R-1135

原本

最　終　報　告　書

4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験

試験番号：R-1135

試験期間：2013 年 8 月 30 日-2014 年 3 月 28 日

試験施設
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1. GLP 陳述書

試験番号　：　R-1135

試験表題　：　4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施したものであります。

- 「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23・03・29 製局第 6 号、環保企発第 110331010 号）

[redacted]　2014 年 3 月 28 日 [redacted]

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

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3. 試験実施概要

3.1 試験番号

R-1135

3.2 試験表題

4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた経口投与による反復投与毒性･生殖発生毒性併合試験

（Combined repeated dose toxicity study with the reproduction / developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats）

3.3 試験目的

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

3.4 試験委託者

厚生労働省　医薬食品局　審査管理課　化学物質安全対策室

〒100-8916　東京都千代田区霞が関 1-2-2

3.5 試験受託者

株式会社ボゾリサーチセンター

〒151-0065　東京都渋谷区大山町 36-7

3.6 試験実施施設

株式会社ボゾリサーチセンター　御殿場研究所

〒412-0039　静岡県御殿場市かまど 1284

3.7 被験物質

製造者	:	東京化成工業株式会社
名称	:	4-tert-ブチルシクロヘキサン-1-イル=アセタート
CAS 番号	:	32210-23-4
官報公示整理番号	:	(3)-2356（化審法）
入手日	:	2013 年 6 月 20 日

3.8　試験日程

試験開始日　：　2013 年　8 月 30 日
被験物質出庫日　：　2013 年　9 月 19 日
動物入荷日　：　2013 年　9 月　4 日
実験開始日（投与開始日）
　：　2013 年　9 月 24 日
交配開始日　：　2013 年 10 月　8 日
分娩開始日　：　2013 年 10 月 31 日
母動物剖検開始日　：　2013 年 11 月　5 日
投与終了剖検日　：　2013 年 11 月　5 日　（雄及び非交配群）
回復開始日　：　2013 年 11 月　5 日
回復終了剖検日　：　2013 年 11 月 19 日
動物試験終了日　：　2013 年 11 月 19 日
実験終了日（病理組織学検査終了日）
　：　2014 年　1 月 15 日
試験終了日　：　2014 年　3 月 28 日

3.9　試験責任者

株式会社ボゾリサーチセンター　御殿場研究所　研究部
[redacted]

3.10　試験担当者

試験主担当者　：
被験物質保存責任者：

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

[redacted]

3.11　試験成績の信頼性に影響を及ぼしたと思われる環境要因

当該試験の動物飼育室において下記の通り温度許容範囲（20°C~26°C）の上限からの逸脱がみられたが、いずれも短時間で 1°C と軽微な逸脱であり、動物に異常はみられなかったことから、試験成績への影響はないと判断した。

逸脱日	逸脱時刻（時間）	温度最高値
2013 年 9 月 5 日	11:00 頃~12:00 頃（約 1 時間）	27°C
2013 年 10 月 4 日~10 月 5 日	23:30 頃~01:00 頃（約 1 時間 30 分）	27°C
2013 年 10 月 5 日	07:00 頃~07:40 頃（約 40 分）	27°C

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

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

1) 血液学検査において、動物番号3108及び4111のAPTTの初回測定時、機器により凝固時間が短いことに起因するエラーが表示され、測定値が得られなかった。そのため、データ取得時間を拡張させた設定による再測定を実施した。その結果、測定値が得られたため、得られた値を採用した。データ採用の判断はSOPに従ったものであること、対処法及びその記録は適切であることを確認したため、試験結果への影響はないと判断した。
2) 血液化学検査において、測定後の精度管理物質測定時に機器故障と判断されたことで、得られたデータの精度が保証できない状況となった。そのため、全例全項目について代替機による再測定（一部項目は再々測定）を実施し、得られた値を採用した。なお、動物番号4005及び3111に関しては、代替機による再測定時、γ-GTPが他の動物より高値を示したため、確認のため2連で測定を実施した（再々、再々々測定）。その結果、再測定値よりも低値を示し、かつ2連の再現性が良好であったことから再々測定値を採用した。なお、γ-GTPの再々及び再々々測定は、代替機による再測定後、速やかに連続作業として同日に行った。これら一連の作業の精度管理として測定した標準サンプルの測定値は、管理範囲内であり問題ないことを確認した。上記に関し、いずれもデータ採用の判断はSOPに従ったものであること、対処法及びその記録は適切であることを確認したため、試験結果への影響はないと判断した。
3) 動物番号4002、1102、1116、1117、1119、3101、4118の上皮小体が標本上欠落していた。しかし、中用量群及び回復群の3例（1119、3101、4118）の上皮小体は検索対象外であり、検索動物では各群5例中1又は2例であり、病理組織学的評価は可能と判断されたため、試験成績へ及ぼす影響はなかった。
4) 一般状態観察において、対照群の投与開始後25日の観察が、試験計画書の規定（投与直後~30分後）を雄で3分、雌で4分超過して実施された。超過は短時間であり、対照群で一般状態に所見はみられていないことから、試験成績に及ぼす影響はなかった。

その他には本試験に関し、試験の信頼性に影響を及ぼす疑いのある事態及び試験計画書に従わなかったことはなかった。

3.13 資料保存

株式会社ボゾリサーチセンターの保存方法に従い、試験計画書（変更書を含む）原本、記録文書、生データ、報告書類（最終報告書は原本）及び標本（被験物質保存サンプルを含む）は株式会社ボゾリサーチセンター御殿場研究所の資料保存施設に最終

報告書提出後 5 年間保存する。期間終了後の保存については、厚生労働省医薬食品局審査管理課化学物質安全対策室と株式会社ボゾリサーチセンター間で協議し、その処置を決定する。ただし、長期保存に耐えられない生体試料（尿、血漿、血清）及び腟垢標本については、試験終了までに廃棄した。また、死産児、死亡児及び生後 4 日生存児については、出生率及び生後 4 日生存率に被験物質投与の影響が認められなかったため試験終了までに廃棄した。

3.14　試験責任者の記名・なつ印

[redacted]　2014 年 3 月 28 日 [redacted]

4. 要約

4-tert-ブチルシクロヘキサン-1-イル=アセタートをコーン油で溶解し、30、100 及び 300 mg/kg の投与量で Sprague-Dawley 系 SPF ラット（交配群として雌雄各 12 匹/群、雌には非交配群として対照群及び 300 mg/kg 投与群に各 10 匹を追加）の雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（42~51 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 300 mg/kg 投与群の一部の動物（交配群雄 5 匹と非交配群雌 5 匹）については、雄及び非交配群雌ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。なお、対照群には媒体であるコーン油を投与した。

4.1 反復投与毒性

いずれの投与群においても死亡動物はみられなかった。

300 mg/kg 群では、雌雄で自発運動の減少、痙攣及びあるいは流涎が投与期間を通じ散見され、非交配群で投与 1 週に立ち上がり回数の低値、投与 2 週に伸びている姿勢が認められた。雌の交配及び非交配群で投与初期に摂餌量の低値又はその傾向を伴った体重増加抑制が認められ、交配群では妊娠期間中の体重も低値を示した。非交配群雌で赤血球数に低値、平均赤血球容積及び平均赤血球血色素量に高値が認められた。雄と雌の交配及び非交配群で肝臓に、雄及び交配群雌で腎臓に、交配群雌で副腎にいずれも重量高値が認められた。雄で腎臓に尿細管上皮細胞の好酸性小体、再生尿細管の増強、顆粒円柱が、雌の交配及び非交配群で肝臓に小葉中心性肝細胞肥大、副腎に束状帯細胞の空胞増加がみられた。

100 mg/kg 群では、雄で腎臓重量に高値が認められた。雄で腎臓に好酸性小体、再生尿細管の増強がみられ、交配群雌で副腎に束状帯細胞の空胞増加がみられた。

30 mg/kg 群では、雄で腎臓に重量高値及び尿細管上皮細胞の好酸性小体がみられた。

なお、尿細管上皮細胞の好酸性小体は抗 α2μ グロブリン免疫組織化学染色では陽性であった。これら変化のうち、腎臓の再生尿細管を除き、いずれの変化も 14 日間の回復期間により消失し、回復性が認められた。

4.2 生殖発生毒性

100 及び 300 mg/kg 群の各 1 例で哺育行動の低下がみられ、それらの全哺育児が死亡し、300 mg/kg 群で生後 4 日生存率に低値傾向が認められた。その他には、親動物及び児動物の生殖発生に関するいずれの検査においても、被験物質投与による影響は認められなかった。

これらの結果から、本試験条件下において、本被験物質の反復投与毒性に対する無影響量は雄で 30 mg/kg 未満、雌で 30 mg/kg、無毒性量は雌雄とも 30 mg/kg と判断した。また、生殖発生毒性に対する無影響量及び無毒性量は雄親動物でいずれも 300 mg/kg、母動物と児動物ではいずれも 30 mg/kg と判断した。

5. 緒言

厚生労働省医薬食品局審査管理課化学物質安全対策室の委託により、4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験を実施したので、その成績を報告する。

なお、本試験は以下の基準を遵守し、ガイドライン等に準拠して、株式会社ボゾリサーチセンターで実施した。また、本試験は試験実施施設の動物実験委員会の承認（承認番号：G130249）を受けて実施した。

5.1 GLP

- 「新規化学物質等に係る試験を実施する試験施設に関する基準」
  （平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23･03･29 製局第 6 号、環保企発第 110331010 号）

5.2 毒性試験ガイドライン

- 「新規化学物質等に係る試験の方法について」
  （平成 23 年 3 月 31 日：薬食発 0331 第 7 号、平成 23･03･29 製局第 5 号、環保企発第 110331009 号）

5.3 動物の福祉

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

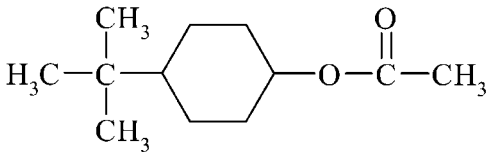
6. 試験材料及び方法

6.1 被験物質及び媒体

6.1.1 被験物質

4-tert-ブチルシクロヘキサン-1-イル=アセタートは理科研株式会社から以下の情報とともに購入した。また、試験開始前に赤外吸収スペクトルの測定により特性が確認されている（試験番号：A-2585、Attached Data 1）。

製造者	:	東京化成工業株式会社
名称	:	4-tert-ブチルシクロヘキサン-1-イル=アセタート
英語名称	:	4-tert-butylcyclohexan-1-yl acetate
製品名	:	酢酸 4-tert-ブチルシクロヘキシル (cis-, trans-混合物)
英語製品名	:	4-tert-Butylcyclohexyl Acetate (cis- and trans-mixture)
CAS 番号	:	32210-23-4
官報公示整理番号	:	(3)-2356（化審法）
構造式又は示性式	:	



分子式	:	$C_{12}H_{22}O_2$
分子量	:	198.31
常温における性状	:	無色透明液体*
沸点/沸騰範囲	:	230°C/3.3kPa*
引火点	:	102°C*
密度	:	0.94*
溶解性	:	不溶；水*
ロット番号	:	AH01
純度（GC）	:	97.4%（異性体合計）
異性体組成	:	異性体構成比は約 7:3 （GC 測定に於いて 4-tert-Butylcyclohexyl Acetate と思われる分子量のピークが 2 つ確認できており、その面積比は 70:30 であるが、どちらのピークが trans 体或いは cis 体であるかは未同定）
不純物	:	不明
比重（20/20）	:	0.9386
屈折率（n20/D）	:	1.4519
保存条件	:	密栓、冷暗所

保存方法　：　気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：3~8°C）に保存した。
保存場所　：　御殿場研究所被験物質保存室、第2研究棟4階被験物質調製室及び生化学部標準物質保存場所
取扱い上の注意　：　作業場の換気を十分に行い、マスク、保護眼鏡、保護手袋等の適切な保護具を着用し、直接の接触を防ぐ。取り扱い後は、手、顔等を良く洗い、うがいをする。
安定性　：　投与期間終了後に株式会社ボゾリサーチセンター御殿場研究所において、残余被験物質の赤外吸収スペクトルを確認した結果、実験実施前に確認した参照スペクトルとほぼ同様であり安定性に問題はなかった（Attached Data 2）。
被験物質残余の処理：　被験物質5 gを保存試料として御殿場研究所の資料保存施設に保存した。動物試験及び分析終了後の残量は全て焼却処分した。

*：製造元の東京化成工業株式会社発行の製品安全データシートに基づく

6.1.2　媒体

名称　：　コーン油
規格　：　生化学用
製造者　：　和光純薬工業株式会社
ロット番号（有効期限）
：　WEK6144（2017年12月24日）、
PDQ0071（2018年8月7日、2018年10月8日）
保存方法　：　室温
保存場所　：　御殿場研究所第2研究棟4階被験物質調製室

なお、媒体については、本試験に先立って実施した被験液中濃度測定法バリデーション及び安定性試験（試験番号：A-2585）[1]において、コーン油中での被験物質の安定性に良好な結果が得られていることから、コーン油を選択した。

6.2　投与液の調製及び保存方法

6.2.1　対照群投与液の採取

対照群投与液として、被験液調製当日の被験物質を取り扱う前に必要量のコーン油を1日使用分ずつ、褐色ガラス瓶に貼付したラベルを確認しながら分注した。

6.2.2　被験液の調製

濃度ごとに必要量の被験物質をガラスシリンジで採り、ビーカーに正確に秤取した。秤取した被験物質をメスシリンダーに移すとともに、ビーカーを少量の媒体で数回洗

い、その液もメスシリンダーに加えた。手で振り攪拌して混合し、完全に溶解したことを目視により確認した。更に媒体をメスシリンダーに加え規定量にメスアップし、6、20 及び 60 mg/mL 液（低、中及び高用量群投与液）を調製した。調製は 7 日に 1 回以上の頻度で最大 7 日分を一括して行った。残液はポリ瓶に回収又はペーパータオル等に吸着させて焼却処分した。

6.2.3 投与液の保存

対照群投与液及び被験液は褐色ガラス瓶に入れ、冷所（冷蔵庫内、許容値：1~10°C、実測値：3~6°C）に保存し、安定性の確認された範囲内で投与に使用した。

6.2.4 被験液の安定性

本被験物質の 1.00 及び 200 mg/mL濃度の被験液（媒体：コーン油）は、褐色ガラス瓶に入れ冷所（冷蔵庫内、許容値：1~10°C）で 8 日間保存後、更に室温下（許容値：1~30°C）で 24 時間保存（冷所 8 日間 + 室温 24 時間）したときに安定であることが試験施設で確認されている（試験番号：A-2585、Attached Data 3） [1]。

6.2.5 被験液の濃度確認

初回投与及び投与 6 週の投与に使用する各濃度の被験液（各 10 mL採取）について、株式会社ボゾリサーチセンター御殿場研究所でGCにより濃度確認を実施した。なお、初回投与に使用する被験液については、投与開始前に確認を行った。その結果、各濃度液における表示値に対する被験物質の割合は 99.8~105.2%であり（Attached Data 4、5）、いずれも許容範囲内（濃度：表示値に対する割合；100.0±10.0%）であったことから、被験液の調製に問題はなかったと考えられた。なお、GCを用いた被験液中濃度測定法バリデーションは株式会社ボゾリサーチセンター御殿場研究所（試験番号：A-2585） [1]で実施された。分析法の概略を以下に示した。

[標準物質]

被験物質から一部分配したものを用いた。

名称	:	4-tert-ブチルシクロヘキサン-1-イル=アセタート
ロット番号	:	AH01
保存条件	:	密栓、冷暗所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：3~8°C）に保存した。
保存場所	:	御殿場研究所　被験物質保存室及び生化学部標準物質保存場所

[測定実測試料の調製]

測定試料を転倒混和した後、任意の場所から n=3 で採取し、以下の表に示すように、アセトンで希釈した測定実測試料を用時調製した。

測定試料濃度 (mg/mL)	1 次希釈		2 次希釈		希釈率
	採取量 (mL)	定容量 (mL)	1 次希釈液 採取量 (mL)	定容量 (mL)	
6	1	30	2.5	10	120
20	1	50	2.5	20	400
60	1	100	2.5	30	1200

溶媒：アセトン

[GC システム]

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

[GC 測定条件]

カラム : DB-5（0.53 mm I.D.×25 m、膜厚 5 μm、Agilent Technologies Inc.）
キャリアガス : He
流量モード : コンスタントフローモード
流量 : 5.0 mL/min
注入口 : スプリット注入口
スプリット比 : 5:1
注入口温度 : 250°C
検出器 : Flame ionization detector（FID）
検出器温度 : 250°C
H_2 流量 : 45 mL/min
Air 流量 : 450 mL/min
メイクアップガス（N_2）流量 : 39 mL/min
オーブン温度 : 170°C（Hold 0 分）→250°C（10°C/min、Hold 2 分）
注入量 : 1 μL

6.3 試験動物種及び系統の選択理由

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

6.4　試験動物

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、筑波飼育センター〕の雄 62 匹及び雌 83 匹をそれぞれ 8 週齢で入手[注)]し、入荷日を馴化 1 日と起算して、3 日間の検疫期間を含む 20 日間の馴化飼育を行った。その間、一般状態の観察（1 回/日）、体重測定（馴化 1、3、9、16 及び 20 日の 5 回）、詳細な一般状態の観察（群分け 5 日前の馴化 15 日に 1 回）を実施した。更に、雄について馴化終了日に陰嚢内の精巣の触診及び陰茎亀頭の観察を実施し、雌については腟垢を検疫期間終了後群分け日まで採取して性周期（検疫期間終了後 14 日間）を調べた。その結果、性周期の異常が 3 例（耳標番号：90、93、143）にみられた。馴化 5 日に雄 1 例（耳標番号：35）が死亡したが、一般状態、体重推移及び剖検（感染症を疑う変化を含め）には異常はみられず、死因は明らかでなかった。それらの異常例を除き、検疫・馴化期間中の一般状態、詳細な一般状態、体重推移、精巣の触診結果及び性周期に異常がなく、性成熟に達した陰茎亀頭であり、健康と思われる雄 61 匹中 48 匹及び雌 80 匹中 68 匹を選択し、10 週齢で投与に使用した。投与開始時の体重の変動範囲は雄で 397~456 g（平均体重：419 g）、雌は 237~290 g（平均体重：262 g）であり、雌雄それぞれ平均体重の±20%以内であった。

なお、動物は検疫・馴化期間中の体重増加量（入荷日~群分け時）により選別後、群分け当日（投与開始の前日）の体重に基づいて、非交配群も含め各群の平均体重ができるだけ均等となるよう各群に割付けた。個体の割付けはコンピュータを用いたブロック配置法及び無作為抽出法の組み合わせ（ブロック配置法で必要な群を構成し、試験群及び群内の個体番号を無作為に割当てた）により行った。供試個体の選択条件を満たして余剰となった雌は交配予備動物として継続飼育したが、使用しなかったため、交配予備動物は全て交配終了後に試験から除外した。その他の雌雄残余動物は群分け当日に試験から除外した。なお、試験から除外された動物は、有効利用を目的として動物管理責任者に移管した（移管日：2013 年 9 月 23 日及び 10 月 21 日）。

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

6.5　飼育条件

動物は、温度 23±3°C（実測値：21~27°C）、相対湿度 50±20%（実測値：37~65%）、換気回数 10~15 回/h、照明 12 時間/日（07:00~19:00）の動物飼育室（飼育室番号：909 号室）でブラケット式金属製網ケージ（W254×D350×H170 mm：リードエンジニアリング株式会社）に交配中を除いて個別に収容した。なお、妊娠 17 日から授乳 4 日までは、床敷（ホワイトフレーク：日本チャールス・リバー株式会社、ロット番号：2013-2）を入れたプラスチック製エコンケージ（W340×D400×H185 mm：日本クレア株式会社）に 1 腹単位で収容した。

飼料は NMF 固形（放射線滅菌、オリエンタル酵母工業株式会社、ロット番号：130523、130619、130718、130822）をステンレス製給餌器により自由に摂取させた。

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

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

6.6 動物の識別

動物は番号（雄：1~62、雌：63~145）が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000 の位は群（対照群、低、中及び高用量の順）、100 の位は性別（0 番を雄、1 番を雌）、10 と 1 の位は個体番号を示す 4 桁の動物番号を設定した。各飼育ケージに投与量（群）ごとに色分けしたケージラベルをつけ、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日（雄及び非交配群の雌）、交尾成立日（交配群の雌雄）及び分娩日（交配群の雌）を明記した。

6.7 投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間は、投与日数として、交配群雌雄ともに交配前 14 日、更に、雄については交配開始後 28 日（計 42 日）、雌については交配期間及び妊娠期間を通して授乳 4 日まで（計 42~51 日）とした。非交配群の雌については 42 日とした。回復動物については、42 日の投与期間が終了した後、被験物質投与に起因した変化の可逆性、持続性並びに遅発性毒性等について観察するため、14 日間の回復期間を設けた。投与回数は反復投与試験で一般的に行われている 1 日 1 回とした。

6.8 投与方法

投与方法は、げっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は 5 mL/kg 体重とし、胃ゾンデを用いて投与液を 08:11~11:56 の間に投与した。ただし、投与時に分娩中であった動物は分娩終了を待って、14:31~14:58 の間に投与した。対照群には媒体のみを同様に投与した。個体ごとの投与液量（表示単位：0.1 mL）は、直近の体重を基準に算出した。

6.9 投与量及び群構成

投与量は 30、100 及び 300 mg/kg の 3 用量とし、試験群はこれらの用量群に媒体を投与する対照群を加え 4 群構成とした。1 群当たりの動物数は交配を行う交配群として各群で雌雄各 12 匹、交配しない非交配群として対照群及び高用量群で雌各 10 匹と

した。なお、対照群及び高用量群における雄の群内番号 8 番以降、非交配群雌の群内番号 18 番以降の各 5 匹は、最終投与終了日以降、回復動物とした。群構成を表 1-1.及び 1-2.に示した。

表 1-1.群構成（雄）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群	
				動物数	動物番号
対照群	0	0	5	12	1001~1012 注1
低用量群	30	6	5	12	2001~2012
中用量群	100	20	5	12	3001~3012
高用量群	300	60	5	12	4001~4012 注1

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

表 1-2.群構成（雌）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群		非交配群	
				動物数	動物番号	動物数	動物番号
対照群	0	0	5	12	1101~1112	10	1113~1122 注2
低用量群	30	6	5	12	2101~2112	−	−
中用量群	100	20	5	12	3101~3112	−	−
高用量群	300	60	5	12	4101~4112	10	4113~4122 注2

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

6.10　投与量の設定根拠

本試験の投与量は、先に実施した「4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）、株式会社ボゾリサーチセンター、試験番号：N-R042、投与量：250、500 及び 1000 mg/kg/day」[2]の結果（Attached Data 6）を参考に設定した。1000 mg/kg投与群では、雌 1/5 例が痙攣、自発運動の減少、軟便、呼吸数減少、被毛の汚染（口腔周囲及び下腹部）、糞量の減少、腹臥/横臥、摂餌量の低値及び体重減少を呈し、投与 5 日に死亡した。剖検では被毛の汚染、脾臓及び胸腺の小型化がみられた。生存例では、雌雄で痙攣、自発運動の減少、糞量減少、下腹部被毛の汚れがみられ、雌雄で投与 4 日に一過性の摂餌量低値を伴った体重減少が、雄で以降も体重増加抑制が認められた。雄で総コレステロール及び尿素窒素の高値、雌で尿素窒素の低値、雌雄で肝臓及び副腎重量の高値、胸腺重量の低値、雄で腎臓重量の高値が認められた。500 mg/kg投与群では、雌雄で投与 4 日に一過性の摂餌量の低値を伴った体重減少又は低値傾向、雌で尿素窒素の低値、雌雄で肝臓重量の高値が認められた。250 mg/kg投与群では、雌で痙攣及び雌雄で肝臓重量の高値が認められた。したがって、反復投与毒性･生殖発生毒性併合試験の投与期間は投与量設定試験の 3 倍以上になること、当該試験が生殖発生毒性試験との併合試験であることを考慮し、本試験では全体の毒性プロファイルを把握するため、またNOAELを求めるため、明らかな毒性徴候の発現が予測される 300 mg/kgを高用量とし、以下公比約 3 で除して 100 及び 30 mg/kgをそれぞれ中及び低用量に設定した。

6.11　観察及び検査の方法

試験日の起算は、投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与 42 日の翌日）を回復 1 日、回復 1 日から 7 日を回復 1 週、交尾成立日を妊娠 0 日、分娩終了日（出産日）を授乳 0 日、出生日を生後 0 日とし、以下に示す項目について、それぞれ記載の時期に観察及び検査を実施した。

6.11.1　一般状態の観察

全個体について、投与期間中は毎日 3 回（投与前、投与直後~30 分後及び投与 1~3 時間後）、回復期間中は毎日 2 回（午前・午後）、剖検日は 1 回（午前）、それぞれ生死、身体の外観、姿勢、行動及び排泄物（尿、糞）などの一般状態における異常の有無を観察した。なお、投与 2 日以降の動物のハンドリングを伴った定期的な観察は、詳細な一般状態の観察と兼ねて行った。

6.11.2　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について行った。雄及び非交配群は投与期間中及び回復期間中毎週 1 回、交配群雌は交配前投与期間中毎週 1 回、交配期間中、妊娠期間中及び授乳期間中は指定された日（交尾動物は妊娠 1、7、14 及び 20 日、未交尾動物は交配開始後 6 日、分娩動物は授乳 4 日）にそれぞれ行った。

機能検査、握力測定及び自発運動量測定は、各群の 5 匹（雄の群内番号 8~12 番、交配群雌の各群の分娩順で動物番号が若い順[注]、非交配群の群内番号 18~22 番）について行った。投与期間中は交配群の雌で授乳 4 日（投与 42~43 日）に、その他は投与期間終了週（投与 6 週、投与 37 日）に、回復期間中は対照群及び高用量群の雌雄で回復期間終了週（回復 2 週、雌雄ともに回復 9 日）に行った。

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

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1101、1102、1106、1108、1112
低用量群	2101、2102、2103、2104、2108
中用量群	3101、3102、3103、3104、3108
高用量群	4101、4103、4104、4109、4110

1)　詳細な一般状態の観察

ケージ内観察は姿勢、痙攣、異常行動を、手に持っての観察はケージからの取り出し易さ、被毛・皮膚の状態、眼・鼻の分泌物、眼球突出、眼瞼閉鎖状態、可視粘膜、自律神経機能（流涙、流涎、立毛、瞳孔径、異常呼吸）、ハンドリングに対する反応、

ハンドリング時の発声を、オープンフィールド内観察は覚醒状態、痙攣、異常行動、常同行動、歩行、姿勢、身繕い、立ち上がり回数、排泄物（排糞数、排尿）を調べた。

2) 機能検査

検査は聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射、空中正向反射、着地開脚幅とした。

3) 握力測定

機能検査に引き続き、CPU ゲージ MODEL-RX-5（アイコーエンジニアリング株式会社）を用いて前肢及び後肢の握力を測定した。

4) 自発運動量の測定

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

6.11.3 体重測定

全個体について、交配群の雄及び非交配群の雌は投与 1、8、15、22、29、36、42 日及び剖検日に、回復動物は更に回復 1、8、14 日及び剖検日に、交配群の雌は投与 1、8、15 及び 22 日、妊娠 0、7、14 及び 20 日、授乳 0 及び 4 日並びに剖検日に体重を測定した。なお、午後の分娩観察時に分娩の終了が確認された個体の授乳 0 日の体重測定（13:50~16:38 の間）を除き、体重測定は測定日の 07:55~10:53 の間（投与期間中は投与前）に行った。剖検日には、前日から約 16 時間絶食させた後、相対器官重量算出に備えて体重を 07:17~08:54 の間に測定した。また、授乳期間中に全哺育児が死亡した母動物については、搬出前に体重を測定したが統計解析からは除外した。

6.11.4 摂餌量測定

全個体について、交配群の雄及び非交配群の雌は投与 2、8、15、30、36 及び 42 日に、回復動物は更に回復 2、8 及び 14 日に、交配群の雌は投与 2、8 及び 15 日、妊娠 1、7、14 及び 20 日並びに授乳 2 及び 4 日に残餌量を測定し、前日の給餌量との差から 1 匹当たりの 1 日摂餌量を算出した。給餌量及び残餌量の測定は測定日の 07:53~11:10 の間（投与期間中は投与前）に行った。

6.11.5 腟垢検査

投与期間中は交配群の雌の全個体について、投与開始日から交尾成立まで毎日（午前）腟垢を採取し、交配前投与期間中の標本について多数の角化上皮細胞から成る腟垢像を発情の指標とし、発情回数及び発情期から次の発情期までの日数（性周期）、観察雌個体数に対する性周期異常を示した個体数の割合を調べた。交配期間中は腟垢内の精子の有無を調べるのに加え腟垢像を発情前期(P)、発情期(E)、発情後期(M)及び発情休止期(D)に分類したが、データは参考とした。

なお、P→E→M→D（→P）の順序で周期的変化を示し、4 又は 5 日の周期を繰り返

す個体を正常、それ以外を性周期異常とした。

6.11.6　交配方法

交配前投与期間終了後、交配群の同投与群内の雌雄を 1:1 で終夜同居させ、翌朝、腟栓形成あるいは腟垢中に精子を確認したものを交尾成立とみなした。交配開始日を 0 日と起算して交尾までに要した日数を求めた。同一雌雄による同居期間は最長 7 日間であった。

6.11.7　分娩及び哺育観察

1)　母動物の観察

交尾成立雌動物は、妊娠 21 日から妊娠 23 日の午前まで 1 日 2 回（午前・午後、妊娠 23 日は午前に 1 回）、分娩の有無並びにその終了を確認するとともに分娩状態（胎盤の処理及び出産児の状態）を観察した。交尾成立から分娩終了までを妊娠期間とし、妊娠期間を 0.5 日単位で求めた。ただし、1 日単位で集計した。なお、分娩終了の確認は 17:00 までとした。

分娩が終了した母動物は授乳 4 日まで出生児を哺育させ、児集め、営巣及び授乳を指標として哺育状態を観察し、授乳 5 日に病理学検査に供した。なお、授乳期間中に全哺育児が死亡した母動物（動物番号 3111 及び 4111）は、その時点で、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、病理学検査に供した。

2)　出生児の観察

生後 0 日に出生児数及び死産児数を数え、合わせて出産児数とした。出産児は口腔内を含む外表異常[注)]の有無を肉眼的に観察して性別を確認した。出生児は体重を個体別に測定した後、母動物に哺育させた。死産児はブアン液で固定して保存した。

生後 4 日まで毎日 1 回、死亡児の有無を確認した。死亡児は肉眼による異常の有無を観察した後、ブアン液で固定して保存した。生後 4 日に全生存児の性別を確認し、個体別に体重を測定した。口腔内を含む外表異常の有無を肉眼的に観察した後、イソフルラン深麻酔下でブアン液に浸漬し、固定して保存した。

