 14.1 | 6.6 | 416 | 193 | 16.8 | 7.8 | 398 | 185 | 0.78 | 0.36 | 5.83 | 2.71 | 491 | 228 |
| F01158 | 274 | 1.87 | 0.68 | 16.1 | 5.9 | 412 | 150 | 15.8 | 5.8 | 420 | 153 | 0.96 | 0.35 | 7.73 | 2.82 | 642 | 234 |
| F01159 | 246 | 1.92 | 0.78 | 16.7 | 6.8 | 407 | 165 | 16.9 | 6.9 | 448 | 182 | 0.82 | 0.33 | 6.98 | 2.84 | 418 | 170 |
| F01160 | 259 | 2.21 | 0.85 | 18.0 | 6.9 | 516 | 199 | 15.1 | 5.8 | 417 | 161 | 0.93 | 0.36 | 6.64 | 2.56 | 575 | 222 |
| F01161 | 237 | 2.01 | 0.85 | 19.4 | 8.2 | 491 | 207 | 16.9 | 7.1 | 445 | 188 | 0.92 | 0.39 | 6.96 | 2.94 | 706 | 298 |
| F01162 | 235 | 1.81 | 0.77 | 13.2 | 5.6 | 403 | 171 | 23.0 | 9.8 | 370 | 157 | 0.87 | 0.37 | 5.91 | 2.51 | 420 | 179 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 244 | 1.96 | 0.80 | 16.3 | 6.7 | 441 | 181 | 17.4 | 7.2 | 416 | 171 | 0.88 | 0.36 | 6.68 | 2.73 | 542 | 222 |
| S.D. | 20 | 0.14 | 0.08 | 2.3 | 0.9 | 49 | 22 | 2.8 | 1.5 | 29 | 16 | 0.07 | 0.02 | 0.72 | 0.17 | 119 | 46 |

(Continued)

Appendix 38-1. (Continued) Individual organ weights of female rats on termination of recovery period

Control group

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F01157 | 1.46 | 0.68 | 64.0 | 29.8 | 79.4 | 36.9 |
| F01158 | 2.02 | 0.74 | 62.4 | 22.8 | 86.5 | 31.6 |
| F01159 | 1.81 | 0.74 | 60.4 | 24.6 | 99.1 | 40.3 |
| F01160 | 1.83 | 0.71 | 79.9 | 30.8 | 96.0 | 37.1 |
| F01161 | 1.65 | 0.70 | 85.9 | 36.2 | 94.0 | 39.7 |
| F01162 | 1.77 | 0.75 | 72.7 | 30.9 | 86.0 | 36.6 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 1.76 | 0.72 | 70.9 | 29.2 | 90.2 | 37.0 |
| S.D. | 0.19 | 0.03 | 10.4 | 4.8 | 7.4 | 3.1 |

Appendix 38-2. Individual organ weights of female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F03357 | 246 | 1.92 | 0.78 | 13.7 | 5.6 | 355 | 144 | 12.6 | 5.1 | 407 | 165 | 1.00 | 0.41 | 7.06 | 2.87 | 469 | 191 |
| F03358 | 244 | 1.78 | 0.73 | 12.6 | 5.2 | 352 | 144 | 19.4 | 8.0 | 361 | 148 | 0.89 | 0.36 | 7.09 | 2.91 | 404 | 166 |
| F03359 | 243 | 1.86 | 0.77 | 12.8 | 5.3 | 408 | 168 | 14.6 | 6.0 | 310 | 128 | 0.79 | 0.33 | 7.43 | 3.06 | 612 | 252 |
| F03360 | 273 | 1.82 | 0.67 | 14.5 | 5.3 | 453 | 166 | 15.1 | 5.5 | 505 | 185 | 0.94 | 0.34 | 7.84 | 2.87 | 431 | 158 |
| F03361 | 242 | 1.90 | 0.79 | 13.3 | 5.5 | 437 | 181 | 18.4 | 7.6 | 384 | 159 | 0.94 | 0.39 | 6.86 | 2.83 | 543 | 224 |
| F03362 | 268 | 1.88 | 0.70 | 13.6 | 5.1 | 438 | 163 | 14.4 | 5.4 | 367 | 137 | 0.93 | 0.35 | 7.18 | 2.68 | 434 | 162 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 253 | 1.86 | 0.74 | 13.4 | 5.3 | 407 | 161 | 15.8 | 6.3 | 389 | 154 | 0.92 | 0.36 | 7.24 | 2.87 | 482 | 192 |
| S.D. | 14 | 0.05 | 0.05 | 0.7 | 0.2 | 44 | 15 | 2.6 | 1.2 | 65 | 21 | 0.07 | 0.03 | 0.35 | 0.12 | 80 | 38 |
| Significance | NS | NS | NS | NS | ## | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (##: $p<0.01$ by Steel's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 38-2. (Continued) Individual organ weights of female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F03357 | 1.81 | 0.74 | 59.5 | 24.2 | 63.4 | 25.8 |
| F03358 | 1.73 | 0.71 | 63.3 | 25.9 | 67.7 | 27.7 |
| F03359 | 1.93 | 0.79 | 63.1 | 26.0 | 94.6 | 38.9 |
| F03360 | 1.73 | 0.63 | 62.6 | 22.9 | 74.1 | 27.1 |
| F03361 | 1.98 | 0.82 | 76.5 | 31.6 | 104.9 | 43.3 |
| F03362 | 2.02 | 0.75 | 56.3 | 21.0 | 68.2 | 25.4 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 1.87 | 0.74 | 63.6 | 25.3 | 78.8 | 31.4 |
| S.D. | 0.13 | 0.07 | 6.9 | 3.6 | 16.9 | 7.7 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 38-3. Individual organ weights of female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Body | Brain | | Pituitary | | Salivary glands | | Thyroids | | Thymus | | Heart | | Liver | | Spleen | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | weight (g) | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (mg) | (mg%) | (g) | (g%) | (g) | (g%) | (mg) | (mg%) |
| F04457 | 249 | 1.83 | 0.73 | 15.2 | 6.1 | 400 | 161 | 15.4 | 6.2 | 522 | 210 | 0.85 | 0.34 | 7.77 | 3.12 | 432 | 173 |
| F04458 | 251 | 1.86 | 0.74 | 13.1 | 5.2 | 407 | 162 | 15.7 | 6.3 | 501 | 200 | 0.95 | 0.38 | 7.89 | 3.14 | 525 | 209 |
| F04459 | 234 | 1.88 | 0.80 | 14.3 | 6.1 | 446 | 191 | 17.5 | 7.5 | 552 | 236 | 0.91 | 0.39 | 7.30 | 3.12 | 485 | 207 |
| F04460 | 261 | 1.93 | 0.74 | 13.6 | 5.2 | 528 | 202 | 16.1 | 6.2 | 454 | 174 | 0.86 | 0.33 | 8.03 | 3.08 | 576 | 221 |
| F04461 | 264 | 1.96 | 0.74 | 16.5 | 6.3 | 465 | 176 | 17.2 | 6.5 | 538 | 204 | 0.92 | 0.35 | 8.09 | 3.06 | 550 | 208 |
| F04462 | 238 | 1.97 | 0.83 | 14.6 | 6.1 | 372 | 156 | 13.7 | 5.8 | 418 | 176 | 0.86 | 0.36 | 7.10 | 2.98 | 483 | 203 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 250 | 1.91 | 0.76 | 14.6 | 5.8 | 436 | 175 | 15.9 | 6.4 | 498 | 200 | 0.89 | 0.36 | 7.70 | 3.08 | 509 | 204 |
| S.D. | 12 | 0.06 | 0.04 | 1.2 | 0.5 | 56 | 19 | 1.4 | 0.6 | 52 | 23 | 0.04 | 0.02 | 0.41 | 0.06 | 52 | 16 |
| Significance | NS | NS | NS | NS | NS | NS | NS | NS | NS | * | * | NS | NS | ** | ** | NS | NS |
| Statistical method | DU | DU | DU | STL | STL | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU | DU |

Significantly different from the control group (*: $p<0.05$, **: $p<0.01$ by Dunnett's test). (Continued)

NS: Not significantly different from the control group.

DU: Analysis by Dunnett's test.

STL: Analysis by Steel's test.