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

6.11.8　尿検査（摂水量測定を含む）

投与期間終了週（投与 6 週、投与 39~40 日）及び回復期間終了週（回復 2 週、回復 11~12 日）に検査を実施した。投与期間中は検査当日の投与後に各群の 5 匹（雄の群内番号 8~12 番、非交配群の群内番号 18~22 番）について、回復期間中は回復動物の全個体について、それぞれ採尿器をセットしたケージに収容し、絶食・自由摂水下で 4 時間尿を、次いで自由摂食・自由摂水下でその後の 20 時間尿を採取した。検査項目を表 2.に示した。採取した最初の 4 時間尿について pH 以下沈渣までの検査と尿量を、その後に得られた 20 時間尿について浸透圧、電解質（ナトリウム、カリウム及び塩素）及び尿量の測定を行った。尿量は 4 時間の尿量と 20 時間の尿量を合計して 1 日量を算出した。電解質は 20 時間尿について濃度を測定し、測定濃度と 24 時間の尿量から 1 日当たりの排泄量を算出した。摂水量は、採尿器をセットしたケージに収容した状態で前日からの 1 日の摂取量を、給水瓶を用いて測定した。

表 2.尿検査の項目、測定法及び使用機器など

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

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

6.11.9　血液学検査

全例について、剖検前日（最終投与日あるいは回復 14 日）から一夜（16~19 時間）絶食させた。そのうちの各群雌雄各 5 匹（動物番号が若い順、ただし、交配群雌は分娩順の 5 匹注）について、イソフルラン麻酔下に開腹し、腹大動脈から EDTA-2K 加採血瓶（SB-41：シスメックス株式会社）に血液を採取した。得られた血液について、次の表 3.-1)に記載した項目及び方法により検査した。なお、採血した全例について、May-Grünwald-Giemsa 染色法による血液塗抹標本を作製した。また、3.8%クエン酸ナトリウム溶液加試験管（血液 9 容に対し 1 容の割合）に採取した血液を遠心分離（3,000 rpm、1,600×g、10 分間）し、得られた血漿について表 3.-2)に記載の項目及び方法により検査した。授乳期間中に全哺育児が死亡した母動物についても採血し同様に検査したが、その成績は統計解析から除外した。

注：交配群雌の検査対象動物を以下に示した。

試験群	動物番号
対照群	1101、1102、1106、1108、1112
低用量群	2101、2102、2103、2104、2108
中用量群	3101、3102、3103、3104、3108
高用量群	4101、4103、4104、4109、4110

表 3.血液学検査の項目、測定法及び使用機器など

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

6.11.10　血液化学検査

血液学検査用試料と同時に採取した血液を凝固促進剤入り試験管（ベノジェクト II-オートセップ：テルモ株式会社）に採り、遠心分離（3,000 rpm、1,670×g、10 分間）し、得られた血清について表 4.-1)に記載の項目及び方法により検査した。また、ヘパリン加試験管（血液 1 mL 当たり約 20 単位のヘパリン）に採取した血液を遠心分離（3,000 rpm、1,600×g、10 分間）して得られた血漿について表 4.-2)に記載の項目及び方法により検査した。授乳期間中に全哺育児が死亡した母動物についても同様に検査したが、その成績は統計解析から除外した。血清の一部（授乳期間中に全哺育児が死亡した母動物を除く）は血中ホルモン測定に備え、約 0.5 mL×3 本をサンプルチューブに分注し、−80°C の冷凍庫（許容範囲：−70°C 以下）に保存した。

表 4.血液化学検査の項目、測定法及び使用機器など

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

6.11.11　血中ホルモン測定

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

6.11.12　病理学検査

1)　剖検及び器官重量測定

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

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

2)　病理組織学検査

全ての個体について、以下に示す全検査対象器官/組織をリン酸緩衝 10 vol%ホルマリン液で固定し、保存した。固定時に肺にはリン酸緩衝 10 vol%ホルマリン液を注入した。ただし、眼球、視神経はリン酸緩衝液で調製した 3 vol%グルタルアルデヒド・2.5 vol%ホルマリン液で固定後、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10 vol%ホルマリン液に置換し保存した。次いで、投与終了時及び回復終了時の計画剖検時に採血を実施した各群雌雄各 5 匹（動物番号が若い順、ただし、交配群雌は分娩順の 5 匹）、授乳期間中に全哺育児が死亡した母動物についてパラフィン包埋した後、切片とし（下線を施した器官・組織は固定・保存のみとした）、ヘマトキシリン・エオジン（H・E）染色標本を作製した。鏡検は、まず投与終了時剖検群における対照群及び高用量群の採血を行った動物、並びに授乳期間中に全哺育児が死亡した母動物の全検査対象器官/組織について行った。両側性の器官については両側を摘出し、坐骨神経、眼球、甲状腺、上皮小体、副腎、顎下腺、腎臓、乳腺（鼠径部）、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、精巣、卵巣、精巣上体及び精嚢（凝固腺含む）は両側並びに子宮は両角部を鏡検した。また、H・E 染色標本による観察の結果、高用量群の雄の腎臓で尿細管上皮細胞に好酸性小体が観察されたため、代表例（動物番号 4001 及び 4002）の腎臓について、抗 α2μ グロブリン抗体を用いた免疫組織化学染色標本を作製し鏡検した。なお、舌下腺、視神経及び皮膚（鼠径部）は H･E 染色標本作製までとし、病理組織学検査は実施しなかった。その結果、高用量群の雄の腎臓、雌の副腎及び肝臓に被験物質投与による影響が疑われたため、中及び低用量群並びに回復終了時剖検群の当該組織について鏡検した。

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

6.12 統計解析

6.12.1 パラメータの算出

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

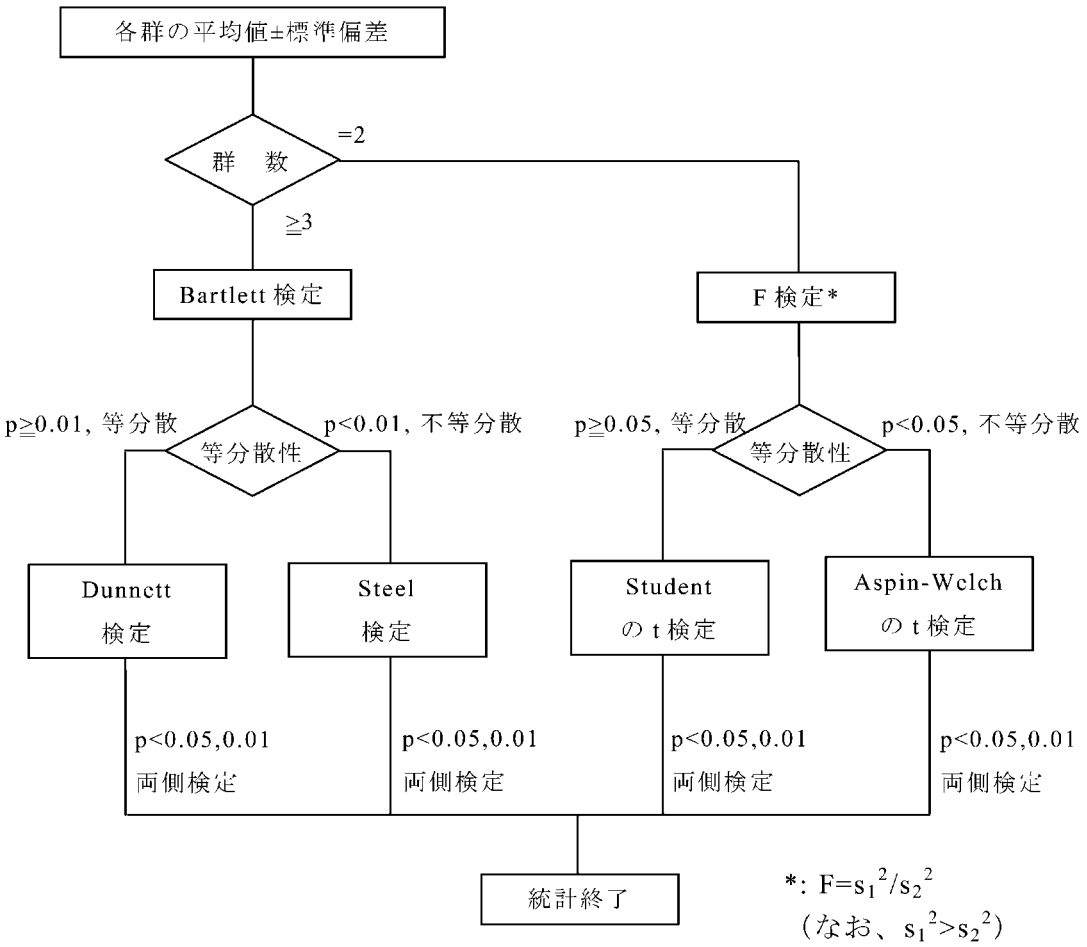
性周期異常率(%) =（性周期異常を示した個体数/観察雌個体数）×100
交尾率(%) =（交尾動物数/同居動物数）×100
授精率(%) =（雌を妊娠させた雄の数/交尾した雄の数）×100
受胎率(%) =（妊娠した雌の数/交尾した雌の数）×100
出産率(%) =（出生児出産雌数/妊娠雌数）×100
妊娠期間(日) = 妊娠 0 日から分娩した日までの日数
着床率(%) =（着床痕数/黄体数）×100
分娩率(%) =（出産児数/着床痕数）×100
死産児率(%) =（死産児数/出産児数）×100
外表異常率(%) =（外表異常児数/出産児数）×100
出生率(%) =（出生児数/出産児数）×100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

6.12.2 検定

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

体重、体重増加量（雄及び非交配群雌：投与 1~42 日及び回復 1~14 日、交配群雌：投与 1~15 日、妊娠 0~20 日及び授乳 0~4 日、出生児：生後 0~4 日）、摂餌量、摂水量、発情期像発現回数、性周期（発情周期）、交尾までに要した日数、妊娠期間、黄体数、着床痕数、生存児数、性比（生後 0 及び 4 日）、オープンフィールド内観察（排糞数、立ち上がり回数）、機能検査（着地開脚幅）、握力及び自発運動量、尿検査の定量的

項目、血液学検査、血液化学検査及び器官重量（含、剖検時体重）は、群ごとに平均値及び標準偏差を求め、次に示す模式図の方法に従って検定した [3] [4] [5]。



着床率、分娩率、死産児率、外表異常率、出生率及び生後 4 日生存率については、群ごとに平均値及び標準偏差を求め、Wilcoxonの順位和検定（有意水準 0.05 及び 0.01、両側）を行った [6]。

性周期異常率、交尾率、授精率、受胎率及び出産率並びに聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射の各反応・反射率は、各群の性周期異常を示した個体数、交尾動物数、雌を妊娠させた雄動物数、妊娠雌動物数、出生児出産雌動物数、正常反射のみられた動物数より算出し、期待度数が 5 以下のセルがみられたためFisherの直接確率計算法により検定（有意水準 0.05 及び 0.01、両側）を行った [7]。

7. 試験結果

7.1 一般状態（Table 1-1~1-11、Appendix 1-1~1-34）

1) 投与期間

いずれの投与群においても死亡動物はみられなかった。

雄では、300 mg/kg 投与群で自発運動の減少が投与 3 日に 1 例でみられ、投与 11 日以降は 1~3 例に散見された。また、痙攣が投与 12 日以降に 1~3 例で、流涎が投与 15 日以降に 1~4 例で散見された。100 mg/kg 以下の投与群では、いずれの動物にも投与期間を通じて異常はみられなかった。

交配群雌では、300 mg/kg 投与群で自発運動の減少が投与 1 日に 4 例でみられ、以降は交配前、妊娠及び授乳期間中、1 例に散見された。また、痙攣が投与 3 日に 1 例で、投与 7 日以降、交配前、妊娠及び授乳の各期間に 1~7 例でみられ、流涎が妊娠 2、8、15~17 日に 1~2 例でみられた。その他、切歯破損が授乳 2~4 日に 1 例（動物番号 4111）でみられたが、発現頻度から偶発性と判断した。なお、本例では授乳 1 日から哺育行動の低下がみられ、授乳 4 日までに全哺育児が死亡した。100 mg/kg 投与群の 1 例（動物番号 3111）で授乳 1 日に哺育行動の低下がみられ、授乳 2 日までに全哺育児が死亡した。100 mg/kg 以下の投与群では、全哺育児死亡母動物を除きいずれの動物にも投与期間を通じて異常はみられなかった。

非交配群雌では、300 mg/kg 投与群で自発運動の減少が投与 1 日に 2 例でみられ、以降は投与 8 日に 6 例でみられた他には投与 32 日までの間、1~2 例で散見された。また、痙攣が投与 2 日に 1 例で、投与 7 日以降、投与期間を通じ 1~5 例でみられ、流涎が投与 16~27 日に 1 例で散見された。

2) 回復期間

いずれの動物にも異常はみられなかった。

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

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

1) 投与期間

雄では、いずれの動物にも異常はみられなかった。

交配群雌では、300 mg/kg 投与群で痙攣が妊娠 7 日に 2 例でみられた。

非交配群雌では、300 mg/kg 投与群で伸びている姿勢が投与 2 週に 1 例でみられた。

2) 回復期間

いずれの動物にも異常はみられなかった。

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

いずれの動物にも投与期間及び回復期間とも被験物質投与に関連すると考えられる異常はみられなかった。

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

1) 投与期間

雄及び交配群雌では、いずれの動物にも被験物質投与に関連すると考えられる異常はみられなかった。なお、非交配群雌の 300 mg/kg 投与群で投与 1 週の立ち上がり回数に対照群と比べ有意な低値が認められた。また、排糞の個数には対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間

いずれの動物にも被験物質投与に関連すると考えられる異常はみられず、立ち上がり回数及び排糞の個数には対照群と 300 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間終了週検査

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

2) 回復期間終了週検査

いずれの動物にも聴覚反応、接近反応、接触反応、痛覚反応、瞳孔反射及び空中正向反射に異常はみられず、着地開脚幅には対照群と 300 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

300 mg/kg 投与群の雄では対照群と比べ前肢の握力に有意な低値が認められたが、前肢のみの変化であり、投与期間終了週測定に異常はみられていないことから、毒性学的意義はないと判断した。

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

1) 投与期間終了週測定

いずれの投与群にも被験物質投与に関連すると考えられる変化はみられなかった。

なお、30 mg/kg 投与群の雄で 50-60 分の間の運動量に対照群と比べ有意な低値が認められたが、用量と関連しない偶発的な有意差と判断した。

2) 回復期間終了週測定

300 mg/kg 投与群の雌雄とも対照群との間に有意差は認められなかった。

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

1)　投与期間

雄では、各被験物質投与群ともに投与期間を通じて対照群と同様な体重推移を示し、有意差は認められなかった。

交配群雌では、300 mg/kg 投与群で投与期間を通じ対照群を下回って推移し、交配前投与期間中の体重増加量、妊娠 7 及び 20 日の体重に対照群と比べ有意な低値が認められた。30 及び 100mg/kg 投与群ともに交配前、妊娠及び授乳の各期間中、対照群と同様な体重推移を示し、有意差は認められなかった。

非交配群雌では、300 mg/kg 投与群で投与期間を通じ対照群を下回って推移し、投与期間中の体重増加量に対照群と比べ有意な低値が認められた。

2)　回復期間

300 mg/kg 投与群の雌雄とも対照群との間に有意差は認められなかった。

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

1)　投与期間

雄では、30 mg/kg 投与群で投与 36 日の摂餌量に対照群と比べ有意な低値が認められたが、用量に依存性のない変化であった。その他各被験物質投与群ともに投与期間を通じて対照群と同様な摂餌量を示し、有意差は認められなかった。

交配群雌では、300 mg/kg 投与群で投与 2 日の摂餌量に対照群と比べ有意な低値が認められた。

非交配群雌では、投与期間中、対照群を下回る傾向を示したが、有意差は認められなかった。

2)　回復期間

300 mg/kg 投与群の雄では、対照群との間に有意差は認められなかった。

300 mg/kg 投与群の雌では、回復 2 及び 8 日の摂餌量に対照群と比べ有意な高値が認められた。

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

1)　投与期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

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

2)　回復期間終了週検査

定性項目については、いずれの動物にも異常はみられなかった。

定量項目については、いずれの検査項目においても 300 mg/kg 投与群と対照群との間に有意差は認められなかった。

7.6　血液学検査（Table 6-1~6-10、Appendix 6-1~6-28）

1)　投与期間終了時検査

雄では、100 mg/kg 投与群で白血球数に対照群と比べ有意な高値が認められたが、用量に依存性のない変化であった。その他いずれの検査項目においても各被験物質投与群と対照群との間に有意差は認められなかった。

交配群雌では、30 及び 100 mg/kg 投与群で血小板数に対照群と比べ有意な低値が認められたが、用量に依存性のない変化であった。その他いずれの検査項目においても各被験物質投与群と対照群との間に有意差は認められなかった。

非交配群雌では、300 mg/kg 投与群で対照群と比べ赤血球数に有意な低値、平均赤血球容積及び平均赤血球血色素量に有意な高値が認められた。

2)　回復期間終了時検査

300 mg/kg 投与群の雄では、対照群と比べ平均赤血球容積に有意な高値が認められたが、4%の軽微な変化であり、投与期間終了時検査には異常がなく、その他の赤血球パラメータに変動はないことから偶発性と判断した。

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

7.7　血液化学検査（Table 7-1~7-10、Appendix 7-1~7-28）

1)　投与期間終了時検査

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

交配群雌では、100 mg/kg 投与群で対照群と比べトリグリセリドに有意な高値が認められたが、用量に依存性のない変化であった。

非交配群雌では、300 mg/kg 投与群で対照群と比べグルコースに有意な低値、カリウムに有意な高値、塩素に有意な低値が認められたが、いずれも個体値は試験施設の背景データ（グルコース：133±26、カリウム：4.3±0.6、塩素：109±4、Mean±2S.D.、N=65、2009/04-2014/03）のほぼ範囲内であることから生理的変動範囲内の偶発的有意差と判断した。

2)　回復期間終了時検査

300 mg/kg 投与群の雄では、対照群と比べ総コレステロール及びリン脂質に有意な高値が認められたが、投与期間終了時検査には異常がなく、いずれも個体値は試験施設の背景データ（総コレステロール：52±28、リン脂質：85±30、Mean±2S.D.、N=65、2009/04-2014/03）の範囲内であることから生理的変動範囲内の偶発的有意差と判断した。

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

7.8　器官重量（Table 8-1~8-10、Appendix 8-1~8-48）

1)　投与期間終了時検査

被験物質投与との関連性が疑われる変化が肝臓、腎臓及び副腎に認められた。

肝臓　:　300 mg/kg 投与群の雄、交配群雌及び非交配群雌で対照群と比べ相対重量に有意な高値が認められた。

腎臓　:　雄の 30 mg/kg 投与群で絶対重量に、100 及び 300 mg/kg 投与群で絶対及び相対重量に、交配群雌の 300 mg/kg 投与群で相対重量に、いずれも対照群と比べ有意な高値が認められた。

副腎　:　交配群雌の 300 mg/kg 投与群で対照群と比べ相対重量に有意な高値が認められた。

その他に対照群と比べ交配群雌の 300 mg/kg 投与群で脳の相対重量に有意な高値、100 及び 300 mg/kg 投与群で心臓の絶対重量に有意な低値が認められたが、いずれも剖検時体重の低値に伴う二次的な変化で毒性学的意義はないと考えられた。

2)　回復期間終了時検査

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

300 mg/kg 投与群の雌では、脳及び心臓の絶対重量に対照群と比べ有意な高値が認められたが、絶対重量のみの変化であり投与終了時検査には異常はないことから偶発性と判断した。

7.9　剖検所見（Table 9-1~9-6、Appendix 9-1~9-116）

1)　投与期間終了時検査

いずれの動物にも被験物質投与に起因すると考えられる変化はみられなかった。

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

授乳期間中に全哺育児が死亡した 300 mg/kg 投与群の 1 例（動物番号 4111）でみられた乳腺の発達不良は、哺育行動の低下に関連した変化と考えられた。一方、100 mg/kg 投与群の 1 例（動物番号 3111）では肉眼的異常はみられなかった。

2)　回復期間終了時検査

対照群の 1/5 例で精巣及び精巣上体の小型化がみられたが、その発現状況から偶発性変化と考えられた。

7.10　病理組織学検査（Table 10-1~10-16、Appendix 9-1~9-116）

1)　投与期間終了時検査

被験物質投与に起因する変化が雄の腎臓、雌の肝臓及び副腎にみられた。総括を表 5-1.~ 表 5-3.に示した。

腎臓　　:　雄の 30 mg/kg 以上の群に尿細管上皮細胞の好酸性小体、100 mg/kg 以上の群に再生尿細管の増強、300 mg/kg 群に顆粒円柱がみられた。好酸性小体は用量依存性に程度が増強し、抗 α2μ グロブリンの免疫組織化学染色標本で陽性を示したことから、α2μ グロブリンに由来するものであった。

表 5-1.病理組織学検査所見（雄）の総括（腎臓）

性別:	雄			
群:	交配群			
器官/組織　投与量(mg/kg):	0	30	100	300
所見　検査例数:	5	5	5	5
腎臓				
尿細管上皮細胞の好酸性小体	0	5	5	5
軽微	0	2	1	0
軽度	0	3	4	2
中等度	0	0	0	3
再生尿細管	2	2	4	5
軽微	2	2	2	1
軽度	0	0	2	4
顆粒円柱	0	0	0	1
軽微	0	0	0	1

肝臓　　:　雌の 300 mg/kg 群の交配群及び非交配群の全例に小葉中心性の肝細胞肥大がみられた。

表 5-2.病理組織学検査所見（交配及び非交配群雌）の総括（肝臓）

性別:	雌				雌	
群:	交配群				非交配群	
器官/組織　投与量(mg/kg):	0	30	100	300	0	300
所見　検査例数:	5	5	5(1)	5(1)	5	5
肝臓						
小葉中心性肝細胞肥大	0	0	0(0)	5(0)	0	5
軽微	0	0	0(0)	4(0)	0	5
軽度	0	0	0(0)	1(0)	0	0

(　)内は全哺育児死亡動物

副腎　　:　雌の 100 mg/kg 以上の交配群及び 300 mg/kg 群の非交配群に束状帯細胞の空胞の増加がみられた。本変化は、非交配群と比較して、交配群でより強くみられた。

表 5-3.病理組織学検査所見（交配及び非交配群雌）の総括（副腎）

性別:	雌				雌	
群:	交配群				非交配群	
器官/組織　投与量(mg/kg):	0	30	100	300	0	300
所見　検査例数:	5	5	5(1)	5(1)	5	5
副腎						
束状帯細胞の空胞の増加	0	0	2(0)	5(1)	0	1
軽微	0	0	2(0)	1(0)	0	0
軽度	0	0	0(0)	4(0)	0	1
中等度	0	0	0(0)	0(1)	0	0

(　)内は全哺育児死亡動物

授乳期間中に全哺育児が死亡した 100 mg/kg 投与群の 1 例（動物番号 3111）では乳腺（鼠径部）に乳汁分泌の減少及び卵巣に大型黄体の減少がみられ、300 mg/kg 投与群の 1 例（動物番号 4111）では乳腺（鼠径部）に乳汁分泌の減少、結腸に杯細胞の萎縮、腎臓に尿細管上皮細胞の空胞化、尿細管の拡張及び壊死、顎下腺に顆粒管の顆粒の減少、胸腺に萎縮、肺に肺胞マクロファージの集簇がみられ、哺育行動の低下あるいは切歯破損に伴う摂餌不良に起因した状態悪化に関連した変化と考えられた。

また、上記の他に、種々の変化がみられたが、いずれもその病理学的性状及び発現状況から被験物質投与と関係しない偶発性変化と判断した。

2)　回復期間終了時検査

300 mg/kg 群の雄の腎臓で軽微又は軽度の再生尿細管が 5/5 例にみられた。

7.11　性周期（Table 11、Appendix 10-1~10-4）

対照群で 1 例に性周期異常がみられたが、被験物質投与群では性周期異常の動物はみられず、性周期異常率、発情期像発現回数及び性周期（発情周期）には対照群と各被験物質投与群との間に有意差は認められなかった。

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

交配 10 日までに全例の交尾が成立し、交尾までに要した日数、交尾率、授精率及び受胎率には対照群と各被験物質投与群との間に有意差は認められなかった。

7.13　分娩成績（Table 13、Appendix 12-1~12-4）並びに分娩及び哺育状態（Table 1-5 及び 1-6、Appendix 1-17~1-24）

出産率、妊娠期間、黄体数、着床痕数、分娩率、死産児率、出生児数及び外表異常率には対照群と各被験物質投与群との間に有意差は認められなかった。100 mg/kg 投与群で着床率に対照群と比べ有意な高値が認められたが、用量に依存性のない変化であった。

妊娠動物の分娩状態では妊娠 21 から 23 日に全例が分娩し、胎盤及び羊膜の処理は

正常に行われた。哺育状態では、100 及び 300 mg/kg 投与群の各 1 例に哺育行動の低下がみられ、全哺育児が死亡した。その他のいずれの母動物にも児集め、営巣及び授乳行動に異常はみられなかった。

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

300 mg/kg 投与群で、統計学的な有意差は認められないものの、生後 4 日生存率に対照群に比して低値傾向が認められた。その他、出生率及び生後 4 日生存率には対照群と各被験物質投与群との間に有意差は認められなかった。

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

出産児並びに出生児の生後 0 及び 4 日の性比には対照群と各被験物質投与群との間に有意差は認められなかった。

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

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

7.17　死亡児の肉眼観察所見（Table 17、Appendix 16-1~16-4）

いずれの死亡児にも肉眼的異常はみられなかった。

7.18　出生児の生後 4 日肉眼観察所見（Table 18、Appendix 17-1~17-4）

いずれの出生児にも肉眼的異常はみられなかった。

8. 考察

4-tert-ブチルシクロヘキサン-1-イル=アセタートの 0（対照群：コーン油）、30、100 及び 300 mg/kg を Sprague-Dawley 系 SPF ラットの雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（42~51 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 300 mg/kg 群の一部の動物については、雌雄ともに 42 日間投与した後 14 日間の回復期間を設け、毒性変化の可逆性を検討した。

8.1 反復投与毒性

いずれの投与群においても死亡動物はみられず、機能検査、握力、自発運動量、尿検査（摂水量を含む）、血液化学検査及び剖検には被験物質投与の影響は認められなかった。

300 mg/kg 投与群の雌雄で自発運動の減少、痙攣及び流涎が投与期間を通じ散見され、非交配群雌で自発運動の減少に関連して立ち上がり回数の低値、伸びている姿勢が認められたことから、自律神経の交感神経及び副交感神経のアンバランスに起因した変化の可能性が考えられ、被験物質投与の影響と判断した。これらの症状は回復期間には消失し、回復性がみられた。

300 mg/kg 投与群の交配及び非交配群雌で投与初期に摂餌量の変動を伴った体重増加抑制が認められ、交配群雌では妊娠期間中の体重も低値を示し、被験物質投与の影響と考えられた。非交配群雌では、回復期間中の摂餌量に高値が認められ、体重増加量も対照群を上回り、速やかに回復すると考えられた。

300 mg/kg 投与群の非交配群雌で赤血球数に低値、平均赤血球容積及び平均赤血球血色素量に高値が認められ、被験物質投与の影響と考えられたが、いずれも 7%未満の軽微な変化であり、網赤血球率等に変動はないことから毒性学的意義は少なく、病理組織学検査に関連する異常はみられないことから、その作用機序は明らかでない。

300 mg/kg 投与群の雄、雌の交配及び非交配群で肝臓重量に高値が認められ、雌の交配及び非交配群では組織所見で小葉中心性肝細胞肥大がみられ、被験物質投与の影響と考えられた。30、100 及び 300 mg/kg 投与群の雄で腎臓重量に高値が認められ、尿細管上皮細胞の好酸性小体の蓄積が重量増加の原因と考えられた。300 mg/kg 投与群の交配群雌でも腎臓重量に高値が認められ、被験物質投与の影響と考えられたが、組織所見には重量増加を示唆する変化はみられないことから、毒性学的意義は少ないと判断した。また、同群では副腎の重量に高値が認められ、組織所見で束状帯細胞の空胞の増加もみられ、被験物質投与の影響と考えられた。

30 mg/kg以上の雄の腎臓にみられた好酸性小体は抗α2μグロブリン免疫組織化学染色では陽性を示したことから、α2μグロブリンに由来するものと考えられた。α2μグロブリンを含む好酸性小体は、背景的に雄ラットの近位尿細管曲部にしばしばみられ、

様々な化学物質の投与により増加することが知られ、さらに尿細管障害を特徴とした病変を誘発することが知られている [8], [9], [10]。本試験においても、個々の上皮細胞内における好酸性小体の異常な蓄積が認められており、100 mg/kg以上の雄の再生尿細管の増強、300 mg/kgの雄の顆粒円柱はそれに関連する変化と考えられ、かつ、腎重量の増加の原因と考えられた。なおα2μグロブリンの蓄積は雄性ラットに種特異的な発現であり人には外挿されないことが知られており[9]、尿細管障害を示唆する変化を伴わず絶対重量のみの変化である 30 mg/kg群の雄の腎重量高値には、毒性学的意義はないと判断した。300 mg/kgの雌にみられた小葉中心性の肝細胞肥大は、その形態及び発現状況から薬物代謝酵素活性の誘導と考えられるが、本試験では明らかでない。肥大した肝細胞は好酸性を呈し、回復期間により速やかに回復した。100 mg/kg以上の雌でみられた副腎の束状帯細胞の空胞増加は交配群でより顕著にみられ、妊娠、分娩及び哺育による特殊な環境により増強された可能性が考えられたが、本被験物質におけるその発現機序については明らかでない。14 日間の回復期間により、上記に示した変化は腎臓の再生尿細管を除き、いずれも消失し、回復性があるものと判断された。なお、腎臓においても、再生尿細管の増強に関連すると考えられる好酸性小体が消失し、他の腎臓の変化も全て消失していることから、回復傾向が伺われた。

8.2 生殖発生毒性

100 及び 300 mg/kg 群の各 1 例で哺育行動の低下がみられ、それらの全哺育児が死亡し、300 mg/kg 群では児の生後 4 日生存率に低値傾向が認められた。300 mg/kg 群では全哺育児死亡母体以外にも、約半数例の児が死亡し生後 4 日生存率が対照群の下限（83.3%）を下回る個体（46.7%、No.4109）が認められ、群平均が試験施設の背景データの下限（85.8%、20 試験、2008/04-2013/03）を下回り、被験物質投与による一般状態の変化に関連して、哺育状態への影響も疑われることから、毒性影響と判断した。100 mg/kg 群の全哺育児死亡母体では、上記 300 mg/kg 群の 2 母体との比較において、分娩成績等に繁殖障害を示唆する特異的な差もみられないことから、同様に被験物質投与との関連性は否定し得ないと判断した。授乳 2 日に切歯破損がみられた 300 mg/kg 群の 1 例では、摂餌不良に伴う一般状態の悪化及びストレスが哺育行動の低下を助長した可能性も考えられた。100 mg/kg 群の 1 例では、授乳時の母動物の卵巣にみられる大型の黄体がほとんどみられないことから、被験物質投与により妊娠、出産及び分娩に伴うホルモン変化に異常をきたしていることが推測され、それによる哺育行動の低下により全哺育児が死亡した可能性が考えられた。

その他にはいずれの投与群においても生殖機能に関するパラメータに被験物質投与の影響は認められないことから、300 mg/kg 群においても雌雄動物の交尾能、授精能及び受胎能、母動物の妊娠維持及び分娩などへの影響はないと判断した。

30 mg/kg 群では、出生児のいずれの検査項目にも被験物質投与による影響は認められないことから、児の子宮内発生、発育及び分化並びに生存性などへの影響はないと判断した。

これらの結果から、本試験条件下で 4-tert-ブチルシクロヘキサン-1-イル=アセタートを反復経口投与することにより、被験物質に起因すると考えられる主な変化として 30 mg/kg 以上の群の雄の腎臓に尿細管上皮細胞の好酸性小体及び重量の増加、100 mg/kg 以上の群の雄の腎臓に再生尿細管の増強及び雌の副腎に束状帯細胞の空胞の増加、300 mg/kg 群の雌の肝臓に重量増加及び小葉中心性肝細胞肥大、雄の肝臓に重量増加及び腎臓に顆粒円柱がみられ、100 及び 300 mg/kg で哺育行動の低下及び全哺育児死亡が、300 mg/kg で児の生後 4 日生存率に低値傾向がみられた。したがって、本被験物質の反復投与毒性に対する無影響量は雄で 30 mg/kg 未満、雌で 30 mg/kg、無毒性量は雌雄とも 30 mg/kg と判断した。また、生殖発生毒性に対する無影響量及び無毒性量は雄親動物でいずれも 300 mg/kg、母動物及び児動物ではいずれも 30 mg/kg と判断した。

9. 文献

[1] [redacted]: 4-tert-ブチルシクロヘキサン-1-イル=アセタートの IR を用いた特性試験及び安定性試験並びに GC を用いた被験液（媒体：コーン油）中濃度測定法バリデーション及び安定性試験（株式会社ボゾリサーチセンター 御殿場研究所、試験番号：A-2585、2013 年）

[2] [redacted]: 4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）（株式会社ボゾリサーチセンター、試験番号：N-R042、2013 年）

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

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

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

[6] Siegel S, Castellan NJ. Jr. Nonparametric statistics for the behavioral sciences. 2nd ed. New York: McGraw-Hill; 1988.