Appendix 38-3. (Continued) Individual organ weights of female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Kidneys | | Adrenals | | Ovaries | |
|---|---|---|---|---|---|---|
| | (g) | (g%) | (mg) | (mg%) | (mg) | (mg%) |
| F04457 | 1.93 | 0.78 | 63.3 | 25.4 | 71.4 | 28.7 |
| F04458 | 1.91 | 0.76 | 69.6 | 27.7 | 95.7 | 38.1 |
| F04459 | 1.91 | 0.82 | 65.2 | 27.9 | 84.6 | 36.2 |
| F04460 | 1.86 | 0.71 | 81.5 | 31.2 | 89.2 | 34.2 |
| F04461 | 2.04 | 0.77 | 58.9 | 22.3 | 68.4 | 25.9 |
| F04462 | 1.69 | 0.71 | 70.4 | 29.6 | 95.0 | 39.9 |
| Number of females | 6 | 6 | 6 | 6 | 6 | 6 |
| Mean | 1.89 | 0.76 | 68.2 | 27.4 | 84.1 | 33.8 |
| S.D. | 0.11 | 0.04 | 7.8 | 3.2 | 11.7 | 5.5 |
| Significance | NS | NS | NS | NS | NS | NS |
| Statistical method | DU | DU | DU | DU | DU | DU |

NS: Not significantly different from the control group.
DU: Analysis by Dunnett's test.

Appendix 39. Individual histopathological findings in a dead female rat

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F04454 | All organs and tissues | Postmortal change: + |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the heart, lung, trachea, liver, pancreas, sublingual gland, submandibular gland, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, thymus, spleen, mandibular lymph node, mesenteric lymph node, kidney, urinary bladder, ovary, uterus, vagina, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, medulla oblongata, spinal cord, sciatic nerve, eyeball, Harderian gland, bone marrow (sternum and femur), bone (sternum and femur), femur muscle, and mammary gland.

Appendix 40-1. Individual histopathological findings in male rats on termination of administration period

Control group

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M01101 | All organs and tissues | No abnormality detected |
| M01102 | All organs and tissues | No abnormality detected |
| M01103 | All organs and tissues | No abnormality detected |
| M01104 | All organs and tissues | No abnormality detected |
| M01105 | Kidney | Cyst, left: ± |
| | Other organs and tissues | No abnormality detected |
| M01106 | All organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the heart, lung, trachea, liver, pancreas, sublingual gland, submandibular gland, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, thymus, spleen, mandibular lymph node, mesenteric lymph node, kidney, urinary bladder, testis, epididymis, seminal vesicle, prostate, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, medulla oblongata, spinal cord, sciatic nerve, eyeball, Harderian gland, bone marrow (sternum and femur), bone (sternum and femur), and femur muscle.

Appendix 40-2. Individual histopathological findings in male rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M02201 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| M02202 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| M02203 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| M02204 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| M02205 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| M02206 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 40-3. Individual histopathological findings in male rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M03301 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| M03302 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| M03303 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| M03304 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| M03305 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| M03306 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 40-4. Individual histopathological findings in male rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M04401 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |
| M04402 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: + |
| | Pituitary | Aberrant craniopharyngeal tissue: ± |
| | Other organs and tissues | No abnormality detected |
| M04403 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: + |
| | Other organs and tissues | No abnormality detected |
| M04404 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: + |
| | Other organs and tissues | No abnormality detected |
| M04405 | Lung | Mineralization, vascular wall, left: ± |
| | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: + |
| | Other organs and tissues | No abnormality detected |
| M04406 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: ± |
| | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the heart, lung, trachea, liver, pancreas, sublingual gland, submandibular gland, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, thymus, spleen, mandibular lymph node, mesenteric lymph node, kidney, urinary bladder, testis, epididymis, seminal vesicle, prostate, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, medulla oblongata, spinal cord, sciatic nerve, eyeball, Harderian gland, bone marrow (sternum and femur), bone (sternum and femur), and femur muscle.

Appendix 41-1. Individual histopathological findings in female rats on termination of administration period

Control group

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F01151 | All organs and tissues | No abnormality detected |
| F01152 | All organs and tissues | No abnormality detected |
| F01153 | All organs and tissues | No abnormality detected |
| F01154 | Eyeball | Dysplasia, retina, left: ± |
| | Other organs and tissues | No abnormality detected |
| F01155 | Lung | Mineralization, vascular wall, left: ± |
| | Other organs and tissues | No abnormality detected |
| F01156 | All organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the heart, lung, trachea, liver, pancreas, sublingual gland, submandibular gland, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, thymus, spleen, mandibular lymph node, mesenteric lymph node, kidney, urinary bladder, ovary, uterus, vagina, pituitary, adrenal, thyroid, parathyroid, cerebrum, cerebellum, medulla oblongata, spinal cord, sciatic nerve, eyeball, Harderian gland, bone marrow (sternum and femur), bone (sternum and femur), femur muscle, and mammary gland.

Appendix 41-2. Individual histopathological findings in female rats on termination of administration period

1,8-dichlorooctane group at 40 mg/kg

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F02251 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F02252 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F02253 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F02254 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Kidney | Cyst, left: ± |
| F02255 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| F02256 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 41-3. Individual histopathological findings in female rats on termination of administration period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F03351 | Liver | Swelling, hepatocyte, periportal: + |
| | Liver | Microgranuloma: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F03352 | Liver | Swelling, hepatocyte, periportal: + |
| | Liver | Microgranuloma: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F03353 | Liver | Swelling, hepatocyte, periportal: + |
| | Liver | Microgranuloma: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F03354 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F03355 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F03356 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 41-4. Individual histopathological findings in female rats on termination of administration period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F04451 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Eyeball | Dysplasia, retina, right: ± |
| | Other organs and tissues | No abnormality detected |
| F04452 | Liver | Swelling, hepatocyte, periportal: + |
| | Liver | Microgranuloma: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F04453 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Other organs and tissues | No abnormality detected |
| F04455 | Liver | Swelling, hepatocyte, periportal: + |
| | Pancreas | Decreased, zymogen granules: + |
| | Parathyroid | Missing |
| | Other organs and tissues | No abnormality detected |
| F04456 | Liver | Swelling, hepatocyte, periportal: + |
| | Liver | Microgranuloma: ± |
| | Pancreas | Decreased, zymogen granules: + |
| | Parathyroid | Missing |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the heart, lung, trachea, liver, pancreas, sublingual gland, submandibular gland, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, thymus, spleen, mandibular lymph node, mesenteric lymph node, kidney, urinary bladder, ovary, uterus, vagina, pituitary, adrenal, thyroid, parathyroid (except for F04455 and F04456), cerebrum, cerebellum, medulla oblongata, spinal cord, sciatic nerve, eyeball, Harderian gland, bone marrow (sternum and femur), bone (sternum and femur), femur muscle, and mammary gland.

Appendix 42-1. Individual histopathological findings in male rats on termination of recovery period

Control group

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M01107 | All organs and tissues | No abnormality detected |
| M01108 | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Kidney | Cyst, left: ± |
| | Other organs and tissues | No abnormality detected |
| M01109 | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |
| M01110 | All organs and tissues | No abnormality detected |
| M01111 | All organs and tissues | No abnormality detected |
| M01112 | All organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 42-2. Individual histopathological findings in male rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M03307 | All organs and tissues | No abnormality detected |
| M03308 | All organs and tissues | No abnormality detected |
| M03309 | All organs and tissues | No abnormality detected |
| M03310 | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |
| M03311 | All organs and tissues | No abnormality detected |
| M03312 | All organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 42-3. Individual histopathological findings in male rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Male No. | Organ/Tissue | Findings |
|---|---|---|
| M04407 | All organs and tissues | No abnormality detected |
| M04408 | All organs and tissues | No abnormality detected |
| M04409 | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |
| M04410 | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |
| M04411 | All organs and tissues | No abnormality detected |
| M04412 | Kidney | Hyaline droplet, tubular epithelium, bilateral: ± |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 43-1. Individual histopathological findings in female rats on termination of recovery period

Control group

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F01157 | All organs and tissues | No abnormality detected |
| F01158 | All organs and tissues | No abnormality detected |
| F01159 | All organs and tissues | No abnormality detected |
| F01160 | All organs and tissues | No abnormality detected |
| F01161 | All organs and tissues | No abnormality detected |
| F01162 | All organs and tissues | No abnormality detected |

Examined the liver, pancreas, and kidney.