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

[8] Haschek WM, Rousseaux CG, Walling MA, Kidney. IV. Mecanism of toxicity, Handbook of Toxicologic Pathology, 2nd ed. Academic Press, 294-298, 2002.

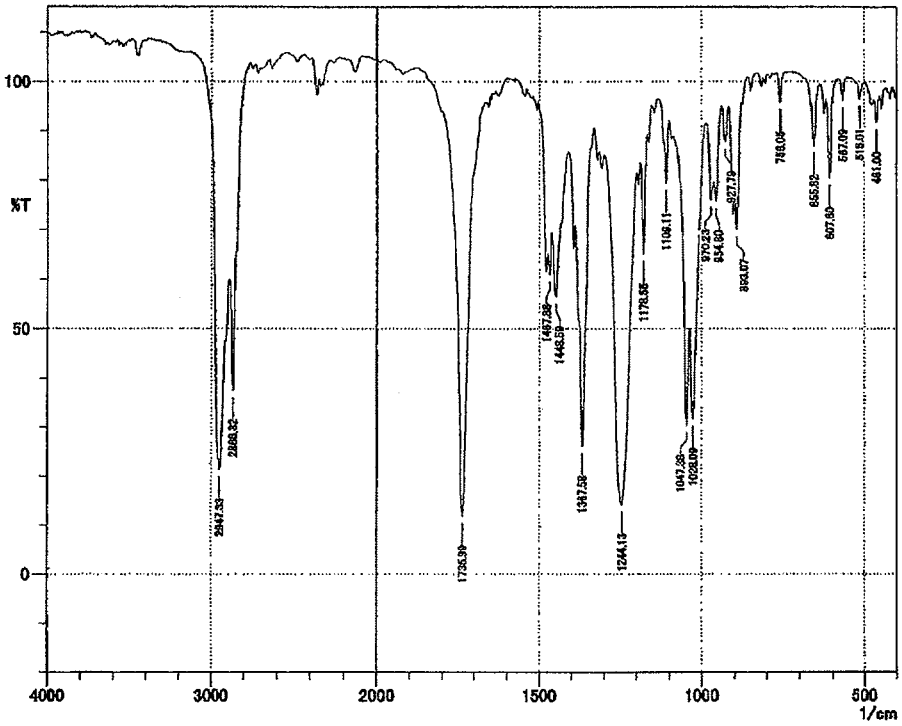
[9] Alden CL and Frith CH. : Urinary System, IV. Mechanisms of toxicity, C. Proximal tubular injury. In : Handbook of Toxicologic Pathology, Academic Press, San Diego: 340-342 (1991)

[10] 伊東信行発行:各論 8 章, 腎臓, In:毒性病理組織学, 日本毒性病理学会, 名古屋, 253（2000）

試験番号：A-2585

試験成績書
(4-tert-ブチルシクロヘキサン-1-イル=アセタートの特性)

ステージ	:	初期値
測定日	:	2013 年 7 月 25 日
被験物質	:	4-tert-ブチルシクロヘキサン-1-イル=アセタート （ロット番号：AH01）
測定項目	:	赤外吸収スペクトル（液膜法）
結果	:	特性のスペクトルを以下に示す。



基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23・03・29 製局第 6 号、環保企発第 110331010 号）

[redacted] 2013 年 7 月 26 日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

試験番号：R-1135

試験成績書
（被験物質の安定性）

ステージ	:	投与期間終了後
測定日	:	2013年11月25日 2013年 7月25日（特性のスペクトル[1)]）
被験物質	:	4-tert-ブチルシクロヘキサン-1-イル=アセタート （ロット番号：AH01）
測定項目	:	赤外吸収スペクトル（液膜法）
判定基準	:	安定性のスペクトルを特性のスペクトル[1)]と比較するとき、同様な赤外吸収スペクトルである。 1) 杉山　文彦：4-tert-ブチルシクロヘキサン-1-イル=アセタートのIRを用いた特性試験及び安定性試験並びにGCを用いた被験液（媒体：コーン油）中濃度測定法バリデーション及び安定性試験（株式会社ボゾリサーチセンター御殿場研究所、試験番号：A-2585）
結果	:	安定性のスペクトルを特性のスペクトルと比較したとき、同様な赤外吸収スペクトルが得られた。なお、赤外吸収スペクトルは次のページに示す。
判定	:	適
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成23年3月31日：薬食発0331第8号、平成23･03･29製局第6号、環保企発第110331010号）

[redacted]　2013 年 12 月 2 日

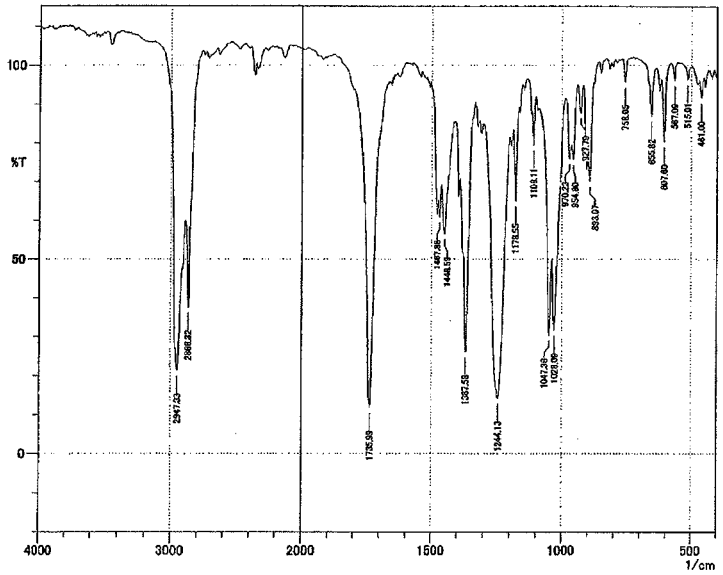
化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

試験番号：R-1135

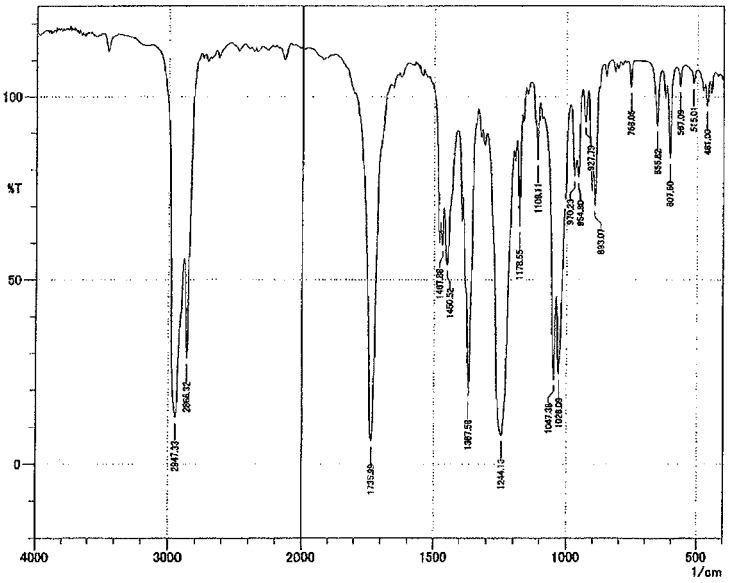
試験成績書
（被験物質の安定性）

結果　　：　赤外吸収スペクトル

（特性のスペクトル）



（安定性のスペクトル）



試験番号：A-2585

試験成績書
（被験液中 4-tert-ブチルシクロヘキサン-1-イル=アセタートの安定性）

被験物質　：　4-tert-ブチルシクロヘキサン-1-イル=アセタート
（ロット番号：AH01）
形態（媒体）　：　溶液（コーン油）
保存条件　：　褐色ガラス瓶にて、冷所（冷蔵庫内、許容値：1~10°C）又は室温保存
保存期間　：　冷所で 8 日間保存した後、室温で 24 時間保存
評価基準
安定性　：　残存率｛調製直後の測定濃度の平均値（100）に対する保存後の測定濃度の平均値の割合｝が 100.0±10.0% 以内。

結果：

調製濃度 (mg/mL)		測定濃度（mg/mL）	
		調製直後	冷所で 8 日間保存した後、室温で 24 時間保存後
1.00		1.00	0.998
		0.998	0.990
		0.974	0.977
	平均値	0.991	0.988
	残存率（%）	100	99.7
200		209	207
		209	207
		213	206
	平均値	210	207
	残存率（%）	100	98.6

判定　：　適

基準　：　「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 日：薬食発 0331 第 8 号、平成 23・03・29 製局第 6 号、環保企発第 110331010 号）

[redacted]　2013 年 8 月 29 日

試験責任者
株式会社ボゾリサーチセンター　御殿場研究所

分析結果

試験番号 : R-1135
項目 : 濃度
ステージ : 初回投与
分析日 : 2013 年 9 月 20 日

測定試料
被験物質 : 4-tert-ブチルシクロヘキサン-1-イル=アセタート
（ロット番号：AH01）
形態 : 溶液
媒体 : コーン油
調製日 : 2013 年 9 月 20 日

測定対象物質 : 4-tert-ブチルシクロヘキサン-1-イル=アセタート

評価基準
濃度 : 表示値に対する割合；100.0±10.0%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値	表示値に対する割合 (%)
6	5.96 6.10 6.09	6.05	100.8
20	20.0 19.9 20.1	20.0	100.0
60	60.1 59.2 60.3	59.9	99.8

判定 : 適

分析結果

試験番号 : R-1135
項目 : 濃度
ステージ : 投与 6 週
分析日 : 2013 年 10 月 25 日

測定試料
被験物質 : 4-tert-ブチルシクロヘキサン-1-イル=アセタート
（ロット番号：AH01）
形態 : 溶液
媒体 : コーン油
調製日 : 2013 年 10 月 25 日

測定対象物質 : 4-tert-ブチルシクロヘキサン-1-イル=アセタート

評価基準
濃度 : 表示値に対する割合；100.0±10.0%

結果：

表示値 (mg/mL)	測定濃度 (mg/mL)	平均値	表示値に対する割合 (%)
6	6.31 6.21 6.28	6.27	104.5
20	21.1 21.1 20.9	21.0	105.0
60	63.0 63.4 62.9	63.1	105.2

判定 : 適

4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた 14 日間反復経口投与毒性試験（投与量設定試験）における所見

試験番号：N-R042

被験物質		媒体 a)	4-tert-ブチルシクロヘキサン-1-イル=アセタート		
投与量(mg/kg)		0	250	500	1000
投与容量 (mL/kg)		5	5	5	5
使用動物数 (♂/♀)		5/5	5/5	5/5	5/5
死亡動物数 (♂/♀)		0/0	0/0	0/0	0/1
死亡発現時期		−	−	−	投与 5 日
一般状態	生存	−	痙攣(♀)	痙攣、自発運動の減少	痙攣、自発運動の減少、被毛の汚れ(下腹部)、糞量の減少
	死亡				痙攣、自発運動の減少、軟便、被毛の汚れ(口腔周囲及び下腹部)、糞量の減少、呼吸数減少、腹臥/横臥
体重			−	減少又は低値傾向 (投与 4 日、♂♀)	減少(投与 4 日、♂♀) ↓(投与 10 及び 14 日、♂)
体重増加量			−	−	↓↓(投与 1-14 日、♂)
摂餌量			−	低値傾向 (投与 4 日、♂♀)	↓↓(投与 4 日、♂♀)
血液学検査			−	−	−
血液化学検査			−	尿素窒素：↓(♀)	総コレステロール：↑(♂) 尿素窒素：↑(♂)、↓↓(♀)
器官重量	絶対		−	肝臓：↑(♂)	肝臓：↑(♂)、↑↑(♀) 胸腺：↓(♂)、↓↓(♀) 副腎：↑↑(♀)
	相対		肝臓:↑(♂♀)	肝臓：↑↑(♂♀)	肝臓：↑↑(♂♀) 胸腺：↓(♂)、↓↓(♀) 副腎：↑↑(♂♀) 腎臓：↑(♂)
剖検	生存	−	−	−	−
	死亡				被毛の汚染、脾臓及び胸腺の小型化

a) ：コーン油
− ：著変なし
/ ：データなし又は判別不明あるいは検定不能
↑又は↓；$p<0.05$，↑↑又は↓↓；$p<0.01$，(対照群との間に有意差あり)

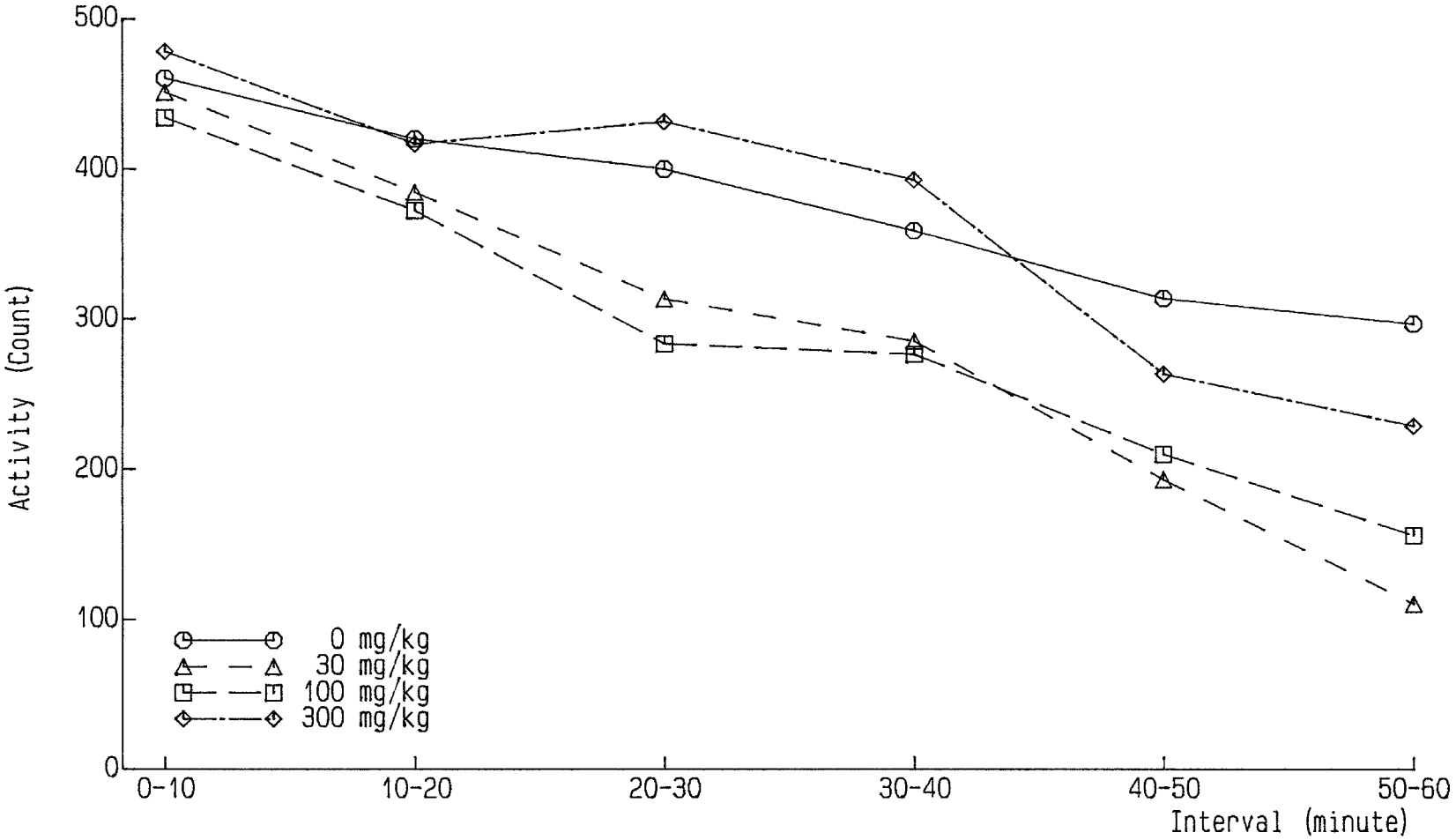


Fig.1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Motor activity of male rats (Week 6 of administration)