Appendix 43-2. Individual histopathological findings in female rats on termination of recovery period

1,8-dichlorooctane group at 200 mg/kg

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F03357 | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| F03358 | All organs and tissues | No abnormality detected |
| F03359 | All organs and tissues | No abnormality detected |
| F03360 | All organs and tissues | No abnormality detected |
| F03361 | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| F03362 | Liver | Swelling, hepatocyte, periportal: ± |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Appendix 43-3. Individual histopathological findings in female rats on termination of recovery period

1,8-dichlorooctane group at 1000 mg/kg

| Female No. | Organ/Tissue | Findings |
|---|---|---|
| F04457 | Liver | Swelling, hepatocyte, periportal: ± |
| | Other organs and tissues | No abnormality detected |
| F04458 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |
| F04459 | All organs and tissues | No abnormality detected |
| F04460 | Liver | Swelling, hepatocyte, periportal: ± |
| | Other organs and tissues | No abnormality detected |
| F04461 | All organs and tissues | No abnormality detected |
| F04462 | Liver | Swelling, hepatocyte, periportal: ± |
| | Pancreas | Decreased, zymogen granules: ± |
| | Other organs and tissues | No abnormality detected |

Grade of histopathological findings: ±: slight, +: mild, 2+: moderate, 3+: marked.
Examined the liver, pancreas, and kidney.

Stability of 1,8-dichlorooctane in test preparations (Study No. 094927)

Test article (Lot No.) : 1,8-dichlorooctane (Lot No. FGN01)
Vehicle : Corn oil
Form : Solution
Method : GC
Date of analysis : June 23, 2008 and July 1, 2008
Testing facility : Hashima Laboratory, Nihon Bioresearch Inc.

Results

| Concentration of analyte (mg/mL) | Storage period | Measured concentrations (mg/mL) | | | Mean concentration (mg/mL) | Recovery rate[2] (%) | Stability[3] (%) |
|---|---|---|---|---|---|---|---|
| | | 1st | 2nd | 3rd | | | |
| 2 | Initial | 2.134 | 2.157 | 2.162 | 2.151 | 107.6 | - |
| | 8 days after preparation [1] | 2.149 | 2.171 | 2.190 | 2.170 | 108.5 | 100.9 |
| 20 | Initial | 20.05 | 19.96 | 20.21 | 20.07 | 100.4 | - |
| | 8 days after preparation [1] | 20.18 | 20.83 | 20.52 | 20.51 | 102.6 | 102.2 |
| 200 | Initial | 196.9 | 201.2 | 200.4 | 199.5 | 99.8 | - |
| | 8 days after preparation [1] | 198.0 | 202.2 | 205.4 | 201.9 | 101.0 | 101.2 |

1) Stored at room temperature (set at 23 °C; values by actual measurement: 22.5 – 23.0°C) and lightproof conditions for 6 hours after being stored under refrigerated (set at 4 °C; values by actual measurement: 2.4 – 6.0°C) and lightproof conditions for 8 days.
2) Acceptable range: within ±10% of the prescribed concentrations.
3) Acceptable range: not less than 90%.

GLP:

This study was conducted in compliance with the OECD Guidelines for Safety Studies on Chemicals (OECD GLP Standards) and the Standards for Testing Facilities for Implementation of Studies of Novel Chemical Substances.

Concentrations of 1,8-dichlorooctane in dosing preparations at the start of administration in male rats

| | |
|---|---|
| Test article (Lot No.): | 1,8-dichlorooctane (Lot No. FGN01) |
| Vehicle: | Corn oil |
| Date of preparation: | August 28, 2008 |
| Form: | Solution |
| Method: | GC |
| Date of analysis: | August 28, 2008 |
| Testing facility: | Hashima Laboratory, Nihon Bioresearch Inc. |

Results

| Concentration of 1,8-dichlorooctane (mg/mL) | Measured concentrations (mg/mL) | | | | Recovery rate (%) |
|---|---|---|---|---|---|
| | 1st | 2nd | 3rd | Mean | |
| 8 | 7.635 | 7.656 | 7.555 | 7.615 | 95.2 |
| 40 | 39.65 | 39.46 | 39.47 | 39.53 | 98.8 |
| 200 | 202.3 | 206.4 | 198.3 | 202.3 | 101.2 |

The concentration of each preparation was within the acceptable range (100 ± 10%).

GLP:

This study was conducted in compliance with the OECD Guidelines for Safety Studies on Chemicals (OECD GLP Standards) and the Standards for Testing Facilities for Implementation of Studies of Novel Chemical Substances.

Concentrations of 1,8-dichlorooctane in dosing preparations at the end of administration in female rats

| | |
|---|---|
| Test article (Lot No.): | 1,8-dichlorooctane (Lot No. FGN01) |
| Vehicle: | Corn oil |
| Date of preparation: | September 25, 2008 |
| Form: | Solution |
| Method: | GC |
| Date of analysis: | September 25, 2008 |
| Testing facility: | Hashima Laboratory, Nihon Bioresearch Inc. |

Results

| Concentration of 1,8-dichlorooctane (mg/mL) | Measured concentrations (mg/mL) | | | | Recovery rate (%) |
|---|---|---|---|---|---|
| | 1st | 2nd | 3rd | Mean | |
| 8 | 7.838 | 7.775 | 7.666 | 7.760 | 97.0 |
| 40 | 41.08 | 40.46 | 41.32 | 40.95 | 102.4 |
| 200 | 205.8 | 205.6 | 206.1 | 205.8 | 102.9 |

The concentration of each preparation was within the acceptable range (100 ± 10%).

GLP:

This study was conducted in compliance with the OECD Guidelines for Safety Studies on Chemicals (OECD GLP Standards) and the Standards for Testing Facilities for Implementation of Studies of Novel Chemical Substances.

Attachment 4-1. General signs in male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Quarantine period | | | | | |
|---|---|---|---|---|---|---|---|
| | | 20-Aug-08 Day 0 | 21-Aug-08 Day 1 | 22-Aug-08 Day 2 | 23-Aug-08 Day 3 | 24-Aug-08 Day 4 | 25-Aug-08 Day 5 |
| M00001 | M01102 | N | N | N | N | N | N |
| M00002 | M04411 | N | N | N | N | N | N |
| M00003 | M04401 | N | N | N | N | N | N |
| M00004 | M04404 | N | N | N | N | N | N |
| M00005 | EG,MA | N | N | N | N | N | N |
| M00006 | EG,MA | N | N | N | N | N | N |
| M00007 | EG | N | N | N | N | N | N |
| M00008 | M03301 | N | N | N | N | N | N |
| M00009 | M01109 | N | N | N | N | N | N |
| M00010 | M01101 | N | N | N | N | N | N |
| M00011 | M01106 | N | N | N | N | N | N |
| M00012 | M03312 | N | N | N | N | N | N |
| M00013 | EG | N | N | N | N | N | N |
| M00014 | M03304 | N | N | N | N | N | N |
| M00015 | M01110 | N | N | N | N | N | N |
| M00016 | M03307 | N | N | N | N | N | N |
| M00017 | M02202 | N | N | N | N | N | N |
| M00018 | M03309 | N | N | N | N | N | N |
| M00019 | M02205 | N | N | N | N | N | N |
| M00020 | M02203 | N | N | N | N | N | N |
| M00021 | M04412 | N | N | N | N | N | N |
| M00022 | EG | N | N | N | N | N | N |
| M00023 | M02201 | N | N | N | N | N | N |
| M00024 | M03310 | N | N | N | N | N | N |
| M00025 | M04405 | N | N | N | N | N | N |

EG: Excluded from grouping because body weight was extremely different from the mean. (Continued)

MA: Monitor animal.

N: Normal.

Attachment 4-1. (Continued) General signs in male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Acclimatization period | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 26-Aug-08 Day 1 | 27-Aug-08 Day 2 | 28-Aug-08 Day 3 | 29-Aug-08 Day 4 | 30-Aug-08 Day 5 | 31-Aug-08 Day 6 | 01-Sep-08 Day 7 # |
| M00001 | M01102 | N | N | N | N | N | N | N |
| M00002 | M04411 | N | N | N | N | N | N | N |
| M00003 | M04401 | N | N | N | N | N | N | N |
| M00004 | M04404 | N | N | N | N | N | N | N |
| M00005 | EG,MA | N | N | N | N | N | N | N |
| M00006 | EG,MA | N | N | N | N | N | N | N |
| M00007 | EG | N | N | N | N | N | N | N * |
| M00008 | M03301 | N | N | N | N | N | N | N |
| M00009 | M01109 | N | N | N | N | N | N | N |
| M00010 | M01101 | N | N | N | N | N | N | N |
| M00011 | M01106 | N | N | N | N | N | N | N |
| M00012 | M03312 | N | N | N | N | N | N | N |
| M00013 | EG | N | N | N | N | N | N | N * |
| M00014 | M03304 | N | N | N | N | N | N | N |
| M00015 | M01110 | N | N | N | N | N | N | N |
| M00016 | M03307 | N | N | N | N | N | N | N |
| M00017 | M02202 | N | N | N | N | N | N | N |
| M00018 | M03309 | N | N | N | N | N | N | N |
| M00019 | M02205 | N | N | N | N | N | N | N |
| M00020 | M02203 | N | N | N | N | N | N | N |
| M00021 | M04412 | N | N | N | N | N | N | N |
| M00022 | EG | N | N | N | N | N | N | N * |
| M00023 | M02201 | N | N | N | N | N | N | N |
| M00024 | M03310 | N | N | N | N | N | N | N |
| M00025 | M04405 | N | N | N | N | N | N | N |

#: Day of grouping.

*: Euthanized.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

N: Normal.

Attachment 4-2. General signs in male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Quarantine period | | | | | |
|---|---|---|---|---|---|---|---|
| | | 20-Aug-08 Day 0 | 21-Aug-08 Day 1 | 22-Aug-08 Day 2 | 23-Aug-08 Day 3 | 24-Aug-08 Day 4 | 25-Aug-08 Day 5 |
| M00026 | M01103 | N | N | N | N | N | N |
| M00027 | M04403 | N | N | N | N | N | N |
| M00028 | M02206 | N | N | N | N | N | N |
| M00029 | M03308 | N | N | N | N | N | N |
| M00030 | M04406 | N | N | N | N | N | N |
| M00031 | EG | N | N | N | N | N | N |
| M00032 | EG | N | N | N | N | N | N |
| M00033 | M04407 | N | N | N | N | N | N |
| M00034 | M03311 | N | N | N | N | N | N |
| M00035 | M04402 | N | N | N | N | N | N |
| M00036 | M01112 | N | N | N | N | N | N |
| M00037 | M04408 | N | N | N | N | N | N |
| M00038 | M01111 | N | N | N | N | N | N |
| M00039 | EG | N | N | N | N | N | N |
| M00040 | M04410 | N | N | N | N | N | N |
| M00041 | EG | N | N | N | N | N | N |
| M00042 | M03303 | N | N | N | N | N | N |
| M00043 | M03306 | N | N | N | N | N | N |
| M00044 | M02204 | N | N | N | N | N | N |
| M00045 | EG | N | N | N | N | N | N |
| M00046 | M01104 | N | N | N | N | N | N |
| M00047 | M01105 | N | N | N | N | N | N |
| M00048 | M03302 | N | N | N | N | N | N |
| M00049 | M04409 | N | N | N | N | N | N |
| M00050 | M01107 | N | N | N | N | N | N |

EG: Excluded from grouping because body weight was extremely different from the mean. (Continued)
N: Normal.

Attachment 4-2. (Continued) General signs in male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Acclimatization period | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 26-Aug-08 Day 1 | 27-Aug-08 Day 2 | 28-Aug-08 Day 3 | 29-Aug-08 Day 4 | 30-Aug-08 Day 5 | 31-Aug-08 Day 6 | 01-Sep-08 Day 7 # |
| M00026 | M01103 | N | N | N | N | N | N | N |
| M00027 | M04403 | N | N | N | N | N | N | N |
| M00028 | M02206 | N | N | N | N | N | N | N |
| M00029 | M03308 | N | N | N | N | N | N | N |
| M00030 | M04406 | N | N | N | N | N | N | N |
| M00031 | EG | N | N | N | N | N | N | N * |
| M00032 | EG | N | N | N | N | N | N | N * |
| M00033 | M04407 | N | N | N | N | N | N | N |
| M00034 | M03311 | N | N | N | N | N | N | N |
| M00035 | M04402 | N | N | N | N | N | N | N |
| M00036 | M01112 | N | N | N | N | N | N | N |
| M00037 | M04408 | N | N | N | N | N | N | N |
| M00038 | M01111 | N | N | N | N | N | N | N |
| M00039 | EG | N | N | N | N | N | N | N * |
| M00040 | M04410 | N | N | N | N | N | N | N |
| M00041 | EG | N | N | N | N | N | N | N * |
| M00042 | M03303 | N | N | N | N | N | N | N |
| M00043 | M03306 | N | N | N | N | N | N | N |
| M00044 | M02204 | N | N | N | N | N | N | N |
| M00045 | EG | N | N | N | N | N | N | N * |
| M00046 | M01104 | N | N | N | N | N | N | N |
| M00047 | M01105 | N | N | N | N | N | N | N |
| M00048 | M03302 | N | N | N | N | N | N | N |
| M00049 | M04409 | N | N | N | N | N | N | N |
| M00050 | M01107 | N | N | N | N | N | N | N |

#: Day of grouping.

*: Euthanized.

EG: Excluded from grouping because body weight was extremely different from the mean.

N: Normal.

Attachment 4-3. General signs in male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Quarantine period | | | | | |
|---|---|---|---|---|---|---|---|
| | | 20-Aug-08 Day 0 | 21-Aug-08 Day 1 | 22-Aug-08 Day 2 | 23-Aug-08 Day 3 | 24-Aug-08 Day 4 | 25-Aug-08 Day 5 |
| M00051 | M03305 | N | N | N | N | N | N |
| M00052 | M01108 | N | N | N | N | N | N |
| Number of males | | 52 | 52 | 52 | 52 | 52 | 52 |
| N | | 52 | 52 | 52 | 52 | 52 | 52 |

N: Normal.

(Continued)

Attachment 4-3. (Continued) General signs in male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Acclimatization period | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 26-Aug-08 Day 1 | 27-Aug-08 Day 2 | 28-Aug-08 Day 3 | 29-Aug-08 Day 4 | 30-Aug-08 Day 5 | 31-Aug-08 Day 6 | 01-Sep-08 Day 7 # |
| M00051 | M03305 | N | N | N | N | N | N | N |
| M00052 | M01108 | N | N | N | N | N | N | N |
| Number of males | | 52 | 52 | 52 | 52 | 52 | 52 | 52 |
| N | | 52 | 52 | 52 | 52 | 52 | 52 | 52 |

#: Day of grouping.
N: Normal.

Attachment 5-1. General signs in female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Quarantine period | | | | | |
|---|---|---|---|---|---|---|---|
| | | 20-Aug-08 Day 0 | 21-Aug-08 Day 1 | 22-Aug-08 Day 2 | 23-Aug-08 Day 3 | 24-Aug-08 Day 4 | 25-Aug-08 Day 5 |
| F00001 | F04455 | N | N | N | N | N | N |
| F00002 | F03358 | N | N | N | N | N | N |
| F00003 | F01157 | N | N | N | N | N | N |
| F00004 | EG | N | N | N | N | N | N |
| F00005 | F04453 | N | N | N | N | N | N |
| F00006 | F04460 | N | N | N | N | N | N |
| F00007 | F01161 | N | N | N | N | N | N |
| F00008 | EG | N | N | N | N | N | N |
| F00009 | F02251 | N | N | N | N | N | N |
| F00010 | F03356 | N | N | N | N | N | N |
| F00011 | F03357 | N | N | N | N | N | N |
| F00012 | F04462 | N | N | N | N | N | N |
| F00013 | F04459 | N | N | N | N | N | N |
| F00014 | EG | N | N | N | N | N | N |
| F00015 | F04454 | N | N | N | N | N | N |
| F00016 | F04452 | N | N | N | N | N | N |
| F00017 | F02255 | N | N | N | N | N | N |
| F00018 | F01158 | N | N | N | N | N | N |
| F00019 | F02253 | N | N | N | N | N | N |
| F00020 | F03361 | N | N | N | N | N | N |
| F00021 | F02252 | N | N | N | N | N | N |
| F00022 | EG | N | N | N | N | N | N |
| F00023 | F03353 | N | N | N | N | N | N |
| F00024 | F01151 | N | N | N | N | N | N |
| F00025 | EG | N | N | N | N | N | N |

EG: Excluded from grouping because body weight was extremely different from the mean. (Continued)
N: Normal.