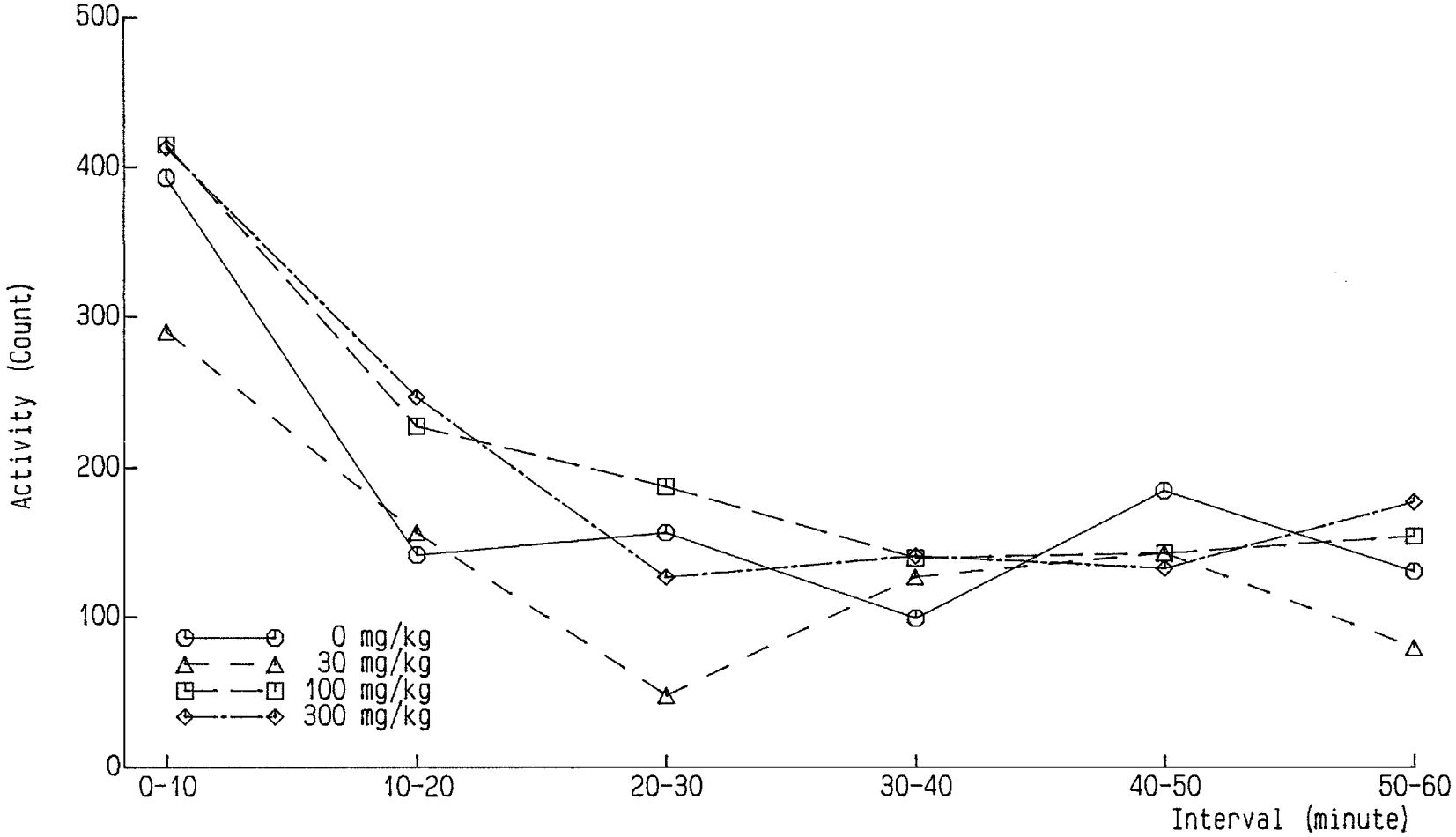


Fig.2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

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

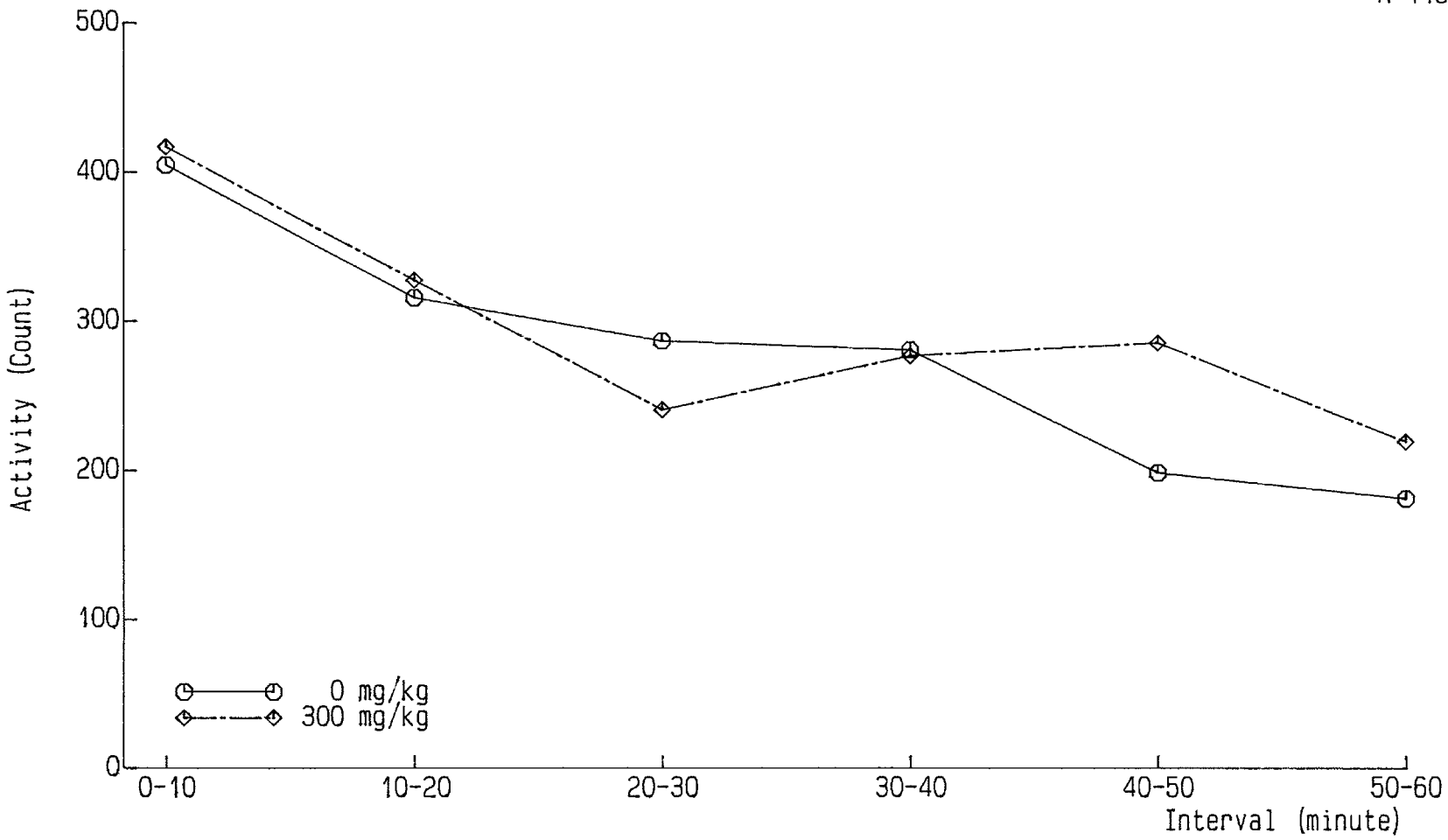


Fig.3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

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

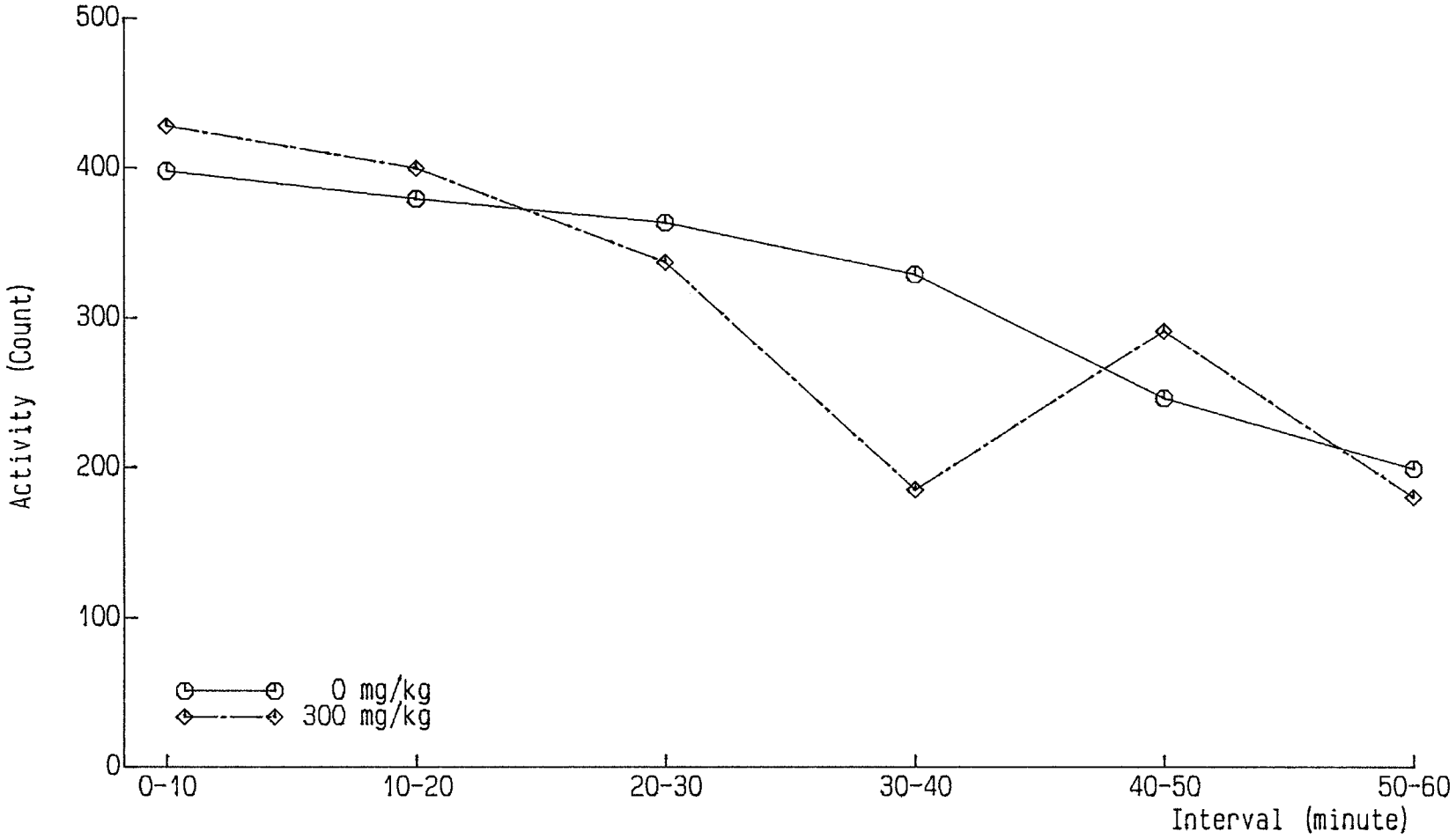


Fig.4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

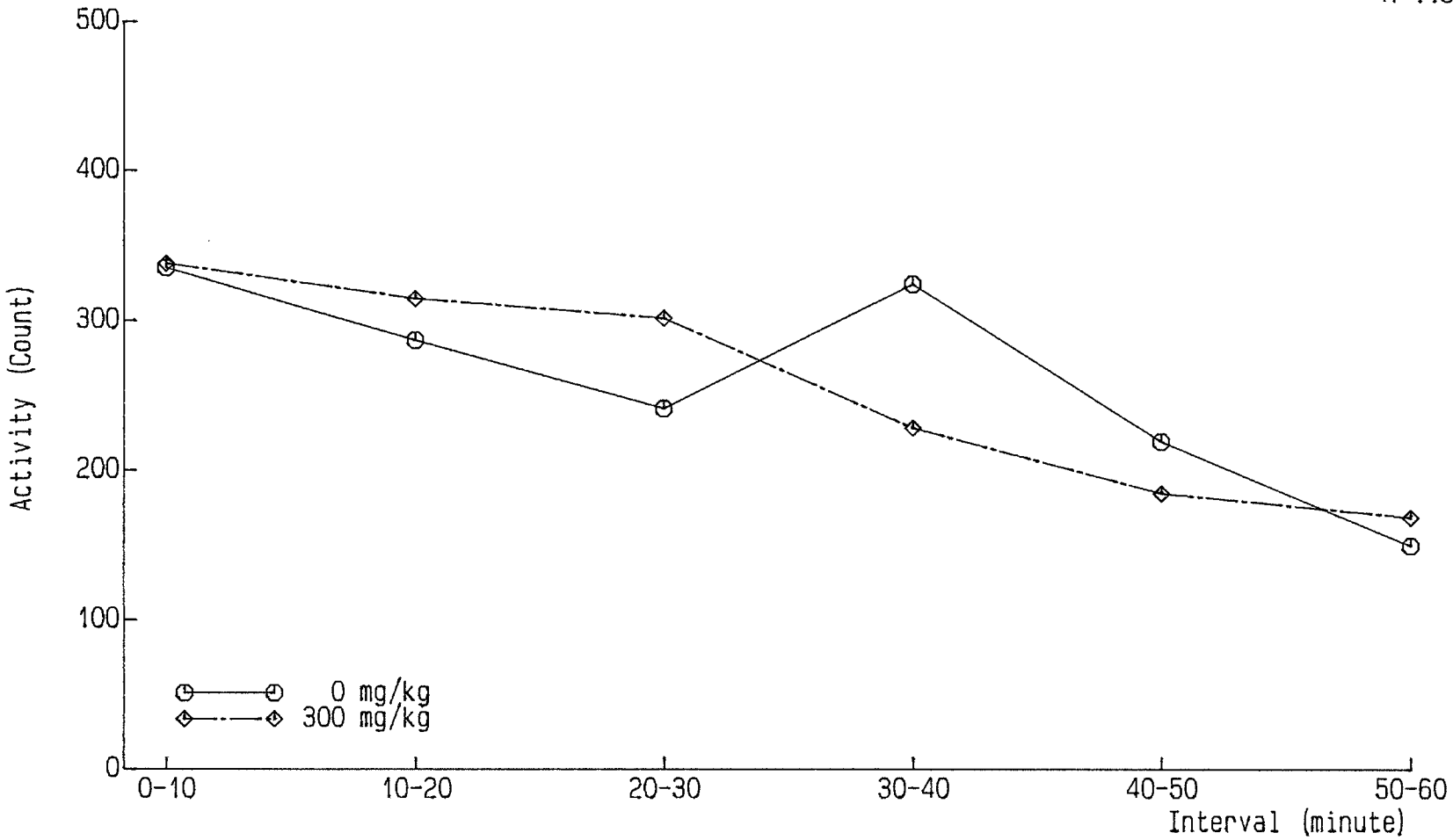


Fig.5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

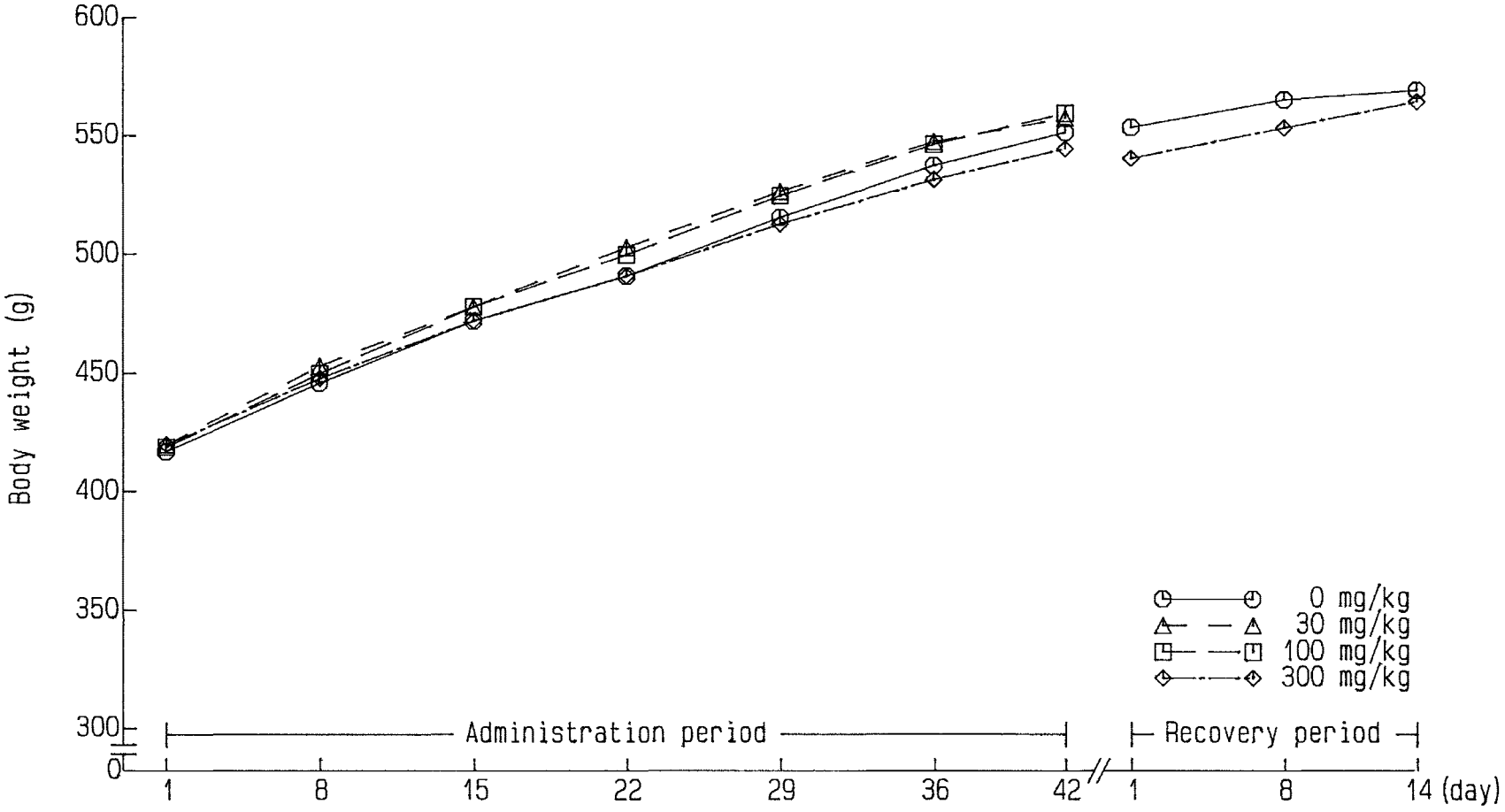


Fig.6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Body weight of male rats

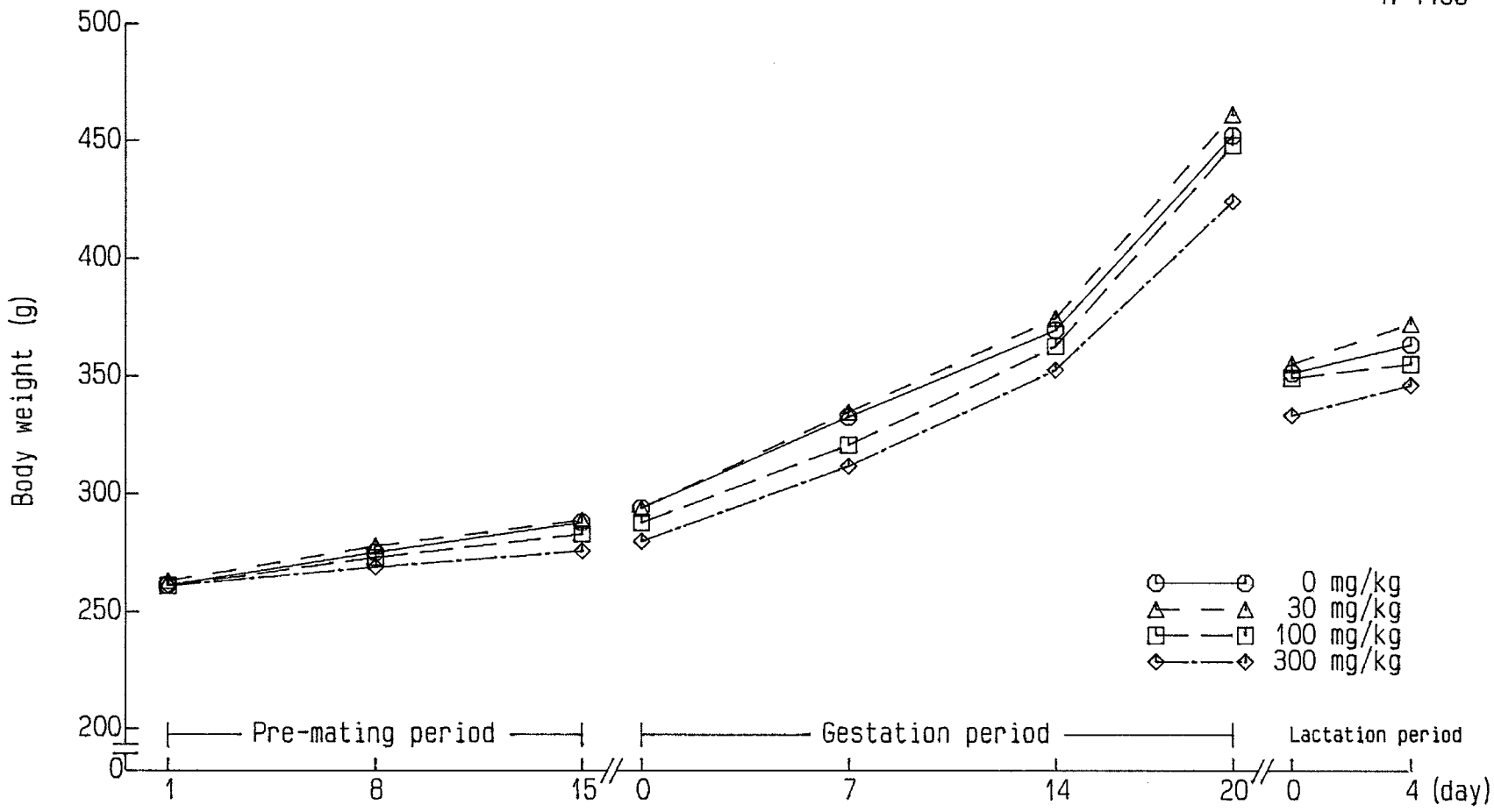


Fig.7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Body weight of female rats (Main group)

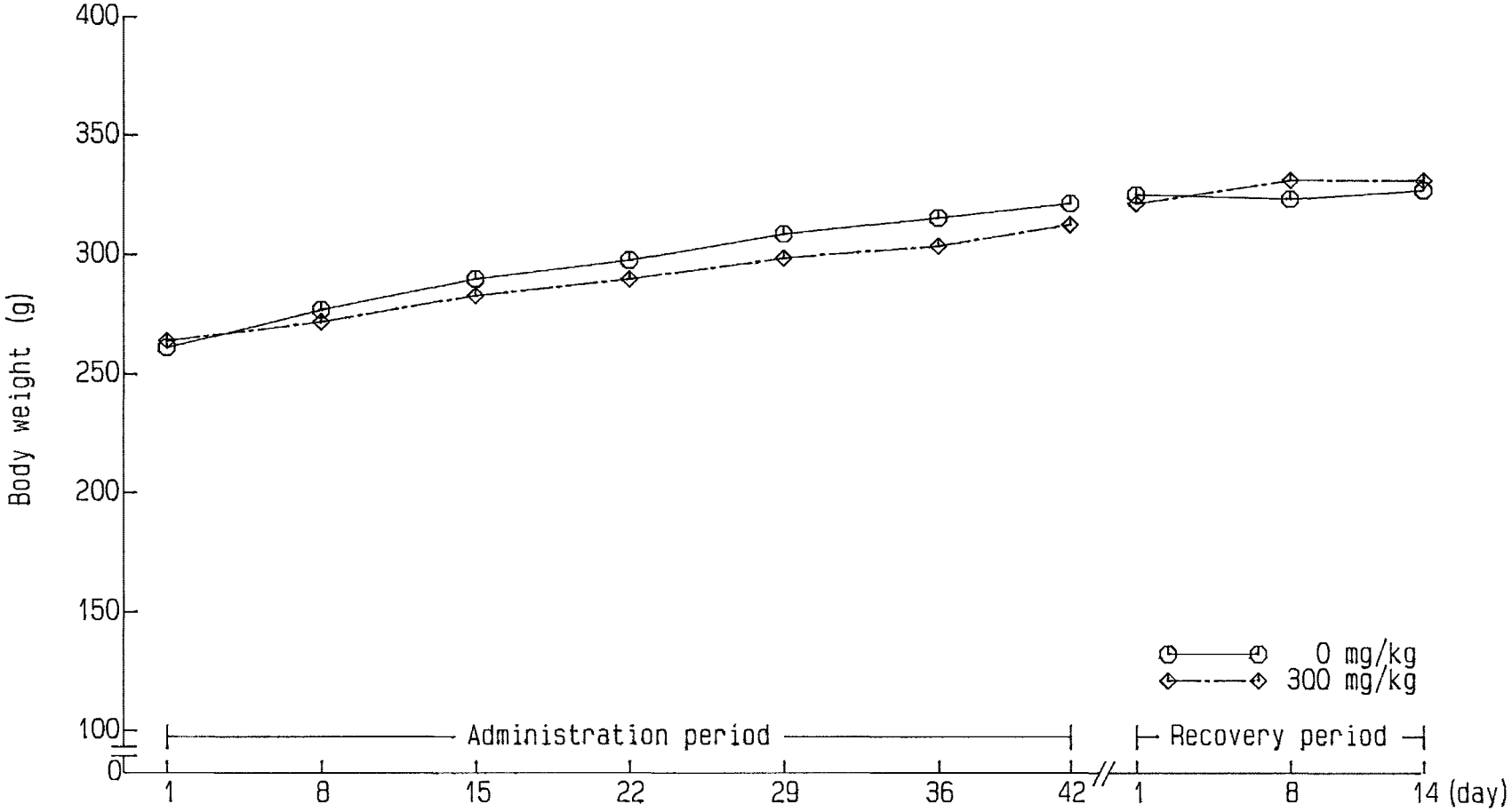


Fig.8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Body weight of female rats (Satellite group)

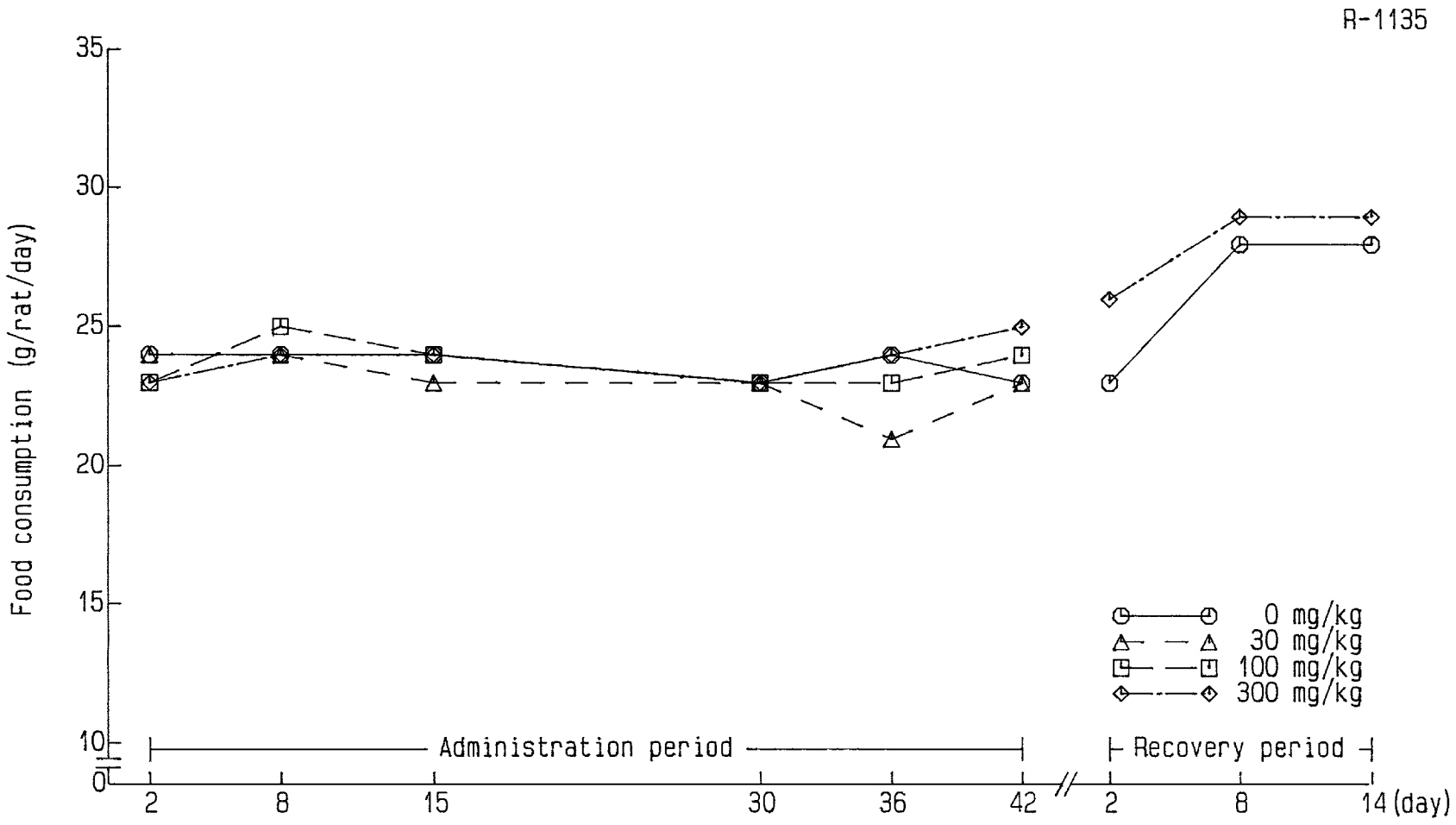


Fig.9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Food consumption of male rats

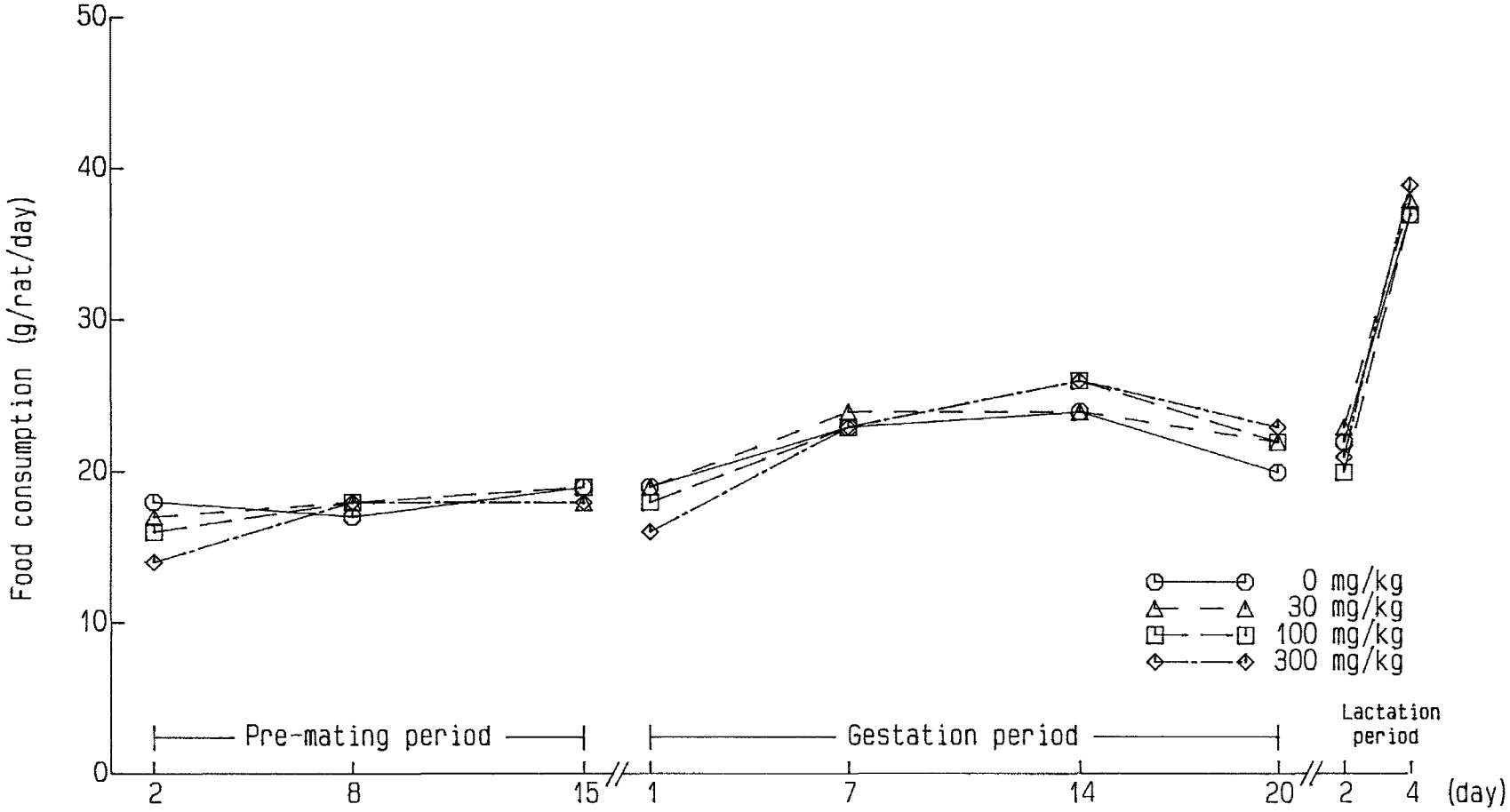


Fig.10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Food consumption of female rats (Main group)

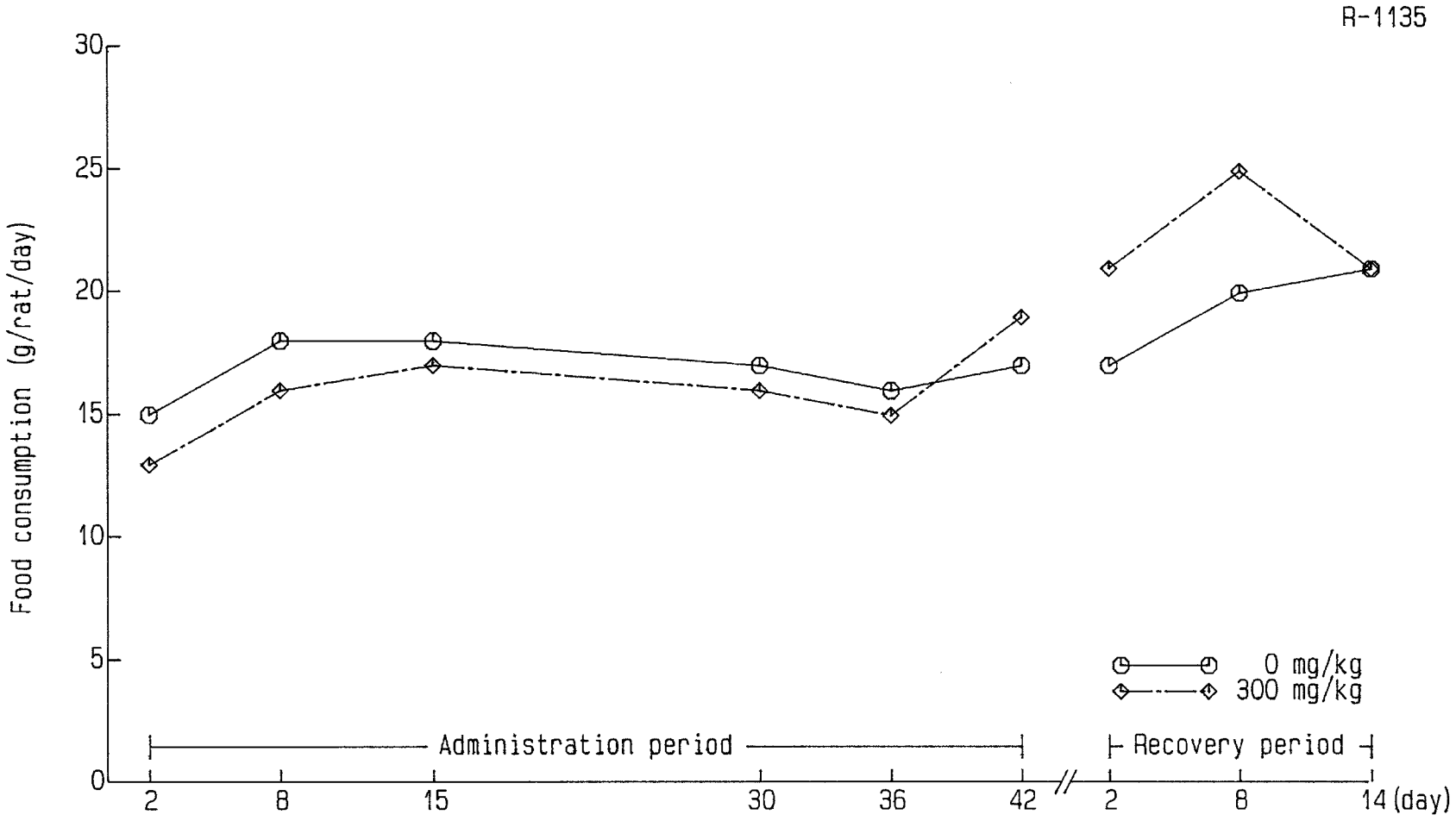


Fig.11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Food consumption of female rats (Satellite group)

Table 1-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in male rats (Administration period)

Dose mg/kg	Signs	Day of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	1	0	0	0	0	0	0	0	1	3	1	2
	Decrease in spontaneous movement	0	0	1	0	0	0	0	0	0	0	1	2	1	1
	Convulsion	0	0	0	0	0	0	0	0	0	0	0	1	0	1

Table 1-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in male rats (Administration period)

Dose mg/kg	Signs	Day of administration 15	16	17	18	19	20	21	22	23	24	25	26	27	28
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	5	4	4	4	3	4	4	4	2	3	3	6	3	4
	Decrease in spontaneous movement	0	0	1	3	1	1	1	1	0	0	0	3	1	0
	Convulsion	2	3	0	0	0	1	1	1	0	0	0	1	3	1
	Salivation	4	2	3	2	3	2	2	3	2	3	3	4	2	3

Table 1-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in male rats (Administration period)

Dose mg/kg	Signs	Day of administration 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
0	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	7
	No. of animals with abnormal findings	3	1	2	4	3	1	4	3	5	5	4	2	2	4	0
	Decrease in spontaneous movement	0	0	0	2	0	0	1	2	2	0	2	1	1	3	0
	Convulsion	2	0	0	1	2	1	2	0	2	3	2	0	0	1	0
	Salivation	2	1	2	2	2	1	1	2	1	2	1	1	1	0	0

a): Day of necropsy

Table 1-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in female rats during the pre-mating period (Main group)

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

Table 1-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in dams during the gestation period (Main group)

Dose mg/kg	Signs	Administration 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
0	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
30	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	0	
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
100	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	3	0
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
300	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	1	0
	No. of dams with abnormal findings	4	3	5	6	5	2	2	3	4	7	7	4	3	2	4	4	6	5	5	5	1	1	0	
	Decrease in spontaneous movement	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	
	Convulsion	3	3	5	6	5	2	2	3	3	7	7	4	3	2	3	4	5	5	5	4	0	1	0	
	Salivation	0	0	2	0	0	0	0	0	1	0	0	0	0	0	0	1	1	1	0	0	0	0	0	

a): Gestation day

Table 1-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in dams during the lactation period (Main group)

Dose mg/kg	Signs	Administration 0	1	2	3	4a)	5b)
0	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
30	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
100	No. of dams	12	12	12	11c)	11	11
	No. of dams with abnormal findings	0	1	0	0	0	0
	Decrease in nursing behavior	0	1	0	0	0	0
300	No. of dams	12	12	12	12	12	11d)
	No. of dams with abnormal findings	0	3	5	3	4	0
	Decrease in spontaneous movement	0	1	1	0	0	0
	Convulsion	0	2	4	2	3	0
	Decrease in nursing behavior	0	1	1	1	0	0
	Fracture of incisors	0	0	1	1	1	0

a): Lactation day
b): Day of necropsy
c): One dam was necropsied on lactation day 2 because all pups died.
d): One dam was necropsied on lactation day 4 because all pups died.

Table 1-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in female rats (Satellite group, Administration period)

Dose mg/kg	Signs	Day of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14
0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No. of animals with abnormal findings	2	2	0	2	1	0	5	6	3	3	2	3	1	1
	Decrease in spontaneous movement	2	2	0	2	1	0	2	6	0	0	1	0	0	1
	Convulsion	0	1	0	0	0	0	4	1	3	3	2	3	1	0

Table 1-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in female rats (Satellite group, Administration period)

Dose mg/kg	Signs	Day of administration 15	16	17	18	19	20	21	22	23	24	25	26	27	28
0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	No. of animals with abnormal findings	3	4	4	4	2	3	4	4	0	1	3	6	4	3
	Decrease in spontaneous movement	0	0	1	0	0	1	0	0	0	0	1	0	0	1
	Convulsion	3	4	2	3	2	2	3	3	0	1	2	5	3	2
	Salivation	0	1	1	1	0	1	1	1	0	0	0	1	1	0

Table 1-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in female rats (Satellite group, Administration period)

Dose mg/kg	Signs	Day of administration 29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
0	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
300	No. of animals	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5
	No. of animals with abnormal findings	3	2	2	4	2	1	4	3	2	1	3	1	1	0	0
	Decrease in spontaneous movement	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	Convulsion	3	2	2	3	2	1	4	3	2	1	3	1	1	0	0

a): Day of necropsy

Table 1-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in male rats (Recovery period)

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

a): Day of necropsy

Table 1-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Clinical signs in female rats (Recovery period)

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

a): Day of necropsy

Table 2-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 3 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 7)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	10
Minor		0	0	0	2a)
Abnormal behavior					
None		12	12	12	12

a): Tonic convulsion

Table 2-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 14)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Gestation day 20)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Posture					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12

Table 2-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	11	11
Posture					
Normal		12	12	11	11
Convulsion					
None		12	12	11	11
Abnormal behavior					
None		12	12	11	11

Table 2-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Posture			
Normal		10	9
Flattened		0	1
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10

Table 2-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: home cage observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: home cage observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Posture			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5

Table 2-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	10	11	12
Soft		1	2	1	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 3 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	12	12
Soft		0	1	0	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	11
Some resistance/avoidance		0	0	0	1
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	12	12
Soft		0	1	0	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	10	12
Soft		0	0	2	0
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	12	12
Reactivity to handling					
Easy		12	12	12	12

Table 2-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	12	12	12
Soft		1	0	0	0
Reactivity to handling					
Easy		11	12	12	12
Slightly awkward		1	0	0	0

Table 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 7)

Parameter / Dose (mg/kg)	0	30	100	300
No. of animals	12	12	12	12
Ease of removal from cage				
Easy	12	12	12	12
Fur condition				
Normal	12	12	12	12
Skin				
Normal	12	12	12	12
Secretions-Eye, Nose				
Absent	12	12	12	12
Exophthalmos				
Absent	12	12	12	12
Palpebral closure				
Normal	12	12	12	12
Mucosal membranes				
Normal	12	12	12	12
Lacrimation				
Normal	12	12	12	12
Piloerection				
Absent	12	12	12	12
Pupil size				
Normal	12	12	12	12
Salivation				
None	12	12	12	12
Abnormal respiration				
Absent	12	12	12	12
Vocalization				
None	12	12	12	12
Reactivity to handling				
Easy	12	12	12	12

Table 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 14)

Parameter / Dose (mg/kg)	0	30	100	300
No. of animals	12	12	12	12
Ease of removal from cage				
Easy	12	12	12	12
Fur condition				
Normal	12	12	12	12
Skin				
Normal	12	12	12	12
Secretions-Eye, Nose				
Absent	12	12	12	12
Exophthalmos				
Absent	12	12	12	12
Palpebral closure				
Normal	12	12	12	12
Mucosal membranes				
Normal	12	12	12	12
Lacrimation				
Normal	12	12	12	12
Piloerection				
Absent	12	12	12	12
Pupil size				
Normal	12	12	12	12
Salivation				
None	12	12	12	12
Abnormal respiration				
Absent	12	12	12	12
Vocalization				
None	12	12	12	12
Reactivity to handling				
Easy	12	12	12	12

Table 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Gestation day 20)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	12	12	12
Soft		1	0	0	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	11	11
Ease of removal from cage					
Easy		12	12	11	11
Fur condition					
Normal		12	12	11	11
Skin					
Normal		12	12	11	11
Secretions-Eye, Nose					
Absent		12	12	11	11
Exophthalmos					
Absent		12	12	11	11
Palpebral closure					
Normal		12	12	11	11
Mucosal membranes					
Normal		12	12	11	11
Lacrimation					
Normal		12	12	11	11
Piloerection					
Absent		12	12	11	11
Pupil size					
Normal		12	12	11	11
Salivation					
None		12	12	11	11
Abnormal respiration					
Absent		12	12	11	11
Vocalization					
None		11	12	11	11
Soft		1	0	0	0
Reactivity to handling					
Easy		11	12	11	11
Slightly awkward		1	0	0	0

Table 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 1 of administration)

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

Table 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 2 of administration)

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

Table 2-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 3 of administration)

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

Table 2-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 4 of administration)

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

Table 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 5 of administration)

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

Table 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Satellite group, Week 6 of administration)

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

Table 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	4
Soft		0	1
Reactivity to handling			
Easy		5	4
Slightly awkward		0	1

Table 2-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: in-the-hand observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Ease of removal from cage			
Easy		5	5
Fur condition			
Normal		5	5
Skin			
Normal		5	5
Secretions-Eye, Nose			
Absent		5	5
Exophthalmos			
Absent		5	5
Palpebral closure			
Normal		5	5
Mucosal membranes			
Normal		5	5
Lacrimation			
Normal		5	5
Piloerection			
Absent		5	5
Pupil size			
Normal		5	5
Salivation			
None		5	5
Abnormal respiration			
Absent		5	5
Vocalization			
None		5	5
Reactivity to handling			
Easy		5	5

Table 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 1 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 3	4± 1	5± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		8	9	10	8
Small amount		4	3	2	4

No significant difference in any treated groups from control group.