Attachment 5-1. (Continued) General signs in female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Acclimatization period | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 26-Aug-08 Day 1 | 27-Aug-08 Day 2 | 28-Aug-08 Day 3 | 29-Aug-08 Day 4 | 30-Aug-08 Day 5 | 31-Aug-08 Day 6 | 01-Sep-08 Day 7 | 02-Sep-08 Day 8 | 03-Sep-08 Day 9 | 04-Sep-08 Day 10 # |
| F00001 | F04455 | N | N | N | N | N | N | N | N | N | N |
| F00002 | F03358 | N | N | N | N | N | N | N | N | N | N |
| F00003 | F01157 | N | N | N | N | N | N | N | N | N | N |
| F00004 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00005 | F04453 | N | N | N | N | N | N | N | N | N | N |
| F00006 | F04460 | N | N | N | N | N | N | N | N | N | N |
| F00007 | F01161 | N | N | N | N | N | N | N | N | N | N |
| F00008 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00009 | F02251 | N | N | N | N | N | N | N | N | N | N |
| F00010 | F03356 | N | N | N | N | N | N | N | N | N | N |
| F00011 | F03357 | N | N | N | N | N | N | N | N | N | N |
| F00012 | F04462 | N | N | N | N | N | N | N | N | N | N |
| F00013 | F04459 | N | N | N | N | N | N | N | N | N | N |
| F00014 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00015 | F04454 | N | N | N | N | N | N | N | N | N | N |
| F00016 | F04452 | N | N | N | N | N | N | N | N | N | N |
| F00017 | F02255 | N | N | N | N | N | N | N | N | N | N |
| F00018 | F01158 | N | N | N | N | N | N | N | N | N | N |
| F00019 | F02253 | N | N | N | N | N | N | N | N | N | N |
| F00020 | F03361 | N | N | N | N | N | N | N | N | N | N |
| F00021 | F02252 | N | N | N | N | N | N | N | N | N | N |
| F00022 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00023 | F03353 | N | N | N | N | N | N | N | N | N | N |
| F00024 | F01151 | N | N | N | N | N | N | N | N | N | N |
| F00025 | EG | N | N | N | N | N | N | N | N | N | N * |

#: Day of grouping.

*: Euthanized.

EG: Excluded from grouping because body weight was extremely different from the mean.

N: Normal.

Attachment 5-2. General signs in female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Quarantine period | | | | | |
|---|---|---|---|---|---|---|---|
| | | 20-Aug-08 Day 0 | 21-Aug-08 Day 1 | 22-Aug-08 Day 2 | 23-Aug-08 Day 3 | 24-Aug-08 Day 4 | 25-Aug-08 Day 5 |
| F00026 | EG | N | N | N | N | N | N |
| F00027 | F03352 | N | N | N | N | N | N |
| F00028 | EG | N | N | N | N | N | N |
| F00029 | F04457 | N | N | N | N | N | N |
| F00030 | F02256 | N | N | N | N | N | N |
| F00031 | EG | N | N | N | N | N | N |
| F00032 | F03360 | N | N | N | N | N | N |
| F00033 | F01154 | N | N | N | N | N | N |
| F00034 | F01155 | N | N | N | N | N | N |
| F00035 | F04458 | N | N | N | N | N | N |
| F00036 | F02254 | N | N | N | N | N | N |
| F00037 | F01160 | N | N | N | N | N | N |
| F00038 | F03351 | N | N | N | N | N | N |
| F00039 | F01152 | N | N | N | N | N | N |
| F00040 | F01159 | N | N | N | N | N | N |
| F00041 | F03355 | N | N | N | N | N | N |
| F00042 | F04456 | N | N | N | N | N | N |
| F00043 | F03359 | N | N | N | N | N | N |
| F00044 | F04451 | N | N | N | N | N | N |
| F00045 | EG | N | N | N | N | N | N |
| F00046 | F03362 | N | N | N | N | N | N |
| F00047 | F01153 | N | N | N | N | N | N |
| F00048 | F03354 | N | N | N | N | N | N |
| F00049 | F01156 | N | N | N | N | N | N |
| F00050 | EG | N | N | N | N | N | N |

EG: Excluded from grouping because body weight was extremely different from the mean. (Continued)
N: Normal.

Attachment 5-2. (Continued) General signs in female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Acclimatization period | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 26-Aug-08 Day 1 | 27-Aug-08 Day 2 | 28-Aug-08 Day 3 | 29-Aug-08 Day 4 | 30-Aug-08 Day 5 | 31-Aug-08 Day 6 | 01-Sep-08 Day 7 | 02-Sep-08 Day 8 | 03-Sep-08 Day 9 | 04-Sep-08 Day 10 # |
| F00026 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00027 | F03352 | N | N | N | N | N | N | N | N | N | N |
| F00028 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00029 | F04457 | N | N | N | N | N | N | N | N | N | N |
| F00030 | F02256 | N | N | N | N | N | N | N | N | N | N |
| F00031 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00032 | F03360 | N | N | N | N | N | N | N | N | N | N |
| F00033 | F01154 | N | N | N | N | N | N | N | N | N | N |
| F00034 | F01155 | N | N | N | N | N | N | N | N | N | N |
| F00035 | F04458 | N | N | N | N | N | N | N | N | N | N |
| F00036 | F02254 | N | N | N | N | N | N | N | N | N | N |
| F00037 | F01160 | N | N | N | N | N | N | N | N | N | N |
| F00038 | F03351 | N | N | N | N | N | N | N | N | N | N |
| F00039 | F01152 | N | N | N | N | N | N | N | N | N | N |
| F00040 | F01159 | N | N | N | N | N | N | N | N | N | N |
| F00041 | F03355 | N | N | N | N | N | N | N | N | N | N |
| F00042 | F04456 | N | N | N | N | N | N | N | N | N | N |
| F00043 | F03359 | N | N | N | N | N | N | N | N | N | N |
| F00044 | F04451 | N | N | N | N | N | N | N | N | N | N |
| F00045 | EG | N | N | N | N | N | N | N | N | N | N * |
| F00046 | F03362 | N | N | N | N | N | N | N | N | N | N |
| F00047 | F01153 | N | N | N | N | N | N | N | N | N | N |
| F00048 | F03354 | N | N | N | N | N | N | N | N | N | N |
| F00049 | F01156 | N | N | N | N | N | N | N | N | N | N |
| F00050 | EG | N | N | N | N | N | N | N | N | N | N * |

#: Day of grouping.

*: Euthanized.

EG: Excluded from grouping because body weight was extremely different from the mean.

N: Normal.

Attachment 5-3. General signs in female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Quarantine period | | | | | |
|---|---|---|---|---|---|---|---|
| | | 20-Aug-08 Day 0 | 21-Aug-08 Day 1 | 22-Aug-08 Day 2 | 23-Aug-08 Day 3 | 24-Aug-08 Day 4 | 25-Aug-08 Day 5 |
| F00051 | F04461 | N | N | N | N | N | N |
| F00052 | F01162 | N | N | N | N | N | N |
| Number of females | | 52 | 52 | 52 | 52 | 52 | 52 |
| N | | 52 | 52 | 52 | 52 | 52 | 52 |

N: Normal.

(Continued)

Attachment 5-3. (Continued) General signs in female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Acclimatization period | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 26-Aug-08 Day 1 | 27-Aug-08 Day 2 | 28-Aug-08 Day 3 | 29-Aug-08 Day 4 | 30-Aug-08 Day 5 | 31-Aug-08 Day 6 | 01-Sep-08 Day 7 | 02-Sep-08 Day 8 | 03-Sep-08 Day 9 | 04-Sep-08 Day 10 # |
| F00051 | F04461 | N | N | N | N | N | N | N | N | N | N |
| F00052 | F01162 | N | N | N | N | N | N | N | N | N | N |
| Number of females | | 52 | 52 | 52 | 52 | 52 | 52 | 52 | 52 | 52 | 52 |
| N | | 52 | 52 | 52 | 52 | 52 | 52 | 52 | 52 | 52 | 52 |

#: Day of grouping.
N: Normal.

Attachment 6-1. Body weights (g) of male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Quarantine period | | Acclimatization period | |
|---|---|---|---|---|---|
| | | 21-Aug-08 | 25-Aug-08 | 01-Sep-08 | |
| | | Day 1 | Day 5 | Day 7 | # |
| M00001 | M01102 | 88 | 126 | 199 | |
| M00002 | M04411 | 90 | 123 | 194 | |
| M00003 | M04401 | 89 | 124 | 184 | |
| M00004 | M04404 | 89 | 125 | 199 | |
| M00005 | EG,MA | 84 | 120 | 173 | |
| M00006 | EG,MA | 86 | 131 H | 204 | |
| M00007 | EG | 85 | 121 | 181 | |
| M00008 | M03301 | 84 | 125 | 195 | |
| M00009 | M01109 | 86 | 122 | 196 | |
| M00010 | M01101 | 90 | 126 | 191 | |
| M00011 | M01106 | 93 H | 131 H | 188 | |
| M00012 | M03312 | 91 | 129 | 194 | |
| M00013 | EG | 89 | 128 | 200 | |
| M00014 | M03304 | 88 | 128 | 196 | |
| M00015 | M01110 | 88 | 121 | 186 | |
| M00016 | M03307 | 89 | 126 | 182 | |
| M00017 | M02202 | 91 | 127 | 199 | |
| M00018 | M03309 | 90 | 124 | 192 | |
| M00019 | M02205 | 90 | 127 | 193 | |
| M00020 | M02203 | 92 | 124 | 185 | |
| M00021 | M04412 | 84 | 119 | 188 | |
| M00022 | EG | 86 | 128 | 205 H | |
| M00023 | M02201 | 87 | 122 | 190 | |
| M00024 | M03310 | 87 | 124 | 188 | |
| M00025 | M04405 | 86 | 125 | 191 | |

#: Day of grouping.

EG: Excluded from grouping because body weight was extremely different from the mean.

MA: Monitor animal.

H: Maximum body weight.

Attachment 6-2. Body weights (g) of male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Quarantine period | | Acclimatization period | |
|---|---|---|---|---|---|
| | | 21-Aug-08 | 25-Aug-08 | 01-Sep-08 | |
| | | Day 1 | Day 5 | Day 7 | # |
| M00026 | M01103 | 85 | 121 | 184 | |
| M00027 | M04403 | 88 | 125 | 193 | |
| M00028 | M02206 | 89 | 126 | 196 | |
| M00029 | M03308 | 87 | 128 | 197 | |
| M00030 | M04406 | 89 | 123 | 185 | |
| M00031 | EG | 91 | 122 | 201 | |
| M00032 | EG | 91 | 131 H | 172 L | |
| M00033 | M04407 | 89 | 124 | 192 | |
| M00034 | M03311 | 88 | 127 | 191 | |
| M00035 | M04402 | 88 | 128 | 197 | |
| M00036 | M01112 | 89 | 125 | 195 | |
| M00037 | M04408 | 88 | 124 | 200 | |
| M00038 | M01111 | 87 | 125 | 196 | |
| M00039 | EG | 88 | 119 | 172 L | |
| M00040 | M04410 | 89 | 123 | 186 | |
| M00041 | EG | 86 | 122 | 179 | |
| M00042 | M03303 | 88 | 123 | 191 | |
| M00043 | M03306 | 86 | 115 L | 185 | |
| M00044 | M02204 | 87 | 118 | 184 | |
| M00045 | EG | 89 | 128 | 204 | |
| M00046 | M01104 | 86 | 125 | 199 | |
| M00047 | M01105 | 83 L | 120 | 188 | |
| M00048 | M03302 | 89 | 128 | 197 | |
| M00049 | M04409 | 83 L | 122 | 188 | |
| M00050 | M01107 | 84 | 129 | 190 | |

#: Day of grouping.

EG: Excluded from grouping because body weight was extremely different from the mean.

L: Minimum body weight.

H: Maximum body weight.

Attachment 6-3. Body weights (g) of male rats during quarantine and acclimatization

| Quarantine/ acclimatization male No. | Male No. | Quarantine period | | Acclimatization period | |
|---|---|---|---|---|---|
| | | 21-Aug-08 | 25-Aug-08 | 01-Sep-08 | |
| | | Day 1 | Day 5 | Day 7 | # |
| M00051 | M03305 | 89 | 123 | 182 | |
| M00052 | M01108 | 88 | 123 | 183 | |
| Number of males | | 52 | 52 | 52 | |
| Mean | | 88 | 124 | 191 | |
| S.D. | | 2 | 3 | 8 | |

#: Day of grouping.

Attachment 7-1. Body weights (g) of female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Quarantine period | | Acclimatization period | |
|---|---|---|---|---|---|
| | | 21-Aug-08 | 25-Aug-08 | 01-Sep-08 | 04-Sep-08 |
| | | Day 1 | Day 5 | Day 7 | Day 10 # |
| F00001 | F04455 | 66 | 98 | 144 | 161 |
| F00002 | F03358 | 70 | 101 | 145 | 159 |
| F00003 | F01157 | 71 | 101 | 138 | 152 |
| F00004 | EG | 74 | 103 | 157 | 169 |
| F00005 | F04453 | 73 | 96 | 137 | 147 |
| F00006 | F04460 | 75 | 106 | 143 | 161 |
| F00007 | F01161 | 73 | 95 | 147 | 157 |
| F00008 | EG | 77 H | 110 H | 165 H | 173 H |
| F00009 | F02251 | 65 | 97 | 141 | 153 |
| F00010 | F03356 | 69 | 98 | 142 | 152 |
| F00011 | F03357 | 71 | 94 | 141 | 156 |
| F00012 | F04462 | 74 | 97 | 148 | 164 |
| F00013 | F04459 | 75 | 104 | 150 | 154 |
| F00014 | EG | 74 | 105 | 155 | 169 |
| F00015 | F04454 | 75 | 100 | 143 | 152 |
| F00016 | F04452 | 69 | 102 | 147 | 161 |
| F00017 | F02255 | 74 | 103 | 144 | 158 |
| F00018 | F01158 | 72 | 104 | 149 | 163 |
| F00019 | F02253 | 75 | 105 | 157 | 163 |
| F00020 | F03361 | 69 | 97 | 142 | 153 |
| F00021 | F02252 | 67 | 98 | 136 | 148 |
| F00022 | EG | 63 L | 90 L | 133 | 145 |
| F00023 | F03353 | 73 | 102 | 148 | 155 |
| F00024 | F01151 | 74 | 101 | 143 | 154 |
| F00025 | EG | 69 | 95 | 141 | 144 |

#: Day of grouping.

EG: Excluded from grouping because body weight was extremely different from the mean.

L: Minimum body weight.

H: Maximum body weight.

Attachment 7-2. Body weights (g) of female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Quarantine period | | Acclimatization period | |
|---|---|---|---|---|---|
| | | 21-Aug-08 | 25-Aug-08 | 01-Sep-08 | 04-Sep-08 |
| | | Day 1 | Day 5 | Day 7 | Day 10 # |
| F00026 | EG | 76 | 110 H | 158 | 169 |
| F00027 | F03352 | 74 | 105 | 150 | 152 |
| F00028 | EG | 70 | 93 | 127 L | 135 L |
| F00029 | F04457 | 73 | 102 | 143 | 152 |
| F00030 | F02256 | 72 | 104 | 153 | 159 |
| F00031 | EG | 70 | 97 | 138 | 144 |
| F00032 | F03360 | 71 | 101 | 148 | 161 |
| F00033 | F01154 | 68 | 97 | 146 | 159 |
| F00034 | F01155 | 72 | 102 | 146 | 154 |
| F00035 | F04458 | 70 | 100 | 146 | 155 |
| F00036 | F02254 | 73 | 104 | 151 | 164 |
| F00037 | F01160 | 75 | 104 | 147 | 164 |
| F00038 | F03351 | 76 | 103 | 147 | 161 |
| F00039 | F01152 | 73 | 103 | 153 | 169 |
| F00040 | F01159 | 73 | 106 | 146 | 162 |
| F00041 | F03355 | 74 | 108 | 159 | 167 |
| F00042 | F04456 | 73 | 106 | 157 | 166 |
| F00043 | F03359 | 70 | 101 | 148 | 165 |
| F00044 | F04451 | 68 | 98 | 143 | 160 |
| F00045 | EG | 71 | 99 | 134 | 143 |
| F00046 | F03362 | 74 | 104 | 148 | 166 |
| F00047 | F01153 | 68 | 99 | 140 | 153 |
| F00048 | F03354 | 75 | 105 | 148 | 164 |
| F00049 | F01156 | 70 | 99 | 143 | 157 |
| F00050 | EG | 70 | 98 | 136 | 146 |

#: Day of grouping.

EG: Excluded from grouping because body weight was extremely different from the mean.

L: Minimum body weight.

H: Maximum body weight.

Attachment 7-3. Body weights (g) of female rats during quarantine and acclimatization

| Quarantine/ acclimatization female No. | Female No. | Quarantine period | | Acclimatization period | |
|---|---|---|---|---|---|
| | | 21-Aug-08 | 25-Aug-08 | 01-Sep-08 | 04-Sep-08 |
| | | Day 1 | Day 5 | Day 7 | Day 10 # |
| F00051 | F04461 | 68 | 100 | 151 | 167 |
| F00052 | F01162 | 70 | 100 | 145 | 148 |
| Number of females | | 52 | 52 | 52 | 52 |
| Mean | | 72 | 101 | 146 | 157 |
| S.D. | | 3 | 4 | 7 | 8 |

#: Day of grouping.