Table 2-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 2 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	5± 1	5± 3	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 1	0± 0
Urination					
None		9	8	11	9
Small amount		3	4	1	3

No significant difference in any treated groups from control group.

Table 2-49 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 3 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	4± 1	4± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 0
Urination					
None		10	10	10	8
Small amount		2	2	2	4

No significant difference in any treated groups from control group.

Table 2-50 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 4 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	1	0	0
Normal		12	11	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 2	4± 2	5± 1	5± 2
Defecation count (Mean±S.D.)		0± 1	0± 0	0± 0	0± 1
Urination					
None		9	8	10	9
Small amount		3	4	2	3

No significant difference in any treated groups from control group.

Table 2-51 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 5 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
No/minimal location		0	1	0	0
Normal		12	11	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 1	6± 3	5± 3	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 1
Urination					
None		8	7	9	8
Small amount		4	5	3	4

No significant difference in any treated groups from control group.

Table 2-52 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 6 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		5± 1	5± 2	6± 2	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 1	0± 0	0± 1
Urination					
None		9	8	9	7
Small amount		3	4	3	5

No significant difference in any treated groups from control group.

Table 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		7± 2	6± 2	8± 2	6± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	11
Small amount		0	0	0	1

No significant difference in any treated groups from control group.

Table 2-54 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		9± 3	7± 2	8± 1	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-55 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 1)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		7± 2	6± 2	7± 1	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	12	10	11
Small amount		1	0	2	1

No significant difference in any treated groups from control group.

Table 2-56 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 7)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 2	7± 2	6± 1	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	12	12	12
Small amount		2	0	0	0

No significant difference in any treated groups from control group.

Table 2-57 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 14)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 1	6± 2	7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	10
Small amount		0	0	1	2

No significant difference in any treated groups from control group.

Table 2-58 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Gestation day 20)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		6± 2	5± 1	6± 1	5± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	12	12

No significant difference in any treated groups from control group.

Table 2-59 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	12	12	11	11
Arousal					
Normal		12	12	11	11
Convulsion					
None		12	12	11	11
Abnormal behavior					
None		12	12	11	11
Stereotypy					
None		12	12	11	11
Gait					
Normal		12	12	11	11
Posture					
Normal		12	12	11	11
Grooming					
None		12	12	11	11
Rearing (Mean±S.D.)		6± 2	6± 2	6± 1	6± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	11

No significant difference in any treated groups from control group.

Table 2-60 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 1 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		7± 2	4± 2**T
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	9
Small amount		0	1

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

Table 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 2 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 3	8± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-62 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		8± 2	8± 4
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		9	10
Small amount		1	0

No significant difference between treated group and control group.

Table 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 4 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 2	10± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-64 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 5 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 2	10± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-65 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	10	10
Arousal			
Normal		10	10
Convulsion			
None		10	10
Abnormal behavior			
None		10	10
Stereotypy			
None		10	10
Gait			
Normal		10	10
Posture			
Normal		10	10
Grooming			
None		10	10
Rearing (Mean±S.D.)		9± 3	9± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		9	10
Small amount		1	0

No significant difference between treated group and control group.

Table 2-66 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 1 of recovery)

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

No significant difference between treated group and control group.

Table 2-67 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in male rats: open field observation (Week 2 of recovery)

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

No significant difference between treated group and control group.

Table 2-68 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Week 1 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		8± 2	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	4
Small amount		0	1

No significant difference between treated group and control group.

Table 2-69 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Detailed clinical signs in female rats: open field observation (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		9± 2	9± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	5

No significant difference between treated group and control group.

Table 2-70 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of male rats (Week 6 of administration)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		95±25	72±30	91±26	87±20

No significant difference in any treated groups from control group.

Table 2-71 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of female rats (Main group, Lactation day 4)

Parameter	Dose (mg/kg)	0	30	100	300
	No. of animals	5	5	5	5
Auditory response					
Normal		5	5	5	5
Approach response					
Normal		5	5	5	5
Touch response					
Normal		5	5	5	5
Tail pinch response					
Normal		5	5	5	5
Pupillary reflex					
Pass, both		5	5	5	5
Aerial righting reflex					
(Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		55±21	51±13	66± 9	44±10

No significant difference in any treated groups from control group.

Table 2-72 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of female rats (Satellite group, Week 6 of administration)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		73± 4	70±26

No significant difference between treated group and control group.

Table 2-73 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of male rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		96±31	69±13

No significant difference between treated group and control group.

Table 2-74 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of female rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	300
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		70± 9	65±13

No significant difference between treated group and control group.

Table 2-75 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Grip strength of male rats (Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1429	865
	S.D.	352	158
30	No.	5	5
	Mean	1519	834
	S.D.	458	216
100	No.	5	5
	Mean	1234	1029
	S.D.	146	103
300	No.	5	5
	Mean	1384	1006
	S.D.	169	91

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

Table 2-76 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Grip strength of female rats (Main group, Lactation day 4)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1301	864
	S.D.	184	129
30	No.	5	5
	Mean	1445	901
	S.D.	121	67
100	No.	5	5
	Mean	1467	890
	S.D.	75	93
300	No.	5	5
	Mean	1405	838
	S.D.	130	206

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

Table 2-77 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Grip strength of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1210	813
	S.D.	100	100
300	No.	5	5
	Mean	1236	785
	S.D.	136	106

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

Table 2-78 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Grip strength of male rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	2017	1064
	S.D.	50	117
300	No.	5	5
	Mean	1690**	1028
	S.D.	163AT	49

No.: No. of animals
**: $p<0.01$ (Significant difference from control group)
AT: Aspin-Welch t-test

Table 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Grip strength of female rats (Week 2 of recovery)

Dose mg/kg		Fore limb g	Hind limb g
0	No.	5	5
	Mean	1544	950
	S.D.	100	154
300	No.	5	5
	Mean	1481	831
	S.D.	219	59

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

Table 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Motor activity of male rats (Week 6 of administration)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	460	420	401	360	315	298	2253
	S.D.	24	32	47	49	104	72	240
30	No.	5	5	5	5	5	5	5
	Mean	451	385	314	286	194	111*	1741
	S.D.	23	38	120	85	139	85D	239
100	No.	5	5	5	5	5	5	5
	Mean	434	373	284	277	211	157	1736
	S.D.	23	83	133	138	143	120	535
300	No.	5	5	5	5	5	5	5
	Mean	478	417	432	394	264	230	2216
	S.D.	50	25	29	71	112	76	125

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

Table 2-81 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Motor activity of female rats (Main group, Lactation day 4)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	393	142	157	99	185	131	1107
	S.D.	59	119	101	87	133	107	418
30	No.	5	5	5	5	5	5	5
	Mean	290	157	48	127	143	80	845
	S.D.	58	90	22	128	113	132	350
100	No.	5	5	5	5	5	5	5
	Mean	415	228	188	140	143	155	1270
	S.D.	73	124	132	132	159	88	578
300	No.	5	5	5	5	5	5	5
	Mean	413	247	127	141	133	178	1239
	S.D.	93	140	171	158	116	118	571

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

Table 2-82 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Motor activity of female rats (Satellite group, Week 6 of administration)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	405	316	287	281	199	182	1670
	S.D.	24	34	109	66	90	99	350
300	No.	5	5	5	5	5	5	5
	Mean	417	328	241	277	286	220	1770
	S.D.	76	129	42	90	113	128	443

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

Table 2-83 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Motor activity of male rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	398	380	364	330	247	200	1919
	S.D.	49	78	32	76	130	136	377
300	No.	5	5	5	5	5	5	5
	Mean	428	400	338	186	292	181	1826
	S.D.	23	41	41	176	159	149	498

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

Table 2-84 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Motor activity of female rats (Week 2 of recovery)

Dose mg/kg		Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
0	No.	5	5	5	5	5	5	5
	Mean	335	287	242	325	220	150	1559
	S.D.	50	55	96	103	99	148	430
300	No.	5	5	5	5	5	5	5
	Mean	338	315	302	229	185	169	1538
	S.D.	71	49	91	110	62	103	339

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

Table 3-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of male rats (Administration period)

Dose mg/kg		Day of administration 1	8	15	22	29	36	42	Gain 1-42
	No.	12	12	12	12	12	12	12	12
0	Mean	417	446	472	491	516	538	552	135
	S.D.	16	17	21	22	24	27	23	18
	No.	12	12	12	12	12	12	12	12
30	Mean	420	453	478	503	527	548	558	138
	S.D.	15	19	21	24	25	27	28	19
	No.	12	12	12	12	12	12	12	12
100	Mean	419	450	478	500	525	547	560	140
	S.D.	17	17	21	23	26	27	24	14
	No.	12	12	12	12	12	12	12	12
300	Mean	420	448	472	491	513	532	545	124
	S.D.	15	17	19	23	26	27	26	20

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

Table 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration 1	8	15	Gain 1-15
	No.	12	12	12	12
0	Mean	261	275	288	27
	S.D.	12	13	13	6
	No.	12	12	12	12
30	Mean	263	278	289	26
	S.D.	14	14	13	8
	No.	12	12	12	12
100	Mean	261	273	283	22
	S.D.	11	14	15	9
	No.	12	12	12	12
300	Mean	261	269	276	15**
	S.D.	12	15	15	6D

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

Table 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of dams during the gestation period (Main group)

Dose mg/kg		Administration 0	7	14	20a)	Gain 0-20
	No.	12	12	12	12	12
0	Mean	294	333	370	453	159
	S.D.	15	16	21	21	14
	No.	12	12	12	12	12
30	Mean	294	335	375	462	168
	S.D.	16	18	25	32	22
	No.	12	12	12	12	12
100	Mean	288	321	363	449	161
	S.D.	16	16	20	21	9
	No.	12	12	12	12	12
300	Mean	280	312**	353	425*	145
	S.D.	13	13D	17	19D	15

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

Table 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of dams during the lactation period (Main group)

Dose mg/kg		Administration 0	Administration 4a)	Gain 0-4
	No.	12	12	12
0	Mean	352	364	12
	S.D.	27	24	12
	No.	12	12	12
30	Mean	356	373	16
	S.D.	20	19	14
	No.	12	11b)	11
100	Mean	350	356	8
	S.D.	28	17	15
	No.	12	11c)	11
300	Mean	334	347	10
	S.D.	21	19	13

Unit: g
No.: No. of dams
a): Lactation day
b): One dam was necropsied on lactation day 2 because all pups died.
c): One dam was necropsied on lactation day 4 because all pups died.
No significant difference in any treated groups from control group.

Table 3-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of female rats (Satellite group, Administration period)

Dose mg/kg		Day of administration 1	8	15	22	29	36	42	Gain 1-42
	No.	10	10	10	10	10	10	10	10
0	Mean	261	277	290	298	309	316	322	60
	S.D.	13	16	15	18	22	24	21	10
	No.	10	10	10	10	10	10	10	10
300	Mean	264	272	283	290	299	304	313	49*
	S.D.	11	14	13	13	16	17	16	9T

Unit: g
No.: No. of animals
*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14	Gain 1-14
	No.	5	5	5	5
0	Mean	554	566	570	16
	S.D.	31	30	28	6
	No.	5	5	5	5
300	Mean	541	554	565	24
	S.D.	27	27	24	10

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

Table 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of female rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14	Gain 1-14
	No.	5	5	5	5
0	Mean	326	324	328	2
	S.D.	18	13	16	7
	No.	5	5	5	5
300	Mean	322	332	332	10
	S.D.	15	14	13	17

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

Table 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of male rats (Administration period)

Dose mg/kg		Day of administration 2	8	15	30	36	42
	No.	12	12	12	12	12	12
0	Mean	24	24	24	23	24	23
	S.D.	2	2	2	2	2	2
	No.	12	12	12	12	12	12
30	Mean	24	24	23	23	21*	23
	S.D.	1	1	2	2	2D	2
	No.	12	12	12	12	12	12
100	Mean	23	25	24	23	23	24
	S.D.	2	3	1	1	2	2
	No.	12	12	12	12	12	12
300	Mean	23	24	24	23	24	25
	S.D.	1	2	2	3	2	2

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

Table 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of female rats during the pre-mating period (Main group)

Dose mg/kg		Day of administration 2	8	15
	No.	12	12	12
0	Mean	18	17	19
	S.D.	2	3	3
	No.	12	12	12
30	Mean	17	18	18
	S.D.	1	3	2
	No.	12	12	12
100	Mean	16	18	19
	S.D.	3	4	2
	No.	12	12	12
300	Mean	14**	18	18
	S.D.	3D	2	2

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

Table 4-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of dams during the gestation period (Main group)

Dose mg/kg		Administration 1	7	14	20a)
	No.	12	12	12	12
0	Mean	19	23	24	20
	S.D.	3	3	4	3
	No.	12	12	12	12
30	Mean	19	24	24	22
	S.D.	2	3	4	3
	No.	12	12	12	12
100	Mean	18	23	26	22
	S.D.	3	3	4	2
	No.	12	12	12	12
300	Mean	16	23	26	23
	S.D.	4	3	4	4

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

Table 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of dams during the lactation period (Main group)

Dose mg/kg		Administration 2	4a)
0	No.	12	12
	Mean	22	37
	S.D.	5	5
30	No.	12	12
	Mean	23	38
	S.D.	6	4
100	No.	11b)	11
	Mean	20	37
	S.D.	4	5
300	No.	12	11c)
	Mean	21	39
	S.D.	8	7

Unit: g/rat/day
No.: No. of dams
a): Lactation day
b): One dam was necropsied on lactation day 2 because all pups died.
c): One dam was necropsied on lactation day 4 because all pups died.
No significant difference in any treated groups from control group.

Table 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of female rats (Satellite group, Administration period)

Dose mg/kg		Day of administration 2	8	15	30	36	42
	No.	10	10	10	10	10	10
0	Mean	15	18	18	17	16	17
	S.D.	3	2	2	2	3	2
	No.	10	10	10	10	10	10
300	Mean	13	16	17	16	15	19
	S.D.	2	3	2	2	3	1

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

Table 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of male rats (Recovery period)

Dose mg/kg		Day of recovery 2	8	14
	No.	5	5	5
0	Mean	23	28	28
	S.D.	3	1	2
	No.	5	5	5
300	Mean	26	29	29
	S.D.	3	3	2

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

Table 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of female rats (Recovery period)

Dose mg/kg		Day of recovery 2	8	14
	No.	5	5	5
0	Mean	17	20	21
	S.D.	2	2	4
	No.	5	5	5
300	Mean	21*	25*	21
	S.D.	2T	3T	4

Unit: g/rat/day
No.: No. of animals
*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 5-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	pH 5.0	5.5	6.0	6.5	7.0	7.5	8.0	8.5	>=9.0	Protein 1) -	+-	+	++	+++	Ketone body 2) -	+-	+	++	+++	Glucose 3) -	+	++	+++	++++
0	5	0	0	0	0	0	1	0	4	0	0	1	4	0	0	0	3	2	0	0	5	0	0	0	0
30	5	0	0	0	0	0	1	0	2	2	0	2	2	1	0	0	2	3	0	0	5	0	0	0	0
100	5	0	0	0	0	0	1	2	2	0	1	1	2	1	0	0	1	4	0	0	5	0	0	0	0
300	5	0	0	0	0	1	1	1	2	0	0	0	2	3	0	1	1	3	0	0	5	0	0	0	0

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

Table 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.	Occult blood 4)					Bilirubin 5)				Urobilinogen 6)				Color 7)		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	**1**	**4**	0	0	0	5	0	0	0	5	0	0	0	0	5	0
30	5	**1**	**4**	0	0	0	5	0	0	0	5	0	0	0	0	5	0
100	5	2	3	0	0	0	5	0	0	0	5	0	0	0	0	5	0
300	5	2	3	0	0	0	5	0	0	0	5	0	0	0	0	5	0

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

Table 5-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 6 of administration)

| | | URINE SEDIMENT | | |

Table 5-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Water intake and urinalysis of male rats (Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	40	16.2	1589	1.30	4.25	1.87
		S.D.	5	1.4	312	0.45	1.03	0.52
30	5	Mean	46	18.4	1528	1.16	3.79	1.53
		S.D.	11	10.5	563	0.39	1.04	0.46
100	5	Mean	48	20.2	1430	1.09	4.06	1.54
		S.D.	11	11.6	506	0.24	0.74	0.35
300	5	Mean	40	14.2	1700	1.17	3.67	1.55
		S.D.	2	3.7	335	0.29	0.89	0.44

No significant difference in any treated groups from control group.

Table 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

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

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

Table 5-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

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

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

Table 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, Week 6 of administration)

| | | URINE SEDIMENT | | |

Table 5-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Water intake and urinalysis of female rats (Satellite group, Week 6 of administration)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	29	8.6	1911	0.68	2.38	1.05
		S.D.	3	4.6	541	0.26	0.76	0.43
300	5	Mean	31	5.2	2118	0.57	1.55	0.78
		S.D.	7	2.8	455	0.32	0.53	0.24

No significant difference between treated group and control group.

Table 5-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

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

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

Table 5-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.	Occult blood 4)					Bilirubin 5)				Urobilinogen 6)				Color 7)		
		-	+-	+	++	+++	-	+	++	+++	+-	+	++	+++	LY	Y	DY
0	5	3	2	0	0	0	5	0	0	0	5	0	0	0	0	5	0
300	5	2	3	0	0	0	5	0	0	0	5	0	0	0	0	5	0

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

Table 5-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

		URINE SEDIMENT																																							
																														CRYSTALLIZATION											
		RBC					WBC					SEC					SREC					Cast			PS					CO				
Dose mg/kg	No.	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	++	+++	-	+-	+	-	+-	+	++	+++	-	+-	+	++	+++
0	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	3	2	0	0	5	0	0	0	0
300	5	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	5	0	0	0	0	5	0	0	0	4	1	0	0	5	0	0	0	0

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

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

Table 5-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Water intake and urinalysis of male rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	46	19.4	1808	1.70	5.49	2.13
		S.D.	10	4.6	233	0.25	0.77	0.36
300	5	Mean	43	16.6	1866	1.56	4.80	1.97
		S.D.	8	5.1	109	0.42	1.48	0.60

No significant difference between treated group and control group.

Table 5-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Week 2 of recovery)

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

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

Table 5-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Week 2 of recovery)

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

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

Table 5-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Week 2 of recovery)

| | | URINE SEDIMENT | | |

Table 5-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Water intake and urinalysis of female rats (Week 2 of recovery)

Dose mg/kg	No.		Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
0	5	Mean	33	10.0	1933	0.86	2.97	1.10
		S.D.	2	2.5	328	0.32	0.55	0.28
300	5	Mean	32	8.4	2364	0.93	3.01	1.18
		S.D.	7	2.4	391	0.24	0.48	0.25

No significant difference between treated group and control group.

Table 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of male rats (End of administration)

Dose mg/kg	No.		RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
0	5	Mean	870	15.5	44.0	50.6	17.8	35.2	2.0	92.4	13.6	18.6	231
		S.D.	61	0.7	2.3	1.5	0.8	0.5	0.2	4.9	2.2	2.4	23
30	5	Mean	864	15.6	44.1	51.2	18.1	35.3	1.9	99.1	12.9	17.8	233
		S.D.	29	0.3	0.7	2.1	0.9	0.3	0.6	9.9	1.1	2.2	34
100	5	Mean	839	15.3	43.3	51.6	18.3	35.4	2.2	96.5	13.9	18.0	265
		S.D.	29	0.4	1.1	1.3	0.6	0.3	0.4	13.1	2.3	2.4	11
300	5	Mean	853	15.3	43.4	50.9	18.0	35.3	1.9	98.2	15.2	19.2	241
		S.D.	18	0.4	0.8	0.3	0.2	0.4	0.2	13.5	1.7	1.6	24

No significant difference in any treated groups from control group.

Table 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of male rats (End of administration)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	66.5	73.6	21.4	1.5	0.4	2.6	0.6	49.4	13.8	0.9	0.2	1.7	0.4
		S.D.	11.7	6.8	6.2	0.7	0.1	0.8	0.3	13.0	2.8	0.4	0.1	0.5	0.2
30	5	Mean	63.2	73.2	22.3	1.5	0.4	2.0	0.5	46.3	14.2	0.9	0.3	1.3	0.4
		S.D.	19.0	2.3	2.1	0.6	0.1	0.6	0.3	14.2	4.5	0.3	0.1	0.5	0.2
100	5	Mean	97.1*	74.2	21.5	1.2	0.3	2.2	0.6	72.0	21.1	1.1	0.3	2.0	0.6
		S.D.	24.3D	6.5	6.0	0.4	0.0	0.8	0.2	18.7	9.0	0.5	0.1	0.5	0.1
300	5	Mean	66.4	67.4	28.4	1.1	0.3	2.2	0.6	44.8	18.8	0.7	0.2	1.4	0.4
		S.D.	7.0	7.6	6.9	0.4	0.1	0.6	0.3	7.5	5.0	0.3	0.1	0.5	0.2

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

Table 6-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
0	5	Mean	711	13.5	38.5	54.3	19.0	34.9	6.4	146.1	11.9	14.8	305
		S.D.	49	0.6	1.6	2.1	0.9	0.3	1.4	19.5	0.9	2.2	66
30	5	Mean	708	13.5	38.3	54.1	19.0	35.1	5.3	114.6**	11.8	14.9	299
		S.D.	17	0.4	1.0	0.9	0.4	0.3	1.1	12.9D	0.4	2.9	68
100	5	Mean	714	13.5	38.4	53.9	18.9	35.2	5.1	123.2*	11.5	13.9	285
		S.D.	12	0.3	0.4	1.3	0.6	0.4	1.0	6.9D	0.6	2.5	55
300	5	Mean	715	13.7	39.3	54.9	19.3	35.0	6.5	136.4	12.4	15.5	275
		S.D.	19	0.3	0.9	1.9	0.6	0.3	1.4	9.7	0.9	1.3	29

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

Table 6-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of female rats (Lactation day 5)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	98.7	57.0	38.6	1.0	0.2	2.4	0.9	55.5	38.8	1.0	0.2	2.4	0.9
		S.D.	21.3	8.9	9.5	0.5	0.1	0.5	0.5	10.9	16.6	0.6	0.1	0.9	0.5
30	5	Mean	118.8	54.7	41.2	0.6	0.2	2.6	0.8	64.8	49.1	0.7	0.3	3.1	0.9
		S.D.	28.4	5.9	5.7	0.2	0.1	0.8	0.2	15.4	15.4	0.2	0.2	1.5	0.1
100	5	Mean	124.3	56.8	38.7	0.5	0.2	2.5	1.2	69.0	49.9	0.6	0.3	2.9	1.5
		S.D.	25.4	9.2	10.2	0.1	0.1	1.0	0.7	7.6	22.5	0.2	0.0	0.9	0.7
300	5	Mean	111.3	58.7	37.0	0.6	0.3	2.7	0.8	65.6	40.9	0.6	0.3	3.0	0.9
		S.D.	23.2	1.8	2.0	0.3	0.1	0.3	0.3	15.2	7.3	0.2	0.1	0.8	0.4

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

Table 6-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	825	15.2	42.4	51.4	18.4	35.8	2.1	111.2	11.7	14.0	179
		S.D.	35	0.8	1.9	0.9	0.5	0.5	0.2	9.8	0.7	2.0	11
300	5	Mean	766*	14.8	40.5	52.8*	19.3*	36.5	2.3	114.4	11.4	13.6	188
		S.D.	27T	0.6	1.4	0.9T	0.5T	0.7	0.6	7.6	0.7	1.4	9

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

Table 6-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of female rats (Satellite group, End of administration)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	48.0	67.3	27.0	2.9	0.3	2.0	0.5	32.1	13.3	1.3	0.1	0.9	0.2
		S.D.	9.0	8.1	8.2	0.6	0.1	0.5	0.2	5.2	5.9	0.2	0.1	0.3	0.1
300	5	Mean	51.0	75.6	18.8	1.9	0.2	2.7	0.7	39.8	8.7	0.8	0.1	1.2	0.4
		S.D.	24.1	10.4	9.3	1.5	0.1	1.2	0.4	22.2	3.2	0.5	0.1	0.4	0.3

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

Table 6-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of male rats (End of recovery)

Dose mg/kg	No.		RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
0	5	Mean	890	15.6	44.4	49.9	17.6	35.2	2.1	101.0	16.4	20.7	252
		S.D.	30	0.1	1.1	1.5	0.6	0.9	0.3	4.6	0.3	2.5	18
300	5	Mean	872	15.8	45.2	51.8*	18.1	35.0	2.1	99.2	14.7	20.5	258
		S.D.	19	0.6	1.7	0.9T	0.4	0.3	0.4	6.8	1.5	3.2	31

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

Table 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of male rats (End of recovery)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	69.6	76.4	17.2	2.3	0.3	3.1	0.7	54.2	11.1	1.4	0.2	2.1	0.5
		S.D.	29.8	6.3	5.7	1.0	0.0	0.5	0.5	26.4	3.9	0.3	0.1	0.9	0.5
300	5	Mean	73.9	78.5	16.6	1.5	0.4	2.4	0.6	57.7	12.6	1.1	0.3	1.8	0.4
		S.D.	28.0	4.5	4.1	0.3	0.1	0.6	0.2	20.9	6.7	0.4	0.1	0.9	0.2

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

Table 6-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of female rats (End of recovery)

Dose mg/kg	No.		RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
0	5	Mean	817	15.2	42.6	52.2	18.7	35.8	2.1	110.3	11.1	14.9	175
		S.D.	36	0.5	1.1	2.3	0.9	0.3	0.5	15.8	0.7	1.8	22
300	5	Mean	804	15.0	42.0	52.2	18.6	35.6	2.1	116.7	11.5	15.6	166
		S.D.	34	0.8	1.9	0.5	0.3	0.4	0.5	12.1	0.8	2.2	19

No significant difference between treated group and control group.

Table 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Hematology of female rats (End of recovery)

Dose mg/kg	No.		WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
0	5	Mean	53.3	76.4	18.6	1.5	0.3	2.4	0.9	40.5	10.1	0.8	0.2	1.4	0.4
		S.D.	20.8	7.1	5.8	0.4	0.2	1.4	0.2	15.4	5.6	0.3	0.2	1.0	0.2
300	5	Mean	59.8	78.5	15.5	1.7	0.3	2.8	1.0	46.7	9.5	1.1	0.2	1.7	0.6
		S.D.	15.5	7.5	6.9	0.6	0.2	0.7	0.7	12.1	5.2	0.5	0.2	0.6	0.4

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

Table 7-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	61	29	46	0	310	13.4	52	33	84	0.1	127
		S.D.	5	5	10	0	35	11.1	9	13	12	0.0	11
30	5	Mean	59	25	50	0	307	12.0	60	28	87	0.1	127
		S.D.	5	4	11	0	96	7.4	9	12	10	0.1	15
100	5	Mean	61	27	48	0	308	11.0	51	34	80	0.0	125
		S.D.	13	6	11	1	43	8.8	5	11	5	0.0	10
300	5	Mean	63	27	48	0	298	17.6	62	29	90	0.0	122
		S.D.	8	4	11	0	48	14.7	14	6	17	0.1	18

No significant difference in any treated groups from control group.

Table 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of male rats (End of administration)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	13	0.27	143	4.5	106	10.0	6.4	5.9	3.3	1.26
		S.D.	1	0.02	1	0.2	1	0.2	0.6	0.1	0.1	0.09
30	5	Mean	13	0.28	144	4.5	106	10.1	6.4	5.8	3.2	1.23
		S.D.	2	0.04	2	0.1	3	0.2	0.5	0.2	0.0	0.10
100	5	Mean	13	0.30	143	4.7	105	10.1	6.5	5.9	3.2	1.19
		S.D.	1	0.03	2	0.2	1	0.3	0.6	0.3	0.1	0.09
300	5	Mean	13	0.29	144	4.7	105	10.1	6.0	5.8	3.3	1.28
		S.D.	2	0.05	1	0.2	1	0.2	0.3	0.2	0.1	0.08

No significant difference in any treated groups from control group.

Table 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	84	51	38	1	199	28.8	62	34	109	0.1	115
		S.D.	17	12	8	1	49	25.7	5	5	6	0.0	11
30	5	Mean	84	52	32	1	184	15.9	52	46	100	0.0	130
		S.D.	21	12	5	1	47	11.6	15	17	20	0.1	11
100	5	Mean	74	47	32	0	272	17.6	59	60*	109	0.0	129
		S.D.	19	11	4	1	61	4.0	8	10D	13	0.1	16
300	5	Mean	68	41	35	0	212	12.9	56	42	99	0.1	128
		S.D.	9	9	6	0	57	5.9	13	16	19	0.1	14

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

Table 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of female rats (Lactation day 5)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	13	0.32	142	4.2	106	10.2	6.8	5.9	3.4	1.39
		S.D.	2	0.05	1	0.6	1	0.2	0.5	0.2	0.1	0.08
30	5	Mean	13	0.30	141	4.2	106	10.5	6.9	6.0	3.5	1.38
		S.D.	2	0.04	1	0.5	2	0.2	0.8	0.3	0.1	0.09
100	5	Mean	11	0.28	141	4.2	104	10.5	7.3	6.1	3.4	1.31
		S.D.	3	0.03	1	0.5	2	0.2	0.8	0.3	0.1	0.04
300	5	Mean	13	0.31	142	4.3	106	10.2	6.8	5.9	3.3	1.31
		S.D.	2	0.04	1	0.5	2	0.3	0.9	0.2	0.1	0.08

No significant difference in any treated groups from control group.