# Background Data

Crl:CD (SD) Male Rats

Hematological findings 10weeks

| Exam.item | Unit | N | Value Mean ± S.D. | Min. | Max. | Range of 2S.D. |
|---|---|---|---|---|---|---|
| RBC | $10^4/\mu L$ | 30 | 789 ± 35 | 739 | 896 | 719 - 859 |
| HGB | g/dL | 30 | 15.1 ± 0.5 | 14.1 | 16.3 | 14.1 - 16.1 |
| HCT | % | 30 | 44.4 ± 1.4 | 41.7 | 47.0 | 41.6 - 47.2 |
| MCV | fL | 30 | 56.3 ± 1.8 | 52.5 | 60.1 | 52.7 - 59.9 |
| MCH | pg | 30 | 19.2 ± 0.6 | 18.0 | 20.4 | 18.0 - 20.4 |
| MCHC | g/dL | 30 | 34.0 ± 0.4 | 33.3 | 34.7 | 33.2 - 34.8 |
| PLT | $10^4/\mu L$ | 30 | 119.4 ± 12.9 | 97.6 | 146.5 | 93.6 - 145.2 |
| RET | % | 30 | 3.55 ± 0.50 | 2.79 | 4.68 | 2.55 - 4.55 |
| PT | sec | 30 | 22.3 ± 4.8 | 14.6 | 33.4 | 12.7 - 31.9 |
| APTT | sec | 30 | 22.6 ± 2.1 | 18.2 | 29.0 | 18.4 - 26.8 |
| Fbg | mg/dL | 30 | 214.3 ± 12.5 | 195.5 | 241.3 | 189.3 - 239.3 |
| WBC | $10^2/\mu L$ | 30 | 66.9 ± 15.0 | 36.2 | 97.8 | 36.9 - 96.9 |
| Differential leukocyte (%) | | | | | | |
| LYMPH | % | 30 | 78.7 ± 7.2 | 61.2 | 90.1 | |
| NEUT | % | 30 | 17.6 ± 6.7 | 6.8 | 33.7 | |
| EO | % | 30 | 1.3 ± 0.5 | 0.6 | 2.5 | |
| BASO | % | 30 | 0.0 ± 0.0 | 0.0 | 0.1 | |
| MONO | % | 30 | 2.5 ± 0.7 | 1.2 | 4.1 | |

N: Number of animals.

Hashima Laboratory, Nihon Bioresearch Inc.

Prepared: 2007.08

# Background Data

Crl:CD (SD) Female Rats

Hematological findings 10 weeks

| Exam.item | Unit | N | Value Mean ± S.D. | Min. | Max. | Range of 2S.D. |
|---|---|---|---|---|---|---|
| RBC | $10^4/\mu L$ | 29 | 767 ± 36 | 682 | 832 | 695 - 839 |
| HGB | g/dL | 29 | 14.7 ± 0.5 | 13.7 | 15.6 | 13.7 - 15.7 |
| HCT | % | 29 | 42.5 ± 1.2 | 39.9 | 44.7 | 40.1 - 44.9 |
| MCV | fL | 29 | 55.5 ± 1.7 | 51.4 | 60.0 | 52.1 - 58.9 |
| MCH | pg | 29 | 19.2 ± 0.6 | 18.1 | 20.4 | 18.0 - 20.4 |
| MCHC | g/dL | 29 | 34.5 ± 0.4 | 33.7 | 35.5 | 33.7 - 35.3 |
| PLT | $10^4/\mu L$ | 29 | 115.6 ± 11.3 | 91.7 | 138.2 | 93.0 - 138.2 |
| RET | % | 29 | 2.92 ± 0.71 | 1.65 | 4.32 | 1.50 - 4.34 |
| PT | sec | 29 | 15.1 ± 0.7 | 13.7 | 16.2 | 13.7 - 16.5 |
| APTT | sec | 29 | 17.1 ± 0.5 | 16.0 | 18.2 | 16.1 - 18.1 |
| Fbg | mg/dL | 29 | 185.6 ± 12.6 | 164.3 | 212.4 | 160.4 - 210.8 |
| WBC | $10^2/\mu L$ | 29 | 47.1 ± 14.3 | 24.8 | 88.5 | 18.5 - 75.7 |
| Differential leukocyte (%) | | | | | | |
| LYMPH | % | 29 | 78.5 ± 7.1 | 65.2 | 87.8 | |
| NEUT | % | 29 | 17.6 ± 6.8 | 8.9 | 30.0 | |
| EO | % | 29 | 1.6 ± 0.5 | 0.6 | 2.6 | |
| BASO | % | 29 | 0.0 ± 0.1 | 0.0 | 0.3 | |
| MONO | % | 29 | 2.3 ± 0.7 | 1.2 | 4.0 | |

N: Number of animals.

Hashima Laboratory, Nihon Bioresearch Inc.

Prepared: 2007.08

# Background Data

Crl:CD (SD) Male Rats

Blood chemical findings 10 weeks

| Exam.item | Unit | N | Value Mean ± S.D. | Min. | Max. | Range of 2S.D. |
|---|---|---|---|---|---|---|
| AST | IU/ L | 30 | 83.7 ± 14.2 | 58.2 | 130.0 | 55.3 - 112.1 |
| ALT | IU/ L | 30 | 28.3 ± 8.3 | 16.9 | 56.9 | 11.7 - 44.9 |
| ALP | IU/ L | 30 | 612.8 ± 123.7 | 380.4 | 904.0 | 365.4 - 860.2 |
| T-Cho | mg/dL | 30 | 56.6 ± 13.0 | 31.4 | 81.2 | 30.6 - 82.6 |
| TG | mg/dL | 30 | 37.3 ± 14.6 | 16.7 | 68.2 | 8.1 - 66.5 |
| T-Bil | mg/dL | 30 | 0.11 ± 0.01 | 0.09 | 0.15 | 0.09 - 0.13 |
| UN | mg/dL | 30 | 15.4 ± 1.8 | 12.4 | 20.6 | 11.8 - 19.0 |
| CRE | mg/dL | 30 | 0.23 ± 0.03 | 0.18 | 0.29 | 0.17 - 0.29 |
| IP | mg/dL | 30 | 8.3 ± 0.7 | 6.5 | 9.5 | 6.9 - 9.7 |
| Ca | mg/dL | 30 | 9.7 ± 0.3 | 9.1 | 10.2 | 9.1 - 10.3 |
| Glu | mg/dL | 30 | 120.3 ± 11.0 | 93.8 | 138.6 | 98.3 - 142.3 |
| Na | mEq/L | 30 | 143.0 ± 1.1 | 140.6 | 144.9 | 140.8 - 145.2 |
| K | mEq/L | 30 | 4.21 ± 0.26 | 3.77 | 4.80 | 3.69 - 4.73 |
| Cl | mEq/L | 30 | 104.8 ± 1.1 | 101.6 | 106.7 | 102.6 - 107.0 |
| TP | g/dL | 30 | 5.54 ± 0.22 | 5.05 | 5.95 | 5.10 - 5.98 |
| A/G | | 30 | 1.09 ± 0.09 | 0.89 | 1.21 | 0.91 - 1.27 |
| alb | % | 30 | 52.1 ± 2.0 | 47.2 | 54.8 | 48.1 - 56.1 |
| $\alpha_1$-glb | % | 30 | 21.0 ± 1.9 | 16.0 | 23.7 | 17.2 - 24.8 |
| $\alpha_2$-glb | % | 30 | 7.3 ± 0.7 | 6.3 | 8.7 | 5.9 - 8.7 |
| β-glb | % | 30 | 15.2 ± 1.2 | 12.7 | 18.0 | 12.8 - 17.6 |
| γ-glb | % | 30 | 4.5 ± 0.9 | 3.2 | 6.8 | 2.7 - 6.3 |
| Alb | g/dL | 30 | 2.88 ± 0.13 | 2.65 | 3.20 | 2.62 - 3.14 |

N: Number of animals.

Hashima Laboratory, Nihon Bioresearch Inc.