Table 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	55	24	33	0	203	10.2	62	18	113	0.0	137
		S.D.	5	6	8	1	66	2.7	19	4	32	0.1	8
300	5	Mean	49	21	34	0	148	8.8	73	22	132	0.0	119*
		S.D.	6	2	8	0	46	2.8	7	4	10	0.1	11T

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

Table 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of female rats (Satellite group, End of administration)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	16	0.36	143	4.2	109	10.2	4.2	6.4	3.9	1.52
		S.D.	1	0.03	1	0.2	1	0.4	0.5	0.5	0.4	0.22
300	5	Mean	15	0.33	143	4.6**	107*	10.6	5.1	6.6	4.0	1.52
		S.D.	1	0.04	1	0.2T	1T	0.1	1.1	0.4	0.2	0.09

*: $p<0.05$; **: $p<0.01$ (Significant difference from control group)
T: Student's t-test

Table 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	63	27	44	0	242	11.3	51	25	80	0.0	135
		S.D.	5	3	5	0	8	3.2	8	6	8	0.1	12
300	5	Mean	66	30	49	0	260	13.2	66*	36	94*	0.1	146
		S.D.	12	4	14	0	52	7.2	7T	15	11T	0.0	11

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

Table 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of male rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	17	0.33	142	4.7	106	9.7	5.7	6.0	3.3	1.23
		S.D.	1	0.02	2	0.1	1	0.3	0.6	0.2	0.1	0.15
300	5	Mean	17	0.33	143	4.4	107	9.6	5.7	5.8	3.2	1.24
		S.D.	2	0.05	1	0.3	2	0.1	0.4	0.2	0.1	0.07

No significant difference between treated group and control group.

Table 7-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
0	5	Mean	99	58	56	1	115	19.0	76	16	135	0.1	133
		S.D.	47	51	17	0	19	12.4	36	4	53	0.0	15
300	5	Mean	72	35	42	0	136	12.1	71	25	127	0.1	123
		S.D.	6	6	10	1	48	5.9	24	19	41	0.0	19

No significant difference between treated group and control group.

Table 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Blood chemistry of female rats (End of recovery)

Dose mg/kg	No.		BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
0	5	Mean	17	0.34	143	4.1	108	10.4	5.2	6.8	4.1	1.50
		S.D.	2	0.03	1	0.3	1	0.5	0.6	0.5	0.4	0.11
300	5	Mean	21	0.38	143	4.3	108	10.2	5.5	6.5	3.8	1.41
		S.D.	4	0.06	1	0.3	3	0.2	0.6	0.4	0.3	0.10

No significant difference between treated group and control group.

Table 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of male rats (End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	7	7	7	7	7	7	7
		Mean	528	2.20	13.2	22.6	316	1.55	13.90
		S.D.	27	0.08	1.8	3.7	72	0.12	1.28
	30	No.	12	12	12	12	12	12	12
		Mean	539	2.16	13.7	24.7	264	1.52	14.18
		S.D.	27	0.06	1.6	4.5	49	0.13	1.15
	100	No.	12	12	12	12	12	12	12
		Mean	536	2.18	13.2	24.8	281	1.59	14.57
		S.D.	26	0.08	1.7	4.2	56	0.14	1.14
	300	No.	7	7	7	7	7	7	7
		Mean	524	2.18	13.2	21.9	286	1.51	15.15
		S.D.	27	0.07	0.7	2.7	51	0.10	1.02
Relative	0	No.		7	7	7	7	7	7
		Mean		0.42	2.5	4.3	60	0.30	2.63
		S.D.		0.03	0.3	0.6	12	0.03	0.16
	30	No.		12	12	12	12	12	12
		Mean		0.40	2.5	4.6	49	0.28	2.63
		S.D.		0.02	0.3	1.0	9	0.02	0.15
	100	No.		12	12	12	12	12	12
		Mean		0.41	2.5	4.6	53	0.30	2.72
		S.D.		0.02	0.3	0.7	11	0.03	0.10
	300	No.		7	7	7	7	7	7
		Mean		0.42	2.5	4.2	54	0.29	2.89**
		S.D.		0.02	0.1	0.4	8	0.01	0.12D

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

Table 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of male rats (End of administration)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
		No.	7	7	7	7	7	7	7
Absolute	0	Mean	0.75	3.42	69	3.51	1382	1.97	1.45
		S.D.	0.05	0.30	17	0.23	96	0.31	0.28
		No.	12	12	12	12	12	12	12
	30	Mean	0.73	3.82*	68	3.57	1377	1.84	1.32
		S.D.	0.12	0.29D	11	0.44	125	0.25	0.20
		No.	12	12	12	12	12	12	12
	100	Mean	0.79	4.08**	68	3.51	1440	1.72	1.31
		S.D.	0.12	0.37D	9	0.34	129	0.27	0.19
		No.	7	7	7	7	7	7	7
	300	Mean	0.78	4.12**	68	3.55	1457	1.81	1.35
		S.D.	0.08	0.39D	6	0.16	121	0.21	0.30
		No.	7	7	7	7	7	7	7
Relative	0	Mean	0.14	0.65	13	0.66	262	0.38	0.28
		S.D.	0.01	0.06	4	0.05	11	0.07	0.05
		No.	12	12	12	12	12	12	12
	30	Mean	0.13	0.71	13	0.66	256	0.34	0.25
		S.D.	0.02	0.04	2	0.08	24	0.04	0.04
		No.	12	12	12	12	12	12	12
	100	Mean	0.15	0.76**	13	0.66	269	0.32	0.24
		S.D.	0.02	0.06D	2	0.06	24	0.05	0.03
		No.	7	7	7	7	7	7	7
	300	Mean	0.15	0.79**	13	0.68	278	0.35	0.26
		S.D.	0.02	0.07D	2	0.04	24	0.04	0.05

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

Table 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of female rats (Main group, End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	12	12	12	12	12	12	12
		Mean	338	2.02	18.3	17.5	197	1.08	10.86
		S.D.	20	0.06	2.8	3.0	60	0.08	0.86
	30	No.	12	12	12	12	12	12	12
		Mean	343	2.00	18.2	17.5	197	1.06	11.13
		S.D.	20	0.10	2.5	2.9	29	0.06	0.55
	100	No.	11	11	11	11	11	11	11
		Mean	330	2.02	17.3	18.2	213	1.01*	11.14
		S.D.	21	0.09	1.7	2.6	52	0.07D	0.99
	300	No.	11	11	11	11	11	11	11
		Mean	319	2.03	18.4	17.5	178	1.00*	11.27
		S.D.	16	0.05	2.1	2.9	47	0.07D	1.08
Relative	0	No.		12	12	12	12	12	12
		Mean		0.60	5.4	5.2	58	0.32	3.21
		S.D.		0.04	0.8	0.8	16	0.03	0.23
	30	No.		12	12	12	12	12	12
		Mean		0.58	5.3	5.1	58	0.31	3.25
		S.D.		0.03	0.7	0.9	9	0.02	0.16
	100	No.		11	11	11	11	11	11
		Mean		0.62	5.3	5.5	64	0.30	3.37
		S.D.		0.05	0.5	0.9	15	0.02	0.19
	300	No.		11	11	11	11	11	11
		Mean		0.64*	5.8	5.5	56	0.31	3.53**
		S.D.		0.03D	0.5	0.9	15	0.02	0.29D

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

Table 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of female rats (Main group, End of administration)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	12	12	12	12	12
		Mean	0.72	2.26	87	120.7	724
		S.D.	0.13	0.17	11	11.9	53
	30	No.	12	12	12	12	12
		Mean	0.67	2.31	88	111.9	668
		S.D.	0.06	0.14	10	12.6	48
	100	No.	11	11	11	11	11
		Mean	0.67	2.27	87	114.6	711
		S.D.	0.11	0.16	11	14.3	80
	300	No.	11	11	11	11	11
		Mean	0.62	2.32	96	117.2	658
		S.D.	0.09	0.16	9	15.2	99
Relative	0	No.	12	12	12	12	12
		Mean	0.21	0.67	26	35.8	214
		S.D.	0.04	0.04	3	3.7	18
	30	No.	12	12	12	12	12
		Mean	0.20	0.67	26	32.6	195
		S.D.	0.01	0.05	4	3.5	12
	100	No.	11	11	11	11	11
		Mean	0.20	0.69	26	34.7	217
		S.D.	0.03	0.06	3	3.8	32
	300	No.	11	11	11	11	11
		Mean	0.19	0.73*	30*	36.7	206
		S.D.	0.03	0.05D	3D	4.7	30

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

Table 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of female rats (Satellite group, End of administration)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	306	1.98	17.7	16.6	358	0.96	8.02
		S.D.	26	0.04	4.3	4.3	105	0.06	0.91
	300	No.	5	5	5	5	5	5	5
		Mean	289	2.00	18.9	17.3	282	0.90	8.69
		S.D.	13	0.05	1.9	1.2	62	0.06	0.76
Relative	0	No.		5	5	5	5	5	5
		Mean		0.65	5.8	5.4	115	0.32	2.61
		S.D.		0.05	1.3	1.1	23	0.02	0.15
	300	No.		5	5	5	5	5	5
		Mean		0.69	6.5	6.0	97	0.31	3.00**
		S.D.		0.02	1.0	0.3	17	0.02	0.16T

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

Table 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of female rats (Satellite group, End of administration)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5
		Mean	0.50	2.01	80	93.1	682
		S.D.	0.03	0.13	12	30.3	105
	300	No.	5	5	5	5	5
		Mean	0.52	2.13	89	111.8	635
		S.D.	0.10	0.30	15	15.4	171
Relative	0	No.	5	5	5	5	5
		Mean	0.16	0.66	26	30.5	223
		S.D.	0.02	0.04	4	10.1	33
	300	No.	5	5	5	5	5
		Mean	0.18	0.74	31	38.6	220
		S.D.	0.03	0.09	5	4.0	59

No significant difference between treated group and control group.

Table 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of male rats (End of recovery)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	538	2.24	13.9	20.6	288	1.47	13.00
		S.D.	27	0.15	1.1	2.4	92	0.13	0.76
	300	No.	5	5	5	5	5	5	5
		Mean	534	2.18	13.7	22.8	259	1.40	13.44
		S.D.	24	0.05	2.1	3.8	31	0.06	1.45
Relative	0	No.		5	5	5	5	5	5
		Mean		0.41	2.6	3.8	54	0.27	2.41
		S.D.		0.02	0.2	0.3	18	0.02	0.09
	300	No.		5	5	5	5	5	5
		Mean		0.41	2.6	4.3	49	0.26	2.51
		S.D.		0.02	0.4	0.8	8	0.02	0.18

No significant difference between treated group and control group.

Table 8-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of male rats (End of recovery)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R+L) g(g/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	0	No.	5	5	5	5	5	5	5
		Mean	0.68	3.54	64	3.36	1340	1.76	1.21
		S.D.	0.10	0.20	14	0.62	213	0.22	0.11
	300	No.	5	5	5	5	5	5	5
		Mean	0.73	3.53	63	3.69	1433	1.68	1.21
		S.D.	0.07	0.43	5	0.22	81	0.24	0.19
Relative	0	No.	5	5	5	5	5	5	5
		Mean	0.13	0.66	12	0.63	250	0.33	0.23
		S.D.	0.02	0.01	2	0.11	43	0.04	0.03
	300	No.	5	5	5	5	5	5	5
		Mean	0.14	0.66	12	0.69	269	0.31	0.23
		S.D.	0.02	0.06	1	0.07	16	0.04	0.03

No significant difference between treated group and control group.

Table 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of female rats (End of recovery)

	Dose mg/kg		Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)	Heart g(g/100g BW)	Liver g(g/100g BW)
		No.	5	5	5	5	5	5	5
Absolute	0	Mean	307	2.01	17.8	17.1	236	0.91	7.71
		S.D.	16	0.04	2.7	2.5	33	0.03	0.86
		No.	5	5	5	5	5	5	5
	300	Mean	310	2.11*	17.7	19.2	278	1.00*	8.21
		S.D.	10	0.08T	3.3	2.3	60	0.07T	0.82
		No.		5	5	5	5	5	5
Relative	0	Mean		0.66	5.8	5.6	77	0.30	2.52
		S.D.		0.02	1.1	0.8	10	0.01	0.28
		No.		5	5	5	5	5	5
	300	Mean		0.68	5.7	6.2	89	0.32	2.65
		S.D.		0.04	1.2	0.7	18	0.03	0.28

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

Table 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Organ weight of female rats (End of recovery)

	Dose mg/kg		Spleen g(g/100g BW)	Kidney (R+L) g(g/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	0	No.	5	5	5	5	5
		Mean	0.56	2.14	76	110.0	654
		S.D.	0.08	0.12	10	11.1	162
	300	No.	5	5	5	5	5
		Mean	0.60	2.20	84	96.8	586
		S.D.	0.07	0.11	4	28.0	123
Relative	0	No.	5	5	5	5	5
		Mean	0.18	0.70	25	35.9	213
		S.D.	0.02	0.05	3	3.8	49
	300	No.	5	5	5	5	5
		Mean	0.19	0.71	27	31.2	190
		S.D.	0.02	0.03	1	9.4	45

No significant difference between treated group and control group.

R-1135

Table 9-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (End of administration period (D42))

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
Findings	Number:	7	12	12	7
Epididymis					
Nodule		1	0	0	0
Kidney					
Dilatation,pelvic		0	0	1	0

M : Male

Table 9-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (End of administration period (D42))

Organs	Sex:	F	F
	Dose(mg/kg):	0	300
Findings	Number:	5	5
All tissues			
Not remarkable		5	5

F : Female

Table 9-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
	Dose(mg/kg):	0	30	100	300
Findings	Number:	12	12	11	11
Lung(bronchus)					
Focus,dark red		0	1	0	0
Stomach					
Focus,dark red,glandular stomach		0	2	1	0

F : Female

Table 9-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Epididymis			
Small		1	0
Testis			
Small		1	0

M : Male

Table 9-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (End of recovery period)

Organs	Sex:	F	F
	Dose(mg/kg):	0	300
Findings	Number:	5	5
All tissues			
Not remarkable		5	5

F : Female

Table 9-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (All littermates died)

Organs	Sex:	F	F
	Dose(mg/kg):	100	300
Findings	Number:	1	1
General descriptions			
Fracture,incisor		0	1
Mammary gland,inguinal			
Undeveloped		0	1
Stomach			
Focus,white,forestomach		0	1

F : Female

Table 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
	Number:	7	12	12	7
Adrenal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Bone+Bone marrow,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebellum(Pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Epididymis					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Granuloma,spermatic		1	0	0	0
mild		1	0	0	0
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Cell infiltration		1	0	0	0
minimal		1	0	0	0
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	5	5	5
Not remarkable		3	0	0	0
Regeneration,tubular		2	2	4	5
minimal		2	2	2	1
mild		0	0	2	4

M : Male

Table 10-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
	Number:	7	12	12	7
Kidney (continued)					
Urinary cast,granular		0	0	0	1
minimal		0	0	0	1
Eosinophilic body,tubular cell		0	5	5	5
minimal		0	2	1	0
mild		0	3	4	2
moderate		0	0	0	3
Hyperplasia,transitional,focal		0	1	0	0
minimal		0	1	0	0
Kidney(alpha2u globulin)					
Number examined		0	0	0	2
Alpha2u globulin immunohistochemistry positive		0	0	0	2
Liver					
Number examined		5	0	0	5
Not remarkable		1	0	0	1
Microgranuloma		4	0	0	4
minimal		4	0	0	4
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		4	0	0	3
Aggregation,alveolar macrophage		1	0	0	2
minimal		1	0	0	2
Lymph node,mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Mammary gland,inguinal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		5	0	0	4
Not remarkable		5	0	0	4
No sample		0	0	0	1
Pituitary					
Number examined		5	0	0	5
Not remarkable		4	0	0	5
Cyst,pars distalis		1	0	0	0
minimal		1	0	0	0
Prostate					
Number examined		5	0	0	5
Not remarkable		2	0	0	0
Cell infiltration		3	0	0	5
minimal		3	0	0	4
mild		0	0	0	1

M : Male

Table 10-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex:	M	M	M	M
	Dose(mg/kg):	0	30	100	300
	Number:	7	12	12	7
Salivary gland,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Seminal vesicle(Coagulating gland)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Skeletal muscle,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spinal cord,thoracic					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spleen					
Number examined		5	0	0	5
Not remarkable		3	0	0	5
Hematopoiesis,extramedullary		2	0	0	0
minimal		2	0	0	0
Stomach					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Testis					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Trachea					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Urinary bladder					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

M : Male

Table 10-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	300
	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	4
Increased vacuole,zona fasciculata		0	1
mild		0	1
Bone+Bone marrow,femoral			
Number examined		5	5
Not remarkable		5	5
Cerebellum(Pons)			
Number examined		5	5
Not remarkable		5	5
Cerebrum			
Number examined		5	5
Not remarkable		5	5
Eye			
Number examined		5	5
Not remarkable		5	5
Heart			
Number examined		5	5
Not remarkable		5	5
Intestine,duodenum			
Number examined		5	5
Not remarkable		5	5
Intestine,jejunum			
Number examined		5	5
Not remarkable		5	5
Intestine,ileum(Peyer's patch)			
Number examined		5	5
Not remarkable		5	5
Intestine,cecum			
Number examined		5	5
Not remarkable		5	5
Intestine,colon			
Number examined		5	5
Not remarkable		5	5
Intestine,rectum			
Number examined		5	5
Not remarkable		5	5
Kidney			
Number examined		5	5
Not remarkable		5	5
Liver			
Number examined		5	5
Not remarkable		2	0
Microgranuloma		3	4
minimal		3	4
Hypertrophy,hepatocytic,centrilobular		0	5
minimal		0	5

F : Female

Table 10-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	0	300
	Number:	5	5
Lung(bronchus)			
Number examined		5	5
Not remarkable		5	4
Aggregation,alveolar macrophage		0	1
minimal		0	1
Lymph node,mesenteric			
Number examined		5	5
Not remarkable		5	5
Lymph node,submandibular			
Number examined		5	5
Not remarkable		5	5
Mammary gland,inguinal			
Number examined		5	5
Not remarkable		5	5
Ovary			
Number examined		5	5
Not remarkable		4	5
Atrophy		1	0
moderate		1	0
Pancreas			
Number examined		5	5
Not remarkable		5	5
Parathyroid			
Number examined		3	5
Not remarkable		3	5
No sample		2	0
Pituitary			
Number examined		5	5
Not remarkable		5	5
Salivary gland,submandibular			
Number examined		5	5
Not remarkable		5	5
Sciatic nerve			
Number examined		5	5
Not remarkable		5	5
Skeletal muscle,femoral			
Number examined		5	5
Not remarkable		5	5
Spinal cord,thoracic			
Number examined		5	5
Not remarkable		5	5
Spleen			
Number examined		5	5
Not remarkable		5	5
Stomach			
Number examined		5	5
Not remarkable		5	5

F : Female

Table 10-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (D42))

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

F : Female

Table 10-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	30	100	300
	Number:	12	12	11	11
Adrenal					
Number examined		5	5	5	5
Not remarkable		5	5	3	0
Increased vacuole,zona fasciculata		0	0	2	5
minimal		0	0	2	1
mild		0	0	0	4
Bone+Bone marrow,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebellum(Pons)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Cerebrum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Eye					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,jejunum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,colon					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,rectum					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Kidney					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Liver					
Number examined		5	5	5	5
Not remarkable		3	4	3	0
Microgranuloma		2	1	2	0
minimal		2	1	2	0

F : Female

Table 10-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs / Findings	Sex:	F	F	F	F
	Dose(mg/kg):	0	30	100	300
	Number:	12	12	11	11
Liver (continued)					
Hypertrophy,hepatocytic,centrilobular		0	0	0	5
minimal		0	0	0	4
mild		0	0	0	1
Lung(bronchus)					
Number examined		5	0	0	5
Not remarkable		2	0	0	4
Aggregation,alveolar macrophage		3	0	0	1
minimal		3	0	0	1
Lymph node,mesenteric					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Lymph node,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Mammary gland,inguinal					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Ovary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Pancreas					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Parathyroid					
Number examined		4	0	0	5
Not remarkable		4	0	0	5
No sample		1	0	0	0
Pituitary					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Salivary gland,submandibular					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Sciatic nerve					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Skeletal muscle,femoral					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spinal cord,thoracic					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Spleen					
Number examined		5	0	0	5
Hematopoiesis,extramedullary		5	0	0	5
minimal		3	0	0	2
mild		2	0	0	3

F : Female

Table 10-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of administration period (L4))

Organs	Sex:	F	F	F	F
	Dose(mg/kg):	0	30	100	300
Findings	Number:	12	12	11	11
Stomach					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Thyroid					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Trachea					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Urinary bladder					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Uterus					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Vagina					
Number examined		5	0	0	5
Not remarkable		5	0	0	5

F : Female

Table 10-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Kidney			
Number examined		5	5
Not remarkable		4	0
Regeneration,tubular		1	5
minimal		1	2
mild		0	3
Hyperplasia,transitional,focal		0	1
minimal		0	1

M : Male

Table 10-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	F	F
	Dose(mg/kg):	0	300
Findings	Number:	5	5
Adrenal			
Number examined		5	5
Not remarkable		5	5
Liver			
Number examined		5	5
Not remarkable		1	3
Microgranuloma		4	2
minimal		4	2

F : Female

Table 10-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (All littermates died)

Organs / Findings	Sex:	F	F
	Dose(mg/kg):	100	300
	Number:	1	1
Adrenal			
Number examined		1	1
Not remarkable		1	0
Increased vacuole,zona fasciculata		0	1
moderate		0	1
Bone+Bone marrow,femoral			
Number examined		1	1
Not remarkable		1	1
Cerebellum(Pons)			
Number examined		1	1
Not remarkable		1	1
Cerebrum			
Number examined		1	1
Not remarkable		1	1
Eye			
Number examined		1	1
Not remarkable		1	1
Heart			
Number examined		1	1
Not remarkable		1	1
Intestine,duodenum			
Number examined		1	1
Not remarkable		1	1
Intestine,jejunum			
Number examined		1	1
Not remarkable		1	1
Intestine,ileum(Peyer's patch)			
Number examined		1	1
Not remarkable		1	1
Intestine,cecum			
Number examined		1	1
Not remarkable		1	1
Intestine,colon			
Number examined		1	1
Not remarkable		1	0
Atrophy,goblet cell		0	1
minimal		0	1
Intestine,rectum			
Number examined		1	1
Not remarkable		1	1
Kidney			
Number examined		1	1
Not remarkable		1	0
Dilatation,tubular		0	1
mild		0	1
Vacuolation,tubular cell		0	1
moderate		0	1
Necrosis,tubular		0	1
mild		0	1

F : Female

Table 10-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (All littermates died)

Organs	Sex:	F	F
	Dose(mg/kg):	100	300
Findings	Number:	1	1
Liver			
Number examined		1	1
Not remarkable		1	1
Lung(bronchus)			
Number examined		1	1
Not remarkable		1	0
Aggregation,alveolar macrophage		0	1
minimal		0	1
Lymph node,mesenteric			
Number examined		1	1
Not remarkable		1	1
Lymph node,submandibular			
Number examined		1	1
Not remarkable		1	1
Mammary gland,inguinal			
Number examined		1	1
Decreased lactation		1	1
mild		0	1
moderate		1	0
Ovary			
Number examined		1	1
Not remarkable		0	1
Decreased large corpus luteum		1	0
moderate		1	0
Pancreas			
Number examined		1	1
Not remarkable		1	1
Parathyroid			
Number examined		1	1
Not remarkable		1	1
Pituitary			
Number examined		1	1
Not remarkable		1	1
Salivary gland,submandibular			
Number examined		1	1
Not remarkable		1	0
Decreased granule,granular duct		0	1
minimal		0	1
Sciatic nerve			
Number examined		1	1
Not remarkable		1	1
Skeletal muscle,femoral			
Number examined		1	1
Not remarkable		1	1
Spinal cord,thoracic			
Number examined		1	1
Not remarkable		1	1

F : Female

Table 10-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (All littermates died)

Organs	Sex:	F	F
	Dose(mg/kg):	100	300
Findings	Number:	1	1
Spleen			
Number examined		1	1
Not remarkable		0	1
Hematopoiesis,extramedullary		1	0
mild		1	0
Stomach			
Number examined		1	1
Not remarkable		1	0
Ulcer,forestomach		0	1
minimal		0	1
Hyperplasia,squamous,forestomach		0	1
mild		0	1
Thymus			
Number examined		1	1
Not remarkable		1	0
Atrophy		0	1
moderate		0	1
Thyroid			
Number examined		1	1
Not remarkable		1	1
Trachea			
Number examined		1	1
Not remarkable		1	1
Urinary bladder			
Number examined		1	1
Not remarkable		1	1
Uterus			
Number examined		1	1
Not remarkable		1	1
Vagina			
Number examined		1	1
Not remarkable		1	1

F : Female

Table 11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Estrous cycle in female rats during the pre-mating period (Main group)

Dose mg/kg	No. of animals	Count of estrus 0	1	2	3	4	Mean±S.D.	Mean duration of cycles Mean±S.D.	Index of animals with abnormal estrous cycle (%)a)
0	12	0	0	0	5	7	3.6±0.5	4.2±0.4	1/12(8.3)
30	12	0	0	0	5	7	3.6±0.5	4.2±0.3	0/12(0.0)
100	12	0	0	0	5	7	3.6±0.5	4.1±0.3	0/12(0.0)
300	12	0	0	0	4	8	3.7±0.5	4.2±0.3	0/12(0.0)

a): (No. of animals with abnormal estrous cycle / No. of animals examined)×100
No significant difference in any treated groups from control group.

Table 12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Mating and fertility of animals

	Male				Female			
Dose mg/kg	No. of males	Days until copulation Mean±S.D.	Copulation index (%) a)	Insemination index (%) b)	No. of females	Days until copulation Mean±S.D.	Copulation index (%) a)	Fertility index (%) c)
0	12	3.0±2.4	12/12(100.0)	12/12(100.0)	12	3.0±2.4	12/12(100.0)	12/12(100.0)
30	12	2.7±2.0	12/12(100.0)	12/12(100.0)	12	2.7±2.0	12/12(100.0)	12/12(100.0)
100	12	2.0±0.9	12/12(100.0)	12/12(100.0)	12	2.0±0.9	12/12(100.0)	12/12(100.0)
300	12	2.6±1.0	12/12(100.0)	12/12(100.0)	12	2.6±1.0	12/12(100.0)	12/12(100.0)

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

Table 13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Delivery data on dams

Dose mg/kg		No. of pregnant females	No. of females with liveborns	Gestation index % a)	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % b)	Delivery index % c)	No. of still-borns (%)d)	No. of live-borns	External e) abnor-malities(%)f)
	Total	12	12	100.0		204	197			2	187	0
0	Mean				22.0	17.0	16.4	96.6	96.0	(1.1)	15.6	(0.0)
	S.D.				0.4	1.5	1.5	3.0	5.1	(2.6)	1.6	(0.0)
	Total	12	12	100.0		205	195			2	184	0
30	Mean				22.0	17.1	16.3	95.2	95.3	(1.0)	15.3	(0.0)
	S.D.				0.0	1.6	1.5	4.2	4.7	(2.3)	1.7	(0.0)
	Total	12	12	100.0		197	195			0	180	0
100	Mean				22.0	16.4	16.3	99.1*	92.4	(0.0)	15.0	(0.0)
	S.D.				0.0	1.4	1.2	2.2J	6.6	(0.0)	1.3	(0.0)
	Total	12	12	100.0		191	183			1	173	0
300	Mean				21.9	15.9	15.3	95.4	95.5	(0.6)	14.4	(0.0)
	S.D.				0.3	1.9	2.9	12.3	6.4	(2.0)	2.7	(0.0)

a): (No. of females which delivered liveborns / No. of pregnant females)×100
b): (No. of implantation sites / No. of corpora lutea)×100
c): (No. of delivered pups / No. of implantation sites)×100
d): (No. of stillborns / No. of delivered pups)×100
e): No. of delivered pups with external abnormalities
f): (No. of delivered pups with external abnormalities / No. of delivered pups)×100
*: $p<0.05$ (Significant difference from control group)
J: Wilcoxon's rank sum test

Table 14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Viability index of pups

Dose mg/kg		No. of dams	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of dams	No. of live pups Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
	Total	12	187	189		12	187	180	
0	Mean		15.6	15.8	98.9		15.6	15.0	96.5
	S.D.		1.6	1.5	2.6		1.6	1.5	5.8
	Total	12	184	186		12	184	180	
30	Mean		15.3	15.5	99.0		15.3	15.0	98.1
	S.D.		1.7	1.8	2.3		1.7	1.3	3.8
	Total	12	180	180		12	180	164	
100	Mean		15.0	15.0	100.0		15.0	13.7	91.2
	S.D.		1.3	1.3	0.0		1.3	4.5	28.8
	Total	12	173	174		12	173	145	
300	Mean		14.4	14.5	99.4		14.4	12.1	85.7
	S.D.		2.7	2.7	2.0		2.7	4.9	30.9

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

Table 15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Sex ratio of pups

Dose mg/kg	No. of dams		Liveborns No. of males	Liveborns No. of females	Stillborns No. of males	Stillborns No. of females	Sex ratio of delivered pups a)	Sex ratio of liveborns b)	No. of dams	Postnatal day 4 No. of males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
		Total	100	87	0	2				95	85	
0	12	Mean	8.3	7.3	0.0	0.2	0.53	0.53	12	7.9	7.1	0.53
		S.D.	2.6	2.1	0.0	0.4	0.15	0.15		2.5	2.3	0.16
		Total	98	86	0	2				95	85	
30	12	Mean	8.2	7.2	0.0	0.2	0.53	0.54	12	7.9	7.1	0.53
		S.D.	2.7	2.9	0.0	0.4	0.16	0.16		2.7	2.8	0.17
		Total	83	97	0	0				73	91	
100	12	Mean	6.9	8.1	0.0	0.0	0.46	0.46	11d)	6.6	8.3	0.44
		S.D.	2.4	2.4	0.0	0.0	0.15	0.15		2.3	2.2	0.14
		Total	86	87	0	1				69	76	
300	12	Mean	7.2	7.3	0.0	0.1	0.50	0.50	11e)	6.3	6.9	0.47
		S.D.	2.0	2.4	0.0	0.3	0.11	0.12		2.6	2.3	0.16

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4
d): All pups from one dam died by postnatal day 2.
e): All pups from one dam died by postnatal day 4.
No significant difference in any treated groups from control group.

Table 16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Body weight of pups

Dose mg/kg		Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
	No.	12	12	12	12	12	12
0	Mean	6.7	10.4	3.7	6.3	9.8	3.5
	S.D.	0.6	1.0	0.6	0.6	0.9	0.6
	No.	12	12	12	12	12	12
30	Mean	6.5	10.4	3.9	6.3	10.1	3.8
	S.D.	0.4	0.8	0.6	0.2	0.6	0.5
	No.	12	11b)	11	12	11b)	11
100	Mean	6.7	10.1	3.3	6.3	9.7	3.3
	S.D.	0.5	0.8	0.7	0.5	0.8	0.7
	No.	12	11c)	11	12	11c)	11
300	Mean	6.7	10.7	4.0	6.2	9.9	3.7
	S.D.	0.5	1.2	0.8	0.5	1.1	0.7

Unit: g
No.: No. of dams
a): Postnatal day
b): All pups from one dam died by postnatal day 2.
c): All pups from one dam died by postnatal day 4.
No significant difference in any treated groups from control group.

Table 17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Externally for gross abnormalities in dead pups

Dose (mg/kg)	0	30	100	300
Male				
No. of pups examined	4	2	3	9
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	2	2	4	8
No. of pups with abnormal findings	0	0	0	0

Table 18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg)	0	30	100	300
Male				
No. of pups examined	95	95	73	69
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	85	85	91	76
No. of pups with abnormal findings	0	0	0	0

Appendix 1-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration														
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
1001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 30

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 30

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 30

Animal number	Day of administration														
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
2001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration														
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
3001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3002	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3004	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3005	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3006	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3008	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3009	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3011	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

a): Day of necropsy
-: No abnormal findings

Appendix 1-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4001	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4002	-	-	-	-	-	-	-	-	-	-	-	A	A	A
4003	-	-	-	-	-	-	-	-	-	-	-	A	-	-
4004	-	-	-	-	-	-	-	-	-	-	A	-	-	-
4005	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4006	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	B	-	B
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4010	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4012	-	-	A	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion

Appendix 1-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4001	BD	D	-	D	D	D	D	D	D	D	D	BD	BD	D
4002	-	-	-	-	-	-	-	-	-	D	-	-	AB	-
4003	-	-	D	-	D	A	-	D	-	-	-	-	-	-
4004	D	-	-	-	-	-	-	-	-	-	-	-	-	-
4005	-	-	-	-	-	B	B	B	-	-	-	A	-	-
4006	-	B	A	A	-	-	A	-	-	-	-	A	-	B
4007	B	-	-	A	-	-	-	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4009	D	BD	D	AD	AD	D	D	AD	D	D	D	AD	BD	D
4010	-	B	-	-	-	-	-	-	-	-	-	-	-	-
4011	-	-	-	-	-	-	-	-	-	-	-	D	-	-
4012	D	-	D	-	-	-	-	-	-	-	D	D	-	D

-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion
D: Salivation

Appendix 1-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration														
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
4001	BD	D	D	D	BD	BD	D	D	D	D	D	D	D	A	-
4002	-	-	-	-	-	-	-	-	-	-	A	-	-	-	-
4003	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4004	-	-	-	-	-	-	-	-	-	B	-	-	-	-	-
4005	-	-	-	-	-	-	-	-	B	B	AB	-	-	-	-
4006	-	-	-	-	B	-	-	-	-	-	-	-	-	-	-
4007	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4008	-	-	-	-	-	-	-	-	-	B	-	-	-	A	
4009	D	-	D	AB	-	-	A	AD	A	D	B	A	A	A	
4010	B	-	-	-	-	-	B	-	B	-	-	-	-	B	
4011	-	-	-	A	-	-	B	-	A	-	-	-	-	-	
4012	-	-	-	D	D	-	-	A	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion
D: Salivation

Appendix 1-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

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

-: No abnormal findings

Appendix 1-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 30

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

-: No abnormal findings

Appendix 1-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

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

-: No abnormal findings

Appendix 1-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

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

-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion

Appendix 1-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 0

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
1101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
1109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d
1110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
1112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	

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

Appendix 1-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 30

Dam number	Administration																						
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
2101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	

a): Gestation day
-: No abnormal findings
d: Delivery

Appendix 1-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 100

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
3101	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3102	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3103	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3104	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	
3108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
3112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d	

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

Appendix 1-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 300

Dam number	Administration																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23a)
4101	-	-	-	-	B	-	-	-	-	-	B	-	-	-	B	B	B	B	-	-	-	-	d	
4102	B	-	-	-	-	-	B	B	-	B	B	-	-	-	-	B	-	B	-	B	-	-	d	
4103	A	B	-	B	-	-	-	-	-	-	-	-	-	-	B	-	-	-	-	-	-	-	d	
4104	-	B	B	B	-	B	-	B	B	-	B	-	-	-	-	-	B	-	B	-	-	-	d	
4105	B	-	-	-	B	-	-	-	B	B	-	B	B	-	-	-	-	-	B	-	-	-	d	
4106	-	-	BD	B	B	-	-	-	D	B	-	-	B	-	A	-	D	BD	-	-	-	-	-/d	
4107	-	-	-	-	-	-	B	-	-	B	B	B	B	B	-	BD	B	-	-	B	-	-	d	
4108	B	-	-	B	-	-	-	-	-	B	-	-	-	-	-	-	-	B	-	-	-	-	d	
4109	-	-	BD	-	B	-	-	-	B	B	-	B	-	B	B	B	B	-	-	B	-	-/d		
4110	-	B	B	B	B	-	-	-	-	B	B	B	-	-	-	-	B	B	B	A	A	-	d	
4111	-	-	B	-	-	-	-	-	-	-	B	-	-	-	-	-	-	-	B	B	-	-	d	
4112	-	-	-	B	-	B	-	B	-	-	B	-	-	-	-	-	-	-	B	-	-	B	d	

a): Gestation day
-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion
D: Salivation
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 0

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

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

Appendix 1-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 30

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

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

Appendix 1-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 100

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

a): Lactation day
b): Day of necropsy
c): Necropsied on lactation day 2 because all pups died
-: No abnormal findings
E: Decrease in nursing behavior

Appendix 1-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 300

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

a): Lactation day
b): Day of necropsy
c): Necropsied on lactation day 4 because all pups died
-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion
E: Decrease in nursing behavior
H: Fracture of incisors

Appendix 1-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1113	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1113	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-

-: No abnormal findings

Appendix 1-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration														
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
1113	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1114	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1115	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1116	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1117	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
1118	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1119	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1120	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1121	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings

Appendix 1-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14
4113	-	-	-	-	-	-	-	-	B	-	-	-	-	-
4114	-	-	-	-	-	-	AB	A	-	-	-	-	-	A
4115	-	-	-	-	-	-	-	A	-	-	-	-	-	-
4116	-	-	-	-	-	-	-	-	-	-	AB	-	-	-
4117	-	-	-	-	-	-	-	A	-	-	-	-	-	-
4118	A	A	-	A	A	-	B	AB	B	-	-	B	B	-
4119	-	-	-	-	-	-	A	A	-	B	-	-	-	-
4120	A	AB	-	A	-	-	B	-	-	B	-	B	-	-
4121	-	-	-	-	-	-	B	A	-	-	B	-	-	-
4122	-	-	-	-	-	-	-	-	B	B	-	B	-	-

-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion

Appendix 1-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 300

Animal number	Day of administration													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
4113	B	B	-	-	-	-	-	-	-	-	-	-	B	-
4114	-	-	A	D	-	-	-	D	-	-	A	-	-	-
4115	-	-	-	-	-	-	B	-	-	-	-	B	B	B
4116	-	-	-	B	B	-	-	B	-	-	-	B	-	-
4117	-	B	B	-	-	D	-	-	-	-	-	D	-	-
4118	-	-	B	B	-	B	-	-	-	-	B	B	D	A
4119	-	BD	D	-	-	AB	D	-	-	-	-	-	-	-
4120	B	-	-	-	B	-	B	B	-	B	-	-	B	-
4121	B	B	-	B	-	-	B	B	-	-	B	B	-	-
4122	-	-	-	-	-	-	-	-	-	-	-	B	-	B

-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion
D: Salivation

Appendix 1-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 300

Animal number	Day of administration														
	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43a)
4113	-	B	B	-	-	B	-	-	-	-	-	-	-	-	-
4114	-	-	-	-	-	-	B	-	-	-	B	-	-	-	-
4115	B	-	-	-	B	-	B	-	-	-	-	-	-	-	-
4116	B	-	-	B	B	-	-	-	-	-	-	-	B	-	-
4117	-	-	-	-	-	-	B	-	-	B	-	-	-	-	-
4118	-	-	-	B	-	-	B	-	B	-	-	-	-	-	
4119	-	-	-	A	-	-	-	B	-	-	B	-	-	-	
4120	B	B	-	-	-	-	-	B	-	-	-	-	-	-	
4121	-	-	-	B	-	-	-	B	-	-	B	B	-	-	
4122	-	-	B	-	-	-	-	-	B	-	-	-	-	-	

a): Day of necropsy
-: No abnormal findings
A: Decrease in spontaneous movement
B: Convulsion

Appendix 1-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Recovery period)
Dose (mg/kg): 0

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Recovery period)
Dose (mg/kg): 300

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Recovery period)
Dose (mg/kg): 0

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Recovery period)
Dose (mg/kg): 300

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

a): Day of necropsy
-: No abnormal findings

Appendix 2-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 1)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 7)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	1d)	0	0	0	0	0	0	1d)	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) Tonic convulsion

Appendix 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Gestation day 20)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-49 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-50 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Posture a)	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-51 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 d)	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) Necropsied on lactation day 2 because all pups died

Appendix 2-52 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11 d)	12
Posture a)	N	N	N	N	N	N	N	N	N	N		N
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) Necropsied on lactation day 4 because all pups died

Appendix 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-54 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-55 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-56 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	F	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-57 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-58 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-59 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-60 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-62 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-64 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Posture a)	N	N	N	N	N	N	N	N	N	N
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-65 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-66 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-67 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-68 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-69 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-70 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 1 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-71 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-72 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: home cage observation
(Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Posture a)	N	N	N	N	N
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0

a) N: Normal, F: Flattened, H: Hunched
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe

Appendix 2-73 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	1	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-74 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	1
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	1	0	0	0	1
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-75 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	1	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-76 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-77 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-78 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	**1**	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-81 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-82 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	1	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-83 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-84 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-85 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-86 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-87 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-88 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-89 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-90 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	1	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-91 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-92 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	1	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-93 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-94 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-95 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	1	0	0	1	0
Reactivity to handling n)	0	0	0	0	0	0	0	1	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-96 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-97 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-98 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-99 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-100 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-101 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-102 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-103 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-104 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-105 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	1	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-106 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-107 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-108 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 1)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-109 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-110 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-111 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-112 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 7)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-113 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-114 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-115 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-116 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-117 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	1	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-118 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-119 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-120 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Gestation day 20)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-121 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	1	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	1	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-122 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-123 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 o)	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
o) Necropsied on lactation day 2 because all pups died

Appendix 2-124 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11 o)	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0		0
Fur condition b)	0	0	0	0	0	0	0	0	0	0		0
Skin c)	0	0	0	0	0	0	0	0	0	0		0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0		0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0		0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0		0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0		0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0		0
Piloerection i)	0	0	0	0	0	0	0	0	0	0		0
Pupil size j)	0	0	0	0	0	0	0	0	0	0		0
Salivation k)	0	0	0	0	0	0	0	0	0	0		0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0		0
Vocalization m)	0	0	0	0	0	0	0	0	0	0		0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0		0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
o) Necropsied on lactation day 4 because all pups died

Appendix 2-125 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-126 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-127 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-128 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-129 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-130 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-131 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-132 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-133 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-134 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-135 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	**1**	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	**1**	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-136 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	1	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-137 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-138 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	1
Reactivity to handling n)	0	0	0	0	1

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-139 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-140 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-141 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-142 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 1 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-143 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-144 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: in-the-hand observation
(Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Ease of removal from cage a)	0	0	0	0	0
Fur condition b)	0	0	0	0	0
Skin c)	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0
Lacrimation h)	0	0	0	0	0
Piloerection i)	0	0	0	0	0
Pupil size j)	0	0	0	0	0
Salivation k)	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0
Vocalization m)	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-145 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	8	3	3	6	6	2	8	4	5	12	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	1	0	1	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-146 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	5	6	2	6	4	3	5	4	6	3
Defecation count	0	0	0	0	0	0	0	0	1	0	0	0
Urination h)	0	0	1	0	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-147 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	4	7	4	4	5	9	5	5	9	6	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-148 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	2	5	5	5	5	5	7	2	7	1
Defecation count	0	1	0	0	0	0	0	0	0	0	0	1
Urination h)	0	1	1	1	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-149 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	5	5	3	7	6	4	5	3	8	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	1	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-150 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	7	5	5	4	4	3	5	2	6	6	4
Defecation count	0	0	0	0	0	0	0	0	2	0	0	0
Urination h)	0	1	1	1	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-151 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	4	8	3	5	8	9	7	0	9	5	4
Defecation count	4	0	0	0	0	0	0	0	1	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-152 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	4	4	7	4	5	3	5	4	3	7	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	1	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-153 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	4	4	6	4	6	8	3	3	4	5	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-154 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	3	5	5	5	4	4	3	2	6	7	5
Defecation count	0	0	0	0	0	0	0	0	4	0	0	0
Urination h)	0	1	0	0	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-155 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	5	5	1	5	2	6	5	1	8	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-156 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	2	2	5	6	6	2	5	5	2	5	2
Defecation count	0	0	1	0	0	0	0	0	0	0	0	0
Urination h)	0	1	1	1	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-157 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	3	5	7	4	6	3	6	10	6	4
Defecation count	2	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	1	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-158 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	U	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	5	5	7	5	0	5	5	2	5	8	2
Defecation count	0	0	0	0	1	0	0	0	1	0	0	0
Urination h)	0	0	1	1	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-159 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	6	4	3	6	6	4	5	7	4	3
Defecation count	1	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-160 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	2	5	7	7	5	3	7	6	1	7	5
Defecation count	0	4	1	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	1	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-161 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	4	8	6	5	6	7	7	3	7	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	1	0	0	0	0	1	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-162 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	U	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	5	5	6	5	0	8	6	3	10	7	4
Defecation count	0	0	0	0	0	0	0	0	2	0	0	0
Urination h)	0	1	1	1	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-163 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	5	6	4	3	1	10	7	9	7	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	1	0	0	0	0	0	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-164 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	4	2	5	8	5	4	5	7	3	9	6
Defecation count	0	2	0	0	0	0	0	0	0	0	0	0
Urination h)	1	1	0	1	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-165 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1001-1012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	5	5	5	3	4	4	4	3	7	5	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	1	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-166 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	7	4	4	6	3	6	7	4	6	8	5
Defecation count	0	0	0	0	0	0	0	0	3	0	0	0
Urination h)	0	1	0	1	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-167 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	2	5	7	5	4	5	10	9	6	8	3	5
Defecation count	1	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	0	1	1	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-168 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	3	3	6	6	6	3	3	6	4	9	9
Defecation count	0	2	0	0	0	0	0	0	0	0	0	0
Urination h)	1	1	0	1	0	0	1	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-169 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	7	6	6	8	9	7	11	2	8	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-170 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	8	8	6	2	7	8	7	4	10	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-171 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	5	9	9	10	6	6	8	12	6	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-172 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	8	3	7	5	3	6	12	1	6	8	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-173 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	9	14	7	8	12	9	8	10	4	7	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-174 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	3	9	6	7	10	5	10	8	9	7	7	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-175 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	9	6	9	8	8	8	11	6	9	9	8	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-176 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	5	8	6	8	8	12	8	9	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-177 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	5	5	5	7	7	9	3	7	7	12	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-178 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	6	6	5	6	6	10	5	7	5	10	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-179 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	8	9	6	8	6	5	5	7	5	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-180 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 1)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	8	4	8	4	6	8	9	3	8	3	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-181 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	9	8	6	7	7	8	6	3	4	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	1	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-182 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	8	6	4	9	8	6	7	4	4	9	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-183 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	5	5	9	5	6	8	6	6	6	6	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-184 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 7)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	5	7	9	4	4	4	6	8	3	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-185 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	7	4	5	5	7	8	4	4	7	6	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-186 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	8	4	5	5	6	7	3	7	8	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-187 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	8	9	8	4	6	8	8	5	5	8
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-188 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 14)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	5	9	5	5	8	7	6	10	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	1	0	0	0	0	0	1

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-189 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	5	6	5	6	9	3	5	3	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-190 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	8	5	4	6	6	5	4	6	4	3	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-191 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	4	5	6	5	3	6	8	5	5	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-192 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Gestation day 20)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	4	7	5	4	5	6	6	3	5	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-193 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	5	5	9	8	9	6	4	3	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-194 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 30

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	5	8	4	4	5	8	9	4	7	7	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-195 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (3101-3112)											
	1	2	3	4	5	6	7	8	9	10	11 i)	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	6	6	5	5	6	6	7	7	7	5		5
Defecation count	0	0	0	0	0	0	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) Necropsied on lactation day 2 because all pups died

Appendix 2-196 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11 i)	12
Arousal a)	0	0	0	0	0	0	0	0	0	0		0
Convulsion b)	0	0	0	0	0	0	0	0	0	0		0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0		0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0		0
Gait e)	0	0	0	0	0	0	0	0	0	0		0
Posture f)	N	N	N	N	N	N	N	N	N	N		N
Grooming g)	0	0	0	0	0	0	0	0	0	0		0
Rearing	4	8	5	7	5	5	5	5	8	5		5
Defecation count	0	0	0	0	0	1	0	0	0	0		0
Urination h)	0	0	0	0	0	0	0	0	0	0		0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) Necropsied on lactation day 4 because all pups died

Appendix 2-197 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	7	6	6	8	10	8	6	6	4	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-198 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 1 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	2	5	1	6	2	6	5	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	1	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-199 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	7	5	4	5	9	11	12	5	9	11
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-200 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 2 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	8	12	11	2	7	8	4	7	7	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-201 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	6	5	9	11	8	8	9	11	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-202 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 3 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	3	11	8	4	12	6	7	13	7	12
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-203 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	10	7	7	12	10	6	8	10	7	10
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-204 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 4 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	13	11	7	8	6	12	12	6	15
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-205 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	11	5	8	11	9	7	9	9	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-206 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 5 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	9	12	9	6	10	10	8	8	10	14
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-207 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1113-1122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	8	4	7	12	10	11	12	10	9	7
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-208 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	5	13	9	5	10	9	10	7	8	12
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-209 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	2	8	5	3
Defecation count	0	0	0	0	0
Urination h)	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-210 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	5	7	4	7	7
Defecation count	0	0	0	0	0
Urination h)	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-211 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	6	4	5	8	2
Defecation count	0	0	0	0	0
Urination h)	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-212 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in male rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	4	7	4	8	8
Defecation count	0	0	0	0	0
Urination h)	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-213 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	8	11	5	8	7
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-214 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 1 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	7	7	9	5	11
Defecation count	0	0	0	0	0
Urination h)	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-215 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	8	11	10	6	10
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-216 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual detailed clinical signs in female rats: open field observation
(Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Arousal a)	0	0	0	0	0
Convulsion b)	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0
Stereotypy d)	0	0	0	0	0
Gait e)	0	0	0	0	0
Posture f)	N	N	N	N	N
Grooming g)	0	0	0	0	0
Rearing	10	11	6	11	9
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-217 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	93	103	70	133	75

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-218 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 30

Parameter	Animal number (2008-2012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	38	93	63	55	111

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-219 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 100

Parameter	Animal number (3008-3012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	102	92	55	80	125

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-220 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	86	96	99	52	100

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-221 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Parameter	Animal number (1101-1112)				
	1	2	6	8	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	31	50	89	54	49

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-222 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 30

Parameter	Animal number (2101-2108)				
	1	2	3	4	8
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	68	56	48	50	31

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-223 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Parameter	Animal number (3101-3108)				
	1	2	3	4	8
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	63	53	71	78	64

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-224 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Parameter	Animal number (4101-4110)				
	1	3	4	9	10
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	44	59	48	33	37

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-225 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	71	76	68	79	72

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-226 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	52	102	83	35	78

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-227 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1008-1012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	50	93	107	137	93

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-228 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4008-4012)				
	8	9	10	11	12
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	51	81	81	64	70

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-229 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Parameter	Animal number (1118-1122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	63	77	66	81	62

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-230 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Week 2 of recovery)
Dose (mg/kg): 300

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
Auditory response a)	0	0	0	0	0
Approach response b)	0	0	0	0	0
Touch response c)	0	0	0	0	0
Tail pinch response d)	0	0	0	0	0
Pupillary reflex e)	P	P	P	P	P
Aerial righting reflex (Total score)	0	0	0	0	0
Landing foot splay (mm)	70	85	56	58	56

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-231 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1008	1338	850
1009	1764	1110
1010	1832	908
1011	1060	751
1012	1151	707
Mean	1429	865
S.D.	352	158

Appendix 2-232 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 30

Animal number	Fore limb g	Hind limb g
2008	793	541
2009	1888	1015
2010	1376	680
2011	1651	897
2012	1889	1036
Mean	1519	834
S.D.	458	216

Appendix 2-233 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Fore limb g	Hind limb g
3008	1469	953
3009	1197	1111
3010	1073	986
3011	1187	1165
3012	1243	932
Mean	1234	1029
S.D.	146	103

Appendix 2-234 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
4008	1127	1016
4009	1322	1120
4010	1475	1059
4011	1568	893
4012	1429	942
Mean	1384	1006
S.D.	169	91

Appendix 2-235 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1101	1344	931
1102	1223	988
1106	1574	950
1108	1295	705
1112	1071	744
Mean	1301	864
S.D.	184	129

Appendix 2-236 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 30

Animal number	Fore limb g	Hind limb g
2101	1624	889
2102	1383	923
2103	1510	991
2104	1384	899
2108	1325	805
Mean	1445	901
S.D.	121	67

Appendix 2-237 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Animal number	Fore limb g	Hind limb g
3101	1526	825
3102	1428	845
3103	1482	1024
3104	1540	948
3108	1358	808
Mean	1467	890
S.D.	75	93

Appendix 2-238 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
4101	1303	796
4103	1285	716
4104	1612	1094
4109	1411	997
4110	1415	589
Mean	1405	838
S.D.	130	206

Appendix 2-239 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1118	1160	771
1119	1059	871
1120	1269	899
1121	1306	656
1122	1256	869
Mean	1210	813
S.D.	100	100

Appendix 2-240 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
4118	1283	697
4119	1105	868
4120	1411	649
4121	1092	828
4122	1289	885
Mean	1236	785
S.D.	136	106

Appendix 2-241 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1008	2049	1012
1009	2062	1083
1010	2023	1112
1011	1934	899
1012	2015	1214
Mean	2017	1064
S.D.	50	117

Appendix 2-242 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
4008	1597	975
4009	1835	994
4010	1646	1071
4011	1880	1012
4012	1493	1089
Mean	1690	1028
S.D.	163	49

Appendix 2-243 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Fore limb g	Hind limb g
1118	1396	737
1119	1590	1064
1120	1557	1125
1121	1664	950
1122	1512	876
Mean	1544	950
S.D.	100	154

Appendix 2-244 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	Fore limb g	Hind limb g
4118	1514	873
4119	1330	872
4120	1798	864
4121	1228	809
4122	1537	736
Mean	1481	831
S.D.	219	59

Appendix 2-245 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1008	485	420	330	346	252	178	2011
1009	452	421	411	434	383	326	2427
1010	426	388	411	363	395	349	2332
1011	481	472	461	360	384	351	2509
1012	454	398	392	296	162	286	1988
Mean	460	420	401	360	315	298	2253
S.D.	24	32	47	49	104	72	240

Unit: Count

Appendix 2-246 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 30

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2008	465	348	317	268	38	26	1462
2009	450	401	379	384	306	38	1958
2010	462	422	116	284	106	237	1627
2011	411	339	431	335	370	136	2022
2012	468	413	325	158	152	119	1635
Mean	451	385	314	286	194	111	1741
S.D.	23	38	120	85	139	85	239

Unit: Count

Appendix 2-247 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3008	436	466	423	386	110	140	1961
3009	468	325	260	241	212	80	1586
3010	438	256	72	50	47	10	873
3011	420	395	354	359	413	284	2225
3012	407	425	310	349	272	273	2036
Mean	434	373	284	277	211	157	1736
S.D.	23	83	133	138	143	120	535

Unit: Count

Appendix 2-248 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	530	453	424	287	191	246	2131
4009	496	421	423	427	244	293	2304
4010	464	425	484	396	140	144	2053
4011	398	399	422	380	322	311	2232
4012	502	388	409	481	423	158	2361
Mean	478	417	432	394	264	230	2216
S.D.	50	25	29	71	112	76	125

Unit: Count

Appendix 2-249 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1101	491	186	122	51	285	150	1285
1102	348	79	92	165	349	280	1313
1106	364	332	331	218	182	168	1595
1108	407	53	153	40	60	15	728
1112	355	61	86	20	51	40	613
Mean	393	142	157	99	185	131	1107
S.D.	59	119	101	87	133	107	418

Unit: Count

Appendix 2-250 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 30

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2101	204	41	23	15	201	49	533
2102	362	168	68	322	32	17	969
2103	284	98	24	14	9	10	439
2104	320	204	63	169	244	12	1012
2108	282	272	61	116	228	314	1273
Mean	290	157	48	127	143	80	845
S.D.	58	90	22	128	113	132	350

Unit: Count

Appendix 2-251 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 100

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3101	483	348	335	285	245	204	1900
3102	470	283	304	279	373	123	1832
3103	315	26	34	14	26	236	651
3104	446	207	184	81	62	195	1175
3108	362	278	83	42	10	16	791
Mean	415	228	188	140	143	155	1270
S.D.	73	124	132	132	159	88	578

Unit: Count

Appendix 2-252 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4101	470	412	412	410	314	156	2174
4103	464	119	48	93	49	112	885
4104	250	107	11	22	30	270	690
4109	457	367	3	144	178	30	1179
4110	425	229	163	35	96	321	1269
Mean	413	247	127	141	133	178	1239
S.D.	93	140	171	158	116	118	571

Unit: Count

Appendix 2-253 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1118	391	281	195	267	148	144	1426
1119	403	335	414	360	300	273	2085
1120	448	354	368	329	220	80	1799
1121	392	278	158	192	73	113	1206
1122	392	330	298	257	254	302	1833
Mean	405	316	287	281	199	182	1670
S.D.	24	34	109	66	90	99	350

Unit: Count

Appendix 2-254 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118	329	254	175	324	289	269	1640
4119	357	197	269	196	118	81	1218
4120	514	456	241	312	379	403	2305
4121	468	477	285	383	399	119	2131
4122	419	254	237	171	247	228	1556
Mean	417	328	241	277	286	220	1770
S.D.	76	129	42	90	113	128	443

Unit: Count

Appendix 2-255 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1008	439	472	354	306	199	254	2024
1009	370	371	390	455	325	315	2226
1010	325	382	402	295	259	100	1763
1011	426	415	346	342	397	315	2241
1012	430	260	326	254	56	15	1341
Mean	398	380	364	330	247	200	1919
S.D.	49	78	32	76	130	136	377

Unit: Count

Appendix 2-256 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	409	393	325	36	28	3	1194
4009	463	449	316	51	276	222	1777
4010	435	410	399	404	438	378	2464
4011	405	336	295	89	353	65	1543
4012	427	414	357	348	367	237	2150
Mean	428	400	338	186	292	181	1826
S.D.	23	41	41	176	159	149	498

Unit: Count

Appendix 2-257 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
1118	292	259	254	340	255	268	1668
1119	406	354	352	489	335	333	2269
1120	364	301	244	289	87	4	1289
1121	320	309	88	300	268	15	1300
1122	291	210	272	209	153	132	1267
Mean	335	287	242	325	220	150	1559
S.D.	50	55	96	103	99	148	430

Unit: Count

Appendix 2-258 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118	315	276	361	194	170	170	1486
4119	329	274	163	271	99	283	1419
4120	433	396	403	393	271	224	2120
4121	241	317	293	191	182	7	1231
4122	370	313	289	98	202	163	1435
Mean	338	315	302	229	185	169	1538
S.D.	71	49	91	110	62	103	339

Unit: Count

Appendix 3-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
1001	413	430	449	453	480	502	531	118
1002	408	437	459	488	504	526	542	134
1003	397	431	453	475	494	523	542	145
1004	444	475	501	509	530	547	557	113
1005	414	442	469	489	515	535	549	135
1006	426	447	476	491	518	545	553	127
1007	442	477	508	532	557	587	587	145
1008	426	460	486	503	531	545	556	130
1009	402	429	444	470	485	499	514	112
1010	410	447	482	490	527	567	580	170
1011	399	426	449	474	496	518	530	131
1012	424	453	482	515	549	567	587	163
Mean	417	446	472	491	516	538	552	135
S.D.	16	17	21	22	24	27	23	18

Unit: g

Appendix 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 30

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
2001	406	441	465	499	529	554	570	164
2002	420	462	487	514	540	567	577	157
2003	434	467	502	530	550	576	585	151
2004	438	481	508	537	572	592	598	160
2005	452	489	517	549	563	581	600	148
2006	412	451	475	498	513	536	555	143
2007	407	433	453	478	495	503	513	106
2008	419	448	468	495	518	534	546	127
2009	413	439	475	494	531	551	552	139
2010	419	452	470	486	506	516	532	113
2011	419	445	469	478	508	528	537	118
2012	397	423	450	478	504	532	530	133
Mean	420	453	478	503	527	548	558	138
S.D.	15	19	21	24	25	27	28	19

Unit: g

Appendix 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
3001	414	435	458	478	515	538	547	133
3002	429	458	485	513	542	555	563	134
3003	402	441	471	494	523	553	564	162
3004	401	427	452	483	504	517	544	143
3005	418	454	476	510	532	560	569	151
3006	419	452	477	500	526	543	557	138
3007	456	490	534	555	591	613	624	168
3008	423	460	489	504	531	549	549	126
3009	416	448	472	483	508	526	543	127
3010	410	446	476	488	507	526	548	138
3011	403	427	457	471	490	517	529	126
3012	442	462	490	517	534	568	577	135
Mean	419	450	478	500	525	547	560	140
S.D.	17	17	21	23	26	27	24	14

Unit: g

Appendix 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4001	423	461	493	518	546	579	594	171
4002	401	428	457	478	505	525	540	139
4003	435	461	475	492	508	519	531	96
4004	414	447	463	485	509	523	534	120
4005	415	438	457	470	488	514	528	113
4006	422	442	465	483	500	517	526	104
4007	450	476	503	521	552	569	586	136
4008	413	447	473	495	519	540	550	137
4009	417	449	462	484	498	521	525	108
4010	441	472	509	535	559	572	576	135
4011	413	434	461	471	487	501	530	117
4012	397	423	450	456	482	500	514	117
Mean	420	448	472	491	513	532	545	124
S.D.	15	17	19	23	26	27	26	20

Unit: g

Appendix 3-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	Gain 1-15
1101	258	279	289	31
1102	253	252	276	23
1103	265	280	292	27
1104	257	280	290	33
1105	238	257	265	27
1106	264	269	295	31
1107	281	293	307	26
1108	263	289	301	38
1109	254	273	276	22
1110	251	262	267	16
1111	271	280	293	22
1112	275	283	299	24
Mean	261	275	288	27
S.D.	12	13	13	6

Unit: g

Appendix 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 30

Animal number	Day of administration 1	8	15	Gain 1-15
2101	271	274	286	15
2102	246	269	276	30
2103	261	275	286	25
2104	267	287	299	32
2105	238	265	278	40
2106	257	273	288	31
2107	258	271	281	23
2108	260	264	280	20
2109	290	314	325	35
2110	267	277	285	18
2111	277	293	292	15
2112	266	277	293	27
Mean	263	278	289	26
S.D.	14	14	13	8