Prepared: 2007.08

# Background Data

Crl:CD (SD) Female Rats

Blood chemical findings 10 weeks

| Exam.item | Unit | N | Value Mean ± S.D. | Min. | Max. | Range of 2S.D. |
|---|---|---|---|---|---|---|
| AST | IU/ L | 29 | 77.9 ± 10.6 | 56.5 | 100.8 | 56.7 - 99.1 |
| ALT | IU/ L | 29 | 20.9 ± 2.4 | 15.6 | 25.1 | 16.1 - 25.7 |
| ALP | IU/ L | 29 | 343.8 ± 65.8 | 248.0 | 454.0 | 212.2 - 475.4 |
| T-Cho | mg/dL | 29 | 73.0 ± 15.3 | 51.4 | 119.2 | 42.4 - 103.6 |
| TG | mg/dL | 29 | 23.7 ± 11.5 | 8.1 | 50.2 | 0.7 - 46.7 |
| T-Bil | mg/dL | 29 | 0.13 ± 0.02 | 0.10 | 0.16 | 0.09 - 0.17 |
| UN | mg/dL | 29 | 17.0 ± 2.3 | 12.9 | 21.4 | 12.4 - 21.6 |
| CRE | mg/dL | 29 | 0.27 ± 0.03 | 0.21 | 0.36 | 0.21 - 0.33 |
| IP | mg/dL | 29 | 6.8 ± 1.0 | 4.8 | 8.6 | 4.8 - 8.8 |
| Ca | mg/dL | 29 | 10.0 ± 0.4 | 9.4 | 10.7 | 9.2 - 10.8 |
| Glu | mg/dL | 29 | 107.5 ± 13.0 | 81.6 | 134.4 | 81.5 - 133.5 |
| Na | mEq/L | 29 | 142.8 ± 1.3 | 140.7 | 144.7 | 140.2 - 145.4 |
| K | mEq/L | 29 | 4.09 ± 0.20 | 3.78 | 4.53 | 3.69 - 4.49 |
| Cl | mEq/L | 29 | 106.3 ± 1.6 | 103.3 | 110.4 | 103.1 - 109.5 |
| TP | g/dL | 29 | 5.98 ± 0.29 | 5.38 | 6.66 | 5.40 - 6.56 |
| A/G | | 29 | 1.25 ± 0.11 | 1.03 | 1.45 | 1.03 - 1.47 |
| alb | % | 29 | 55.4 ± 2.1 | 50.8 | 59.2 | 51.2 - 59.6 |
| $\alpha_1$-glb | % | 29 | 18.9 ± 1.6 | 13.8 | 22.5 | 15.7 - 22.1 |
| $\alpha_2$-glb | % | 29 | 6.4 ± 0.8 | 5.3 | 9.3 | 4.8 - 8.0 |
| β-glb | % | 29 | 14.6 ± 1.3 | 12.4 | 17.7 | 12.0 - 17.2 |
| γ-glb | % | 29 | 4.8 ± 1.0 | 3.1 | 7.6 | 2.8 - 6.8 |
| Alb | g/dL | 29 | 3.31 ± 0.25 | 2.90 | 3.94 | 2.81 - 3.81 |

N: Number of animals.

Hashima Laboratory, Nihon Bioresearch Inc.

Prepared: 2007.08

# 信頼性保証陳述書

試験番号 : 502227

表　　題 : 1,8-ジクロロオクタンのラットを用いる28日間反復経口投与毒性試験及び14日間回復試験

当試験が新規化学物質等に係る試験を実施する試験施設に関する基準について (平成 15 年 11 月 21 日，薬食発第 1121003 号，平成 15・11・17 製局第 3 号，環保企発第 031121004 号，平成 20 年 7 月 4 日最終改正) 及び OECD PRINCIPLES OF GOOD LABORATORY PRACTICE (OECD 化学物質の安全性試験の実施に関する基準，1997 年 11 月 26 日) に従って実施され，この最終報告書には試験の方法が正確に記載され，かつ生データが正確に反映されていることを保証する．

(調査の状況は，別紙 1～2 のとおりである．)

2011 年　9 月 13 日

株式会社日本バイオリサーチセンター　羽島研究所

信頼性保証部門責任者 [redacted]

別紙 1

| | 調 査 項 目 | 調査実施日 | 運営管理者及び試験責任者への報告日 |
|---|---|---|---|
| 1. | 試験計画書 | 2008年 8月 19日 | 2008年 8月 20日 |
| 2. | コンピュータプロトコール | 2008年 8月 20日 | 2008年 8月 20日 |
| 3. | 動物の受け入れ | 2008年 8月 20日 | 2008年 8月 20日 |
| 4. | 試験計画書変更書 (No.1) | 2008年 8月 27日 | 2008年 8月 28日 |
| 5. | 被験物質の管理 | 2008年 8月 28日 | 2008年 8月 28日 |
| 6. | 検体の調製 | 2008年 8月 28日 | 2008年 8月 28日 |
| 7. | 群分け及び個体識別 | 2008年 9月 1日 | 2008年 9月 2日 |
| 8. | 投与 | 2008年 9月 2日 | 2008年 9月 2日 |
| 9. | 動物飼育管理 | 2008年 9月 2日 | 2008年 9月 2日 |
| 10. | 体重測定・摂餌量測定・摂水量測定 | 2008年 9月 5日 | 2008年 9月 8日 |
| 11. | 一般状態観察 | 2008年 9月 5日 | 2008年 9月 8日 |
| 12. | 投与 | 2008年 9月 5日 | 2008年 9月 8日 |
| 13. | 行動機能 (FOB) 観察 (投与7日，雄) | 2008年 9月 8日 | 2008年 9月 8日 |
| 14. | 尿検査 (投与期間終了前，雄) | 2008年 9月 24日 ～ 9月 25日 | 2008年 9月 25日 |
| 15. | 自発運動量測定 | 2008年 9月 30日 | 2008年 10月 1日 |
| 16. | 剖検・採血・器官重量測定 (投与期間終了時，雄) | 2008年 9月 30日 | 2008年 10月 1日 |
| 17. | 血液学検査 (血漿分取・測定) [投与期間終了時，雄] | 2008年 9月 30日 | 2008年 10月 1日 |
| 18. | 血液生化学検査 (血清分取・測定・保存用血清の保管) [投与期間終了時，雄] | 2008年 9月 30日 | 2008年 10月 1日 |
| 19. | 感覚反応検査 | 2008年 10月 1日 | 2008年 10月 1日 |
| 20. | 握力測定 | 2008年 10月 1日 | 2008年 10月 1日 |
| 21. | 体重測定・摂餌量測定・摂水量測定 | 2008年 10月 3日 | 2008年 10月 3日 |
| 22. | 一般状態観察 | 2008年 10月 3日 | 2008年 10月 3日 |
| 23. | 動物飼育管理 | 2008年 10月 3日 | 2008年 10月 3日 |
| 24. | 剖検・採血・器官重量測定 (投与期間終了時，雌) | 2008年 10月 3日 | 2008年 10月 3日 |

別紙 2

| 調 査 項 目 | 調査実施日 | 運営管理者及び試験責任者への報告日 |
|---|---|---|
| 25. 尿検査 (回復期間終了前，雄) | 2008年 10月 8日 | 2008年 10月 9日 |
| | ～ 10月 9日 | |
| 26. 剖検・採血・器官重量測定 (回復期間終了時，雄) | 2008年 10月 14日 | 2008年 10月 20日 |
| 27. 標本作製 (病理：切り出し) | 2008年 10月 14日 | 2008年 10月 20日 |
| 28. 剖検・採血・器官重量測定 (回復期間終了時，雌) | 2008年 10月 17日 | 2008年 10月 20日 |
| 29. 血液学検査 (血漿分取・測定) [回復期間終了時，雌] | 2008年 10月 17日 | 2008年 10月 20日 |
| 30. 血液生化学検査 (血清分取・測定・保存用血清の保管) [回復期間終了時，雌] | 2008年 10月 17日 | 2008年 10月 20日 |
| 31. 標本作製 (病理：薄切) | 2008年 12月 12日 | 2008年 12月 15日 |
| 32. 生データ | 2009年 1月 23日 | 2009年 1月 30日 |
| | ～ 1月 27日 | |
| 33. 標本 | 2009年 1月 27日 | 2009年 1月 30日 |
| 34. 最終報告書 (一次案) | 2009年 1月 26日 | 2009年 1月 30日 |
| | ～ 1月 30日 | |
| 35. 生データ (再調査) | 2009年 2月 9日 | 2009年 2月 9日 |
| 36. 最終報告書 (一次案) (再調査) | 2009年 2月 9日 | 2009年 2月 9日 |
| 37. 最終報告書 | 2011年 9月 13日 | 2011年 9月 13日 |