Unit: g

Appendix 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	Day of administration 1	8	15	Gain 1-15
3101	253	262	272	19
3102	266	278	291	25
3103	259	268	275	16
3104	284	300	309	25
3105	267	276	288	21
3106	251	270	295	44
3107	247	261	270	23
3108	247	245	255	8
3109	263	282	284	21
3110	265	279	285	20
3111	268	286	301	33
3112	263	273	274	11
Mean	261	273	283	22
S.D.	11	14	15	9

Unit: g

Appendix 3-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	Gain 1-15
4101	263	279	286	23
4102	243	247	251	8
4103	259	273	276	17
4104	274	288	285	11
4105	267	266	286	19
4106	250	245	253	3
4107	255	269	275	20
4108	254	266	275	21
4109	285	297	300	15
4110	265	267	284	19
4111	247	257	257	10
4112	265	272	280	15
Mean	261	269	276	15
S.D.	12	15	15	6

Unit: g

Appendix 3-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 0	7	14	20a)	Gain 0-20
1101	291	329	364	449	158
1102	271	315	338	413	142
1103	298	335	373	464	166
1104	316	352	387	473	157
1105	270	312	353	446	176
1106	292	347	374	451	159
1107	313	352	386	454	141
1108	307	336	381	460	153
1109	285	324	359	434	149
1110	279	304	337	430	151
1111	305	339	383	472	167
1112	301	351	410	489	188
Mean	294	333	370	453	159
S.D.	15	16	21	21	14

Unit: g
a): Gestation day

Appendix 3-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 30

Dam number	Administration 0	7	14	20a)	Gain 0-20
2101	283	315	347	442	159
2102	290	329	380	470	180
2103	283	344	387	467	184
2104	298	342	371	458	160
2105	276	321	364	455	179
2106	299	331	358	428	129
2107	285	324	350	425	140
2108	273	316	351	439	166
2109	329	381	432	544	215
2110	309	349	398	492	183
2111	312	343	392	474	162
2112	293	329	369	455	162
Mean	294	335	375	462	168
S.D.	16	18	25	32	22

Unit: g
a): Gestation day

Appendix 3-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 100

Dam number	Administration 0	7	14	20a)	Gain 0-20
3101	276	315	358	443	167
3102	299	329	379	470	171
3103	276	319	365	443	167
3104	318	346	391	486	168
3105	296	330	374	461	165
3106	293	334	386	457	164
3107	276	313	351	442	166
3108	259	286	323	412	153
3109	295	322	359	444	149
3110	282	322	357	441	159
3111	305	333	376	468	163
3112	279	302	340	421	142
Mean	288	321	363	449	161
S.D.	16	16	20	21	9

Unit: g
a): Gestation day

Appendix 3-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 0	7	14	20a)	Gain 0-20
4101	286	323	356	409	123
4102	256	288	319	392	136
4103	277	311	348	418	141
4104	286	329	372	439	153
4105	295	327	365	439	144
4106	265	301	333	405	140
4107	287	322	374	440	153
4108	282	298	335	411	129
4109	298	315	355	435	137
4110	283	318	375	460	177
4111	259	304	350	426	167
4112	284	311	351	429	145
Mean	280	312	353	425	145
S.D.	13	13	17	19	15

Unit: g
a): Gestation day

Appendix 3-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 0	Administration 4a)	Gain 0-4
1101	344	369	25
1102	319	338	19
1103	351	367	16
1104	366	386	20
1105	332	329	-3
1106	358	375	17
1107	368	363	-5
1108	380	384	4
1109	328	349	21
1110	311	328	17
1111	365	391	26
1112	402	394	-8
Mean	352	364	12
S.D.	27	24	12

Unit: g
a): Lactation day

Appendix 3-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 30

Dam number	Administration 0	Administration 4a)	Gain 0-4
2101	335	342	7
2102	347	375	28
2103	365	387	22
2104	349	394	45
2105	349	369	20
2106	367	369	2
2107	343	371	28
2108	338	337	-1
2109	394	400	6
2110	383	385	2
2111	375	383	8
2112	330	360	30
Mean	356	373	16
S.D.	20	19	14

Unit: g
a): Lactation day

Appendix 3-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 100

Dam number	Administration 0	Administration 4a)	Gain 0-4
3101	328	347	19
3102	381	373	-8
3103	350	364	14
3104	387	382	-5
3105	370	365	-5
3106	373	375	2
3107	346	339	-7
3108	291	331	40
3109	337	340	3
3110	338	349	11
3111b)	370		
3112	323	346	23
Mean	350	356	8
S.D.	28	17	15

Unit: g
a): Lactation day
b): Necropsied on lactation day 2 because all pups died

Appendix 3-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 0	Administration 4a)	Gain 0-4
4101	351	346	-5
4102	299	324	25
4103	311	334	23
4104	339	364	25
4105	361	374	13
4106	333	320	-13
4107	344	353	9
4108	325	332	7
4109	348	345	-3
4110	356	375	19
4111b)	300		
4112	340	349	9
Mean	334	347	10
S.D.	21	19	13

Unit: g
a): Lactation day
b): Necropsied on lactation day 4 because all pups died

Appendix 3-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
1113	251	272	278	283	290	300	301	50
1114	254	256	273	278	286	284	294	40
1115	261	271	293	301	310	316	324	63
1116	285	301	314	337	352	363	364	79
1117	268	281	297	304	312	318	325	57
1118	275	302	314	315	332	347	341	66
1119	237	257	275	277	278	295	300	63
1120	263	283	292	301	320	312	329	66
1121	258	282	290	295	296	305	318	60
1122	259	268	276	289	312	317	319	60
Mean	261	277	290	298	309	316	322	60
S.D.	13	16	15	18	22	24	21	10

Unit: g

Appendix 3-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats (Satellite group, Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4113	251	257	282	291	299	289	308	57
4114	265	272	279	281	297	315	320	55
4115	247	248	264	264	271	283	288	41
4116	268	271	287	301	308	299	317	49
4117	260	266	276	282	284	288	295	35
4118	258	270	271	289	294	303	314	56
4119	263	269	279	286	291	292	296	33
4120	270	273	285	294	309	313	322	52
4121	285	294	296	306	321	329	341	56
4122	270	295	309	307	320	329	325	55
Mean	264	272	283	290	299	304	313	49
S.D.	11	14	13	13	16	17	16	9

Unit: g

Appendix 3-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14	Gain 1-14
1008	556	566	565	9
1009	513	523	532	19
1010	582	595	598	16
1011	535	552	558	23
1012	586	592	597	11
Mean	554	566	570	16
S.D.	31	30	28	6

Unit: g

Appendix 3-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Recovery period)
Dose (mg/kg): 300

Animal number	Day of recovery 1	8	14	Gain 1-14
4008	553	571	577	24
4009	521	525	536	15
4010	584	593	598	14
4011	529	545	566	37
4012	520	537	550	30
Mean	541	554	565	24
S.D.	27	27	24	10

Unit: g

Appendix 3-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 1	8	14	Gain 1-14
1118	351	341	353	2
1119	305	307	310	5
1120	335	332	325	-10
1121	317	323	323	6
1122	321	319	329	8
Mean	326	324	328	2
S.D.	18	13	16	7

Unit: g

Appendix 3-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats (Recovery period)
Dose (mg/kg): 300

Animal number	Day of recovery 1	8	14	Gain 1-14
4118	320	319	314	-6
4119	299	314	331	32
4120	325	337	327	2
4121	341	343	338	-3
4122	324	345	349	25
Mean	322	332	332	10
S.D.	15	14	13	17

Unit: g

Appendix 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 2	8	15	30	36	42
1001	21	22	22	22	22	24
1002	21	24	22	22	21	22
1003	22	26	24	26	25	27
1004	22	26	26	19	22	24
1005	24	25	24	24	23	22
1006	25	23	25	22	25	19
1007	27	28	25	23	26	23
1008	26	25	26	23	23	23
1009	24	24	25	23	21	26
1010	27	25	24	23	29	24
1011	23	20	23	22	23	23
1012	21	25	21	23	22	23
Mean	24	24	24	23	24	23
S.D.	2	2	2	2	2	2

Unit: g/rat/day

Appendix 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 30

Animal number	Day of administration 2	8	15	30	36	42
2001	23	26	25	24	24	25
2002	23	25	23	23	20	23
2003	23	25	26	22	21	23
2004	25	25	23	26	23	27
2005	25	24	24	23	20	21
2006	23	24	23	22	20	23
2007	25	23	23	22	20	22
2008	25	23	20	20	21	24
2009	23	23	27	24	23	23
2010	22	24	19	19	19	20
2011	22	23	23	23	23	21
2012	24	26	21	22	23	20
Mean	24	24	23	23	21	23
S.D.	1	1	2	2	2	2

Unit: g/rat/day

Appendix 4-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 100

Animal number	Day of administration 2	8	15	30	36	42
3001	17	22	24	22	25	23
3002	24	30	25	23	21	23
3003	23	26	25	25	25	26
3004	23	24	24	23	21	25
3005	22	23	24	23	25	24
3006	23	28	23	23	23	25
3007	25	32	28	25	25	24
3008	22	22	25	23	23	23
3009	23	25	24	21	23	22
3010	20	23	24	23	22	25
3011	25	23	23	24	23	20
3012	23	23	24	22	25	23
Mean	23	25	24	23	23	24
S.D.	2	3	1	1	2	2

Unit: g/rat/day

Appendix 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 2	8	15	30	36	42
4001	24	26	23	29	28	26
4002	20	23	24	19	22	22
4003	23	25	24	25	24	24
4004	23	26	20	24	24	27
4005	24	21	24	23	26	24
4006	24	23	22	20	22	23
4007	21	26	27	24	24	26
4008	23	22	26	20	23	25
4009	23	25	23	21	24	23
4010	24	24	27	23	23	25
4011	22	24	24	22	23	26
4012	22	23	29	29	21	26
Mean	23	24	24	23	24	25
S.D.	1	2	2	3	2	2

Unit: g/rat/day

Appendix 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

Animal number	Day of administration 2	8	15
1101	18	16	20
1102	20	12	18
1103	18	19	20
1104	17	19	21
1105	17	19	17
1106	18	14	23
1107	14	19	18
1108	18	23	20
1109	16	16	17
1110	17	15	11
1111	18	18	20
1112	22	14	19
Mean	18	17	19
S.D.	2	3	3

Unit: g/rat/day

Appendix 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 30

Animal number	Day of administration 2	8	15
2101	16	14	18
2102	17	20	18
2103	17	19	18
2104	17	19	19
2105	20	21	21
2106	17	19	18
2107	14	20	19
2108	16	14	18
2109	18	21	22
2110	16	20	16
2111	17	19	16
2112	15	13	18
Mean	17	18	18
S.D.	1	3	2

Unit: g/rat/day

Appendix 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	Day of administration 2	8	15
3101	20	15	19
3102	21	17	21
3103	18	15	21
3104	17	22	20
3105	14	21	19
3106	17	18	22
3107	15	18	16
3108	14	10	16
3109	14	18	17
3110	19	18	19
3111	14	23	21
3112	9	20	16
Mean	16	18	19
S.D.	3	4	2

Unit: g/rat/day

Appendix 4-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	Day of administration 2	8	15
4101	14	19	19
4102	17	15	14
4103	16	20	19
4104	17	22	17
4105	10	15	20
4106	17	19	21
4107	12	18	16
4108	13	17	17
4109	13	19	18
4110	14	14	18
4111	11	18	15
4112	11	17	18
Mean	14	18	18
S.D.	3	2	2

Unit: g/rat/day

Appendix 4-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 1	7	14	20a)
1101	18	23	23	19
1102	20	24	21	19
1103	20	21	25	20
1104	15	24	26	19
1105	20	21	19	20
1106	19	25	22	17
1107	23	22	23	18
1108	18	26	24	19
1109	18	24	21	22
1110	17	17	19	17
1111	15	23	27	23
1112	25	26	33	26
Mean	19	23	24	20
S.D.	3	3	4	3

Unit: g/rat/day
a): Gestation day

Appendix 4-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 30

Dam number	Administration 1	7	14	20a)
2101	18	21	19	23
2102	24	24	28	22
2103	19	31	28	25
2104	19	24	20	17
2105	19	20	24	22
2106	19	23	18	20
2107	16	26	22	21
2108	17	22	25	21
2109	20	30	31	25
2110	19	26	26	24
2111	18	24	27	21
2112	18	21	22	17
Mean	19	24	24	22
S.D.	2	3	4	3

Unit: g/rat/day
a): Gestation day

Appendix 4-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 100

Dam number	Administration 1	7	14	20a)
3101	21	25	25	22
3102	19	25	30	21
3103	22	22	28	22
3104	22	21	29	27
3105	19	23	27	20
3106	18	23	32	21
3107	21	25	24	23
3108	14	18	20	20
3109	16	22	22	20
3110	19	25	26	18
3111	15	25	28	24
3112	11	16	18	20
Mean	18	23	26	22
S.D.	3	3	4	2

Unit: g/rat/day
a): Gestation day

Appendix 4-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 1	7	14	20a)
4101	19	24	25	19
4102	11	20	18	25
4103	21	23	26	17
4104	14	25	26	23
4105	17	24	26	24
4106	19	31	36	31
4107	18	22	28	20
4108	13	18	23	18
4109	7	23	24	25
4110	19	22	30	26
4111	17	21	27	21
4112	17	20	25	21
Mean	16	23	26	23
S.D.	4	3	4	4

Unit: g/rat/day
a): Gestation day

Appendix 4-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 0

Dam number	Administration 2	4a)
1101	19	35
1102	20	36
1103	27	33
1104	21	42
1105	18	26
1106	31	43
1107	18	32
1108	19	42
1109	27	39
1110	20	37
1111	28	43
1112	21	36
Mean	22	37
S.D.	5	5

Unit: g/rat/day
a): Lactation day

Appendix 4-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 30

Dam number	Administration 2	4a)
2101	26	41
2102	21	41
2103	28	43
2104	32	37
2105	17	41
2106	28	42
2107	31	38
2108	15	36
2109	15	31
2110	17	34
2111	20	36
2112	22	37
Mean	23	38
S.D.	6	4

Unit: g/rat/day
a): Lactation day

Appendix 4-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 100

Dam number	Administration 2	4a)
3101	12	47
3102	18	31
3103	21	36
3104	22	41
3105	20	36
3106	20	32
3107	14	28
3108	25	41
3109	19	34
3110	21	40
3111b)		
3112	25	36
Mean	20	37
S.D.	4	5

Unit: g/rat/day
a): Lactation day
b): Necropsied on lactation day 2 because all pups died

Appendix 4-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 300

Dam number	Administration 2	4a)
4101	19	28
4102	23	40
4103	22	39
4104	26	42
4105	24	42
4106	33	42
4107	22	47
4108	19	46
4109	19	23
4110	24	44
4111b)	0	
4112	21	41
Mean	21	39
S.D.	8	7

Unit: g/rat/day
a): Lactation day
b): Necropsied on lactation day 4 because all pups died

Appendix 4-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats (Satellite group, Administration period)
Dose (mg/kg): 0

Animal number	Day of administration 2	8	15	30	36	42
1113	14	18	17	14	18	15
1114	18	13	20	18	14	20
1115	15	17	20	17	9	19
1116	20	20	18	19	19	20
1117	13	18	21	17	15	18
1118	14	21	20	14	17	13
1119	16	16	20	19	18	17
1120	14	18	15	17	11	17
1121	16	20	16	16	17	17
1122	11	17	16	20	17	16
Mean	15	18	18	17	16	17
S.D.	3	2	2	2	3	2

Unit: g/rat/day

Appendix 4-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats (Satellite group, Administration period)
Dose (mg/kg): 300

Animal number	Day of administration 2	8	15	30	36	42
4113	16	16	19	14	10	17
4114	12	17	17	17	18	20
4115	13	10	18	13	19	20
4116	17	16	20	16	13	19
4117	13	15	18	16	11	18
4118	15	18	12	15	17	18
4119	14	17	14	16	16	17
4120	13	16	17	19	13	20
4121	11	17	16	16	19	20
4122	10	21	18	15	18	17
Mean	13	16	17	16	15	19
S.D.	2	3	2	2	3	1

Unit: g/rat/day

Appendix 4-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 2	8	14
1008	25	28	27
1009	25	28	30
1010	20	28	26
1011	23	29	29
1012	20	26	29
Mean	23	28	28
S.D.	3	1	2

Unit: g/rat/day

Appendix 4-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Recovery period)
Dose (mg/kg): 300

Animal number	Day of recovery 2	8	14
4008	24	30	29
4009	25	23	29
4010	26	32	27
4011	25	29	30
4012	31	29	32
Mean	26	29	29
S.D.	3	3	2

Unit: g/rat/day

Appendix 4-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats (Recovery period)
Dose (mg/kg): 0

Animal number	Day of recovery 2	8	14
1118	19	16	20
1119	17	21	22
1120	18	20	15
1121	19	22	22
1122	14	20	25
Mean	17	20	21
S.D.	2	2	4

Unit: g/rat/day

Appendix 4-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats (Recovery period)
Dose (mg/kg): 300

Animal number	Day of recovery 2	8	14
4118	18	21	16
4119	19	25	23
4120	23	27	19
4121	21	23	22
4122	23	27	26
Mean	21	25	21
S.D.	2	3	4

Unit: g/rat/day

Appendix 5-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1008	8.5	+	+-	-	+-	-	+-	Y
1009	7.5	+	+	-	+-	-	+-	Y
1010	8.5	+	+	-	-	-	+-	Y
1011	8.5	+	+-	-	+-	-	+-	Y
1012	8.5	+-	+-	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	+-	-
1010	-	-	+-	-	-	-	-
1011	-	-	+-	-	-	+-	-
1012	-	-	+-	-	-	+-	-

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

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

Appendix 5-3

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	43	18.5	1512	1.22	4.59	1.78
1009	45	15.4	1088	0.80	2.55	1.08
1010	35	15.9	1862	1.43	5.13	2.26
1011	41	14.9	1664	1.07	4.06	1.82
1012	35	16.4	1820	2.00	4.91	2.43
Mean	40	16.2	1589	1.30	4.25	1.87
S.D.	5	1.4	312	0.45	1.03	0.52

Appendix 5-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 30

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
2008	7.5	+-	+-	-	+-	-	+-	Y
2009	>=9.0	+-	+-	-	+-	-	+-	Y
2010	>=9.0	+	+	-	+-	-	+-	Y
2011	8.5	+	+	-	+-	-	+-	Y
2012	8.5	++	+	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 30

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
2008	-	-	+-	-	-	+-	-
2009	-	-	+-	-	-	+-	-
2010	-	-	+-	-	-	+-	-
2011	-	-	+-	-	-	+-	-
2012	-	-	+-	-	-	+-	-

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

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

Appendix 5-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 30

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
2008	63	34.7	766	1.11	4.30	1.67
2009	50	19.7	1576	1.77	5.24	2.25
2010	36	7.0	2290	0.81	2.54	1.04
2011	36	11.6	1730	0.86	3.16	1.30
2012	46	19.1	1276	1.26	3.71	1.41
Mean	46	18.4	1528	1.16	3.79	1.53
S.D.	11	10.5	563	0.39	1.04	0.46

Appendix 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
3008	8.0	+-	+-	-	+-	-	+-	Y
3009	8.5	++	+	-	-	-	+-	Y
3010	7.5	+	+	-	+-	-	+-	Y
3011	8.5	-	+	-	-	-	+-	Y
3012	8.0	+	+	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
3008	-	-	+-	-	-	+-	-
3009	-	-	+-	-	-	+-	-
3010	-	-	+-	-	-	-	-
3011	-	-	+-	-	-	+	-
3012	-	-	+-	-	-	+-	-

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

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

Appendix 5-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 100

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
3008	44	20.1	1542	1.21	4.87	1.53
3009	39	16.6	1424	1.36	3.99	1.76
3010	39	8.4	2044	0.79	2.88	1.06
3011	64	39.4	638	1.18	4.14	1.97
3012	54	16.6	1504	0.90	4.43	1.36
Mean	48	20.2	1430	1.09	4.06	1.54
S.D.	11	11.6	506	0.24	0.74	0.35

Appendix 5-10

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4008	7.5	++	+	-	-	-	+-	Y
4009	7.0	+	+	-	-	-	+-	Y
4010	8.5	++	+	-	+-	-	+-	Y
4011	8.0	++	+-	-	+-	-	+-	Y
4012	8.5	+	-	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+-	-
4009	-	-	+-	-	-	+	-
4010	-	-	+-	-	-	+-	-
4011	-	-	+-	-	-	+-	-
4012	-	-	+-	-	-	+	-

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

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

Appendix 5-12

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 300

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	42	15.9	1272	1.21	3.03	1.24
4009	40	17.7	1556	1.56	4.19	1.88
4010	43	15.8	1606	1.20	3.67	1.42
4011	38	8.1	1952	0.75	2.62	1.09
4012	39	13.7	2116	1.15	4.86	2.14
Mean	40	14.2	1700	1.17	3.67	1.55
S.D.	2	3.7	335	0.29	0.89	0.44

Appendix 5-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1118	7.5	-	-	-	+	-	+-	Y
1119	7.5	-	-	-	-	-	+-	Y
1120	6.0	++	+-	-	-	+	+-	Y
1121	7.0	+-	-	-	-	-	+-	Y
1122	7.5	++	+-	-	-	-	+-	Y

1) - : 0 mg/dL	+- : 15 mg/dL	+ : 30 mg/dL	++ : 100 mg/dL	+++ : >=300 mg/dL
2) - : 0 mg/dL	+- : 5 mg/dL	+ : 15 mg/dL	++ : 40 mg/dL	+++ : 80 mg/dL
3) - : 0 mg/dL	+ : 100 mg/dL	++ : 250 mg/dL	+++ : 500 mg/dL	++++ : >=1000 mg/dL
4) - : 0 mg/dL	+- : 0.015 mg/dL	+ : 0.062 mg/dL	++ : 0.135 mg/dL	+++ : 0.405 mg/dL
5) - : 0 mg/dL	+ : 0.8 mg/dL	++ : 1.6 mg/dL	+++ : 3.2 mg/dL	
6) +- : 0.1-1.0 E.U./dL	+ : 2.0 E.U./dL	++ : 4.0 E.U./dL	+++ : >=8.0 E.U./dL	
7) LY : Light yellow	Y : Yellow	DY : Dark yellow		

Appendix 5-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	+-	-
1119	-	-	+-	-	-	-	-
1120	-	-	+-	-	-	+-	-
1121	-	-	+-	-	-	+-	-
1122	-	-	+-	-	-	+-	-

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

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

Appendix 5-15

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	35	15.6	1084	1.03	2.74	1.22
1119	28	10.2	1934	0.82	3.38	1.63
1120	28	3.7	2604	0.41	1.54	0.56
1121	26	7.5	1996	0.69	2.55	1.16
1122	30	5.8	1938	0.44	1.71	0.68
Mean	29	8.6	1911	0.68	2.38	1.05
S.D.	3	4.6	541	0.26	0.76	0.43

Appendix 5-16

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118	7.0	-	-	-	-	-	+-	Y
4119	6.5	+	+-	-	-	-	+-	Y
4120	6.5	+-	+-	-	-	-	+-	Y
4121	6.5	+-	+-	-	-	-	+-	Y
4122	6.5	+-	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	-	-
4119	-	-	+-	-	-	+-	-
4120	-	-	+-	-	-	+-	-
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	-	-

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

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

Appendix 5-18

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 300

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	43	10.0	1702	1.12	2.42	1.18
4119	26	4.0	2138	0.32	1.37	0.54
4120	26	4.1	2676	0.57	1.67	0.82
4121	27	3.1	2444	0.48	1.17	0.71
4122	33	4.6	1630	0.35	1.11	0.66
Mean	31	5.2	2118	0.57	1.55	0.78
S.D.	7	2.8	455	0.32	0.53	0.24

Appendix 5-19

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1008	>=9.0	+	+-	-	+-	-	+-	Y
1009	8.0	+-	+-	-	-	-	+-	Y
1010	8.0	+-	+-	-	-	-	+-	Y
1011	>=9.0	+-	-	-	-	-	+-	Y
1012	8.5	+	-	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1008	-	-	+-	-	-	+-	-
1009	-	-	+-	-	-	+	-
1010	-	-	+-	-	-	+-	-
1011	-	-	+-	-	-	+	-
1012	-	-	+-	-	-	+-	-

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

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

Appendix 5-21

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1008	62	22.5	1582	1.35	5.63	1.98
1009	44	17.4	1972	1.91	5.33	2.30
1010	35	16.5	2098	1.78	5.47	2.05
1011	48	25.9	1572	1.92	6.58	2.64
1012	43	14.9	1816	1.52	4.43	1.67
Mean	46	19.4	1808	1.70	5.49	2.13
S.D.	10	4.6	233	0.25	0.77	0.36

Appendix 5-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4008	8.0	+	+	-	-	-	+-	Y
4009	8.5	+	+	-	+-	-	+-	Y
4010	>=9.0	++	+-	-	+-	-	+-	Y
4011	>=9.0	+	-	-	+-	-	+-	Y
4012	>=9.0	++	-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4008	-	-	+-	-	-	+-	-
4009	-	-	+-	-	-	+-	-
4010	-	-	+-	-	-	+	-
4011	-	-	+-	-	-	+-	-
4012	-	-	+-	-	-	+-	-

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

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

Appendix 5-24

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	44	19.7	1772	1.73	5.72	2.05
4009	35	9.7	1802	0.89	2.59	1.09
4010	47	15.0	1990	1.59	4.31	1.92
4011	53	23.2	1786	2.04	6.48	2.78
4012	34	15.3	1980	1.56	4.91	2.02
Mean	43	16.6	1866	1.56	4.80	1.97
S.D.	8	5.1	109	0.42	1.48	0.60

Appendix 5-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
1118	7.0	-	-	-	-	-	+-	Y
1119	6.0	-	-	-	-	-	+-	Y
1120	7.0	+-	-	-	-	+	+-	Y
1121	6.0	+	-	-	-	-	+-	Y
1122	7.0	-	-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
1118	-	-	+-	-	-	-	-
1119	-	-	+-	-	-	-	-
1120	-	-	+-	-	-	+-	-
1121	-	-	+-	-	-	-	-
1122	-	-	+-	-	-	-	-

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

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

Appendix 5-27

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 0

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
1118	31	12.3	1828	1.33	3.49	1.33
1119	34	11.6	1954	0.95	3.65	1.44
1120	33	8.5	1846	0.54	2.62	0.83
1121	32	6.3	2464	0.57	2.51	0.86
1122	35	11.1	1572	0.93	2.57	1.04
Mean	33	10.0	1933	0.86	2.97	1.10
S.D.	2	2.5	328	0.32	0.55	0.28

Appendix 5-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118	6.5	+-	-	-	-	-	+-	Y
4119	6.5	+	-	-	-	-	+-	Y
4120	7.0	+	-	-	-	+	+-	Y
4121	7.0	+	+-	-	-	-	+-	Y
4122	8.5	-	-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118	-	-	+-	-	-	+-	-
4119	-	-	+-	-	-	+-	-
4120	-	-	+-	-	-	-	-
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	+-	-

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

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

Appendix 5-30

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual water intake and urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 300

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118	34	9.8	1998	1.04	3.07	1.27
4119	37	6.7	2628	0.76	2.76	0.96
4120	34	8.3	2226	0.71	2.84	1.16
4121	20	5.6	2908	0.85	2.58	0.95
4122	36	11.5	2060	1.29	3.80	1.56
Mean	32	8.4	2364	0.93	3.01	1.18
S.D.	7	2.4	391	0.24	0.48	0.25

Appendix 6-1

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 0

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
1001	958	16.6	47.7	49.8	17.3	34.8	2.1	98.1	17.5	22.1	257
1002	873	14.9	42.8	49.0	17.1	34.9	1.8	88.9	12.0	15.3	224
1003	888	15.6	44.9	50.5	17.6	34.8	2.0	95.3	13.3	18.4	243
1004	796	15.2	42.2	53.0	19.1	36.0	2.2	86.0	12.5	18.1	196
1005	837	15.1	42.6	50.9	18.0	35.4	1.9	93.8	12.6	19.1	233
Mean	870	15.5	44.0	50.6	17.8	35.2	2.0	92.4	13.6	18.6	231
S.D.	61	0.7	2.3	1.5	0.8	0.5	0.2	4.9	2.2	2.4	23

Appendix 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1001	60.9	69.5	25.8	2.0	0.5	1.5	0.6	42.3	15.7	1.2	0.3	0.9	0.4
1002	87.3	82.0	13.5	1.2	0.3	2.6	0.4	71.7	11.8	1.0	0.3	2.2	0.3
1003	61.6	66.1	28.3	1.0	0.3	3.3	1.1	40.7	17.5	0.6	0.2	2.0	0.7
1004	59.4	71.0	22.5	2.3	0.3	3.3	0.6	42.2	13.4	1.4	0.2	2.0	0.4
1005	63.4	79.3	16.7	0.8	0.4	2.3	0.5	50.3	10.6	0.5	0.2	1.5	0.3
Mean	66.5	73.6	21.4	1.5	0.4	2.6	0.6	49.4	13.8	0.9	0.2	1.7	0.4
S.D.	11.7	6.8	6.2	0.7	0.1	0.8	0.3	13.0	2.8	0.4	0.1	0.5	0.2

LUC: Large unstained cells

Appendix 6-3

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 30

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
2001	896	15.6	44.3	49.5	17.4	35.2	2.9	106.7	14.6	20.3	219
2002	886	15.2	43.2	48.8	17.1	35.1	1.6	91.4	12.1	14.3	249
2003	825	15.9	44.7	54.1	19.3	35.6	2.1	110.0	12.0	17.7	275
2004	862	15.7	44.8	52.0	18.2	35.0	1.4	86.6	13.2	18.4	183
2005	849	15.6	43.7	51.4	18.3	35.7	1.5	100.8	12.5	18.2	237
Mean	864	15.6	44.1	51.2	18.1	35.3	1.9	99.1	12.9	17.8	233
S.D.	29	0.3	0.7	2.1	0.9	0.3	0.6	9.9	1.1	2.2	34

Appendix 6-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 30

Animal number	WBC 10E2/μL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/μL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
2001	77.5	74.0	21.4	1.7	0.4	2.2	0.3	57.4	16.6	1.3	0.3	1.7	0.2
2002	66.3	69.3	25.9	1.7	0.5	2.0	0.5	46.0	17.2	1.1	0.4	1.3	0.4
2003	82.1	75.0	22.0	0.6	0.4	1.3	0.8	61.5	18.0	0.5	0.4	1.0	0.7
2004	34.5	74.3	21.5	2.1	0.3	1.6	0.2	25.7	7.4	0.7	0.1	0.6	0.1
2005	55.7	73.5	20.7	1.4	0.6	3.0	0.9	41.0	11.6	0.8	0.3	1.7	0.5
Mean	63.2	73.2	22.3	1.5	0.4	2.0	0.5	46.3	14.2	0.9	0.3	1.3	0.4
S.D.	19.0	2.3	2.1	0.6	0.1	0.6	0.3	14.2	4.5	0.3	0.1	0.5	0.2

LUC: Large unstained cells

Appendix 6-5

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 100

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
3001	872	15.3	43.4	49.8	17.6	35.3	2.3	104.5	14.7	17.6	273
3002	851	15.1	43.1	50.6	17.7	35.0	1.9	107.4	11.6	17.2	271
3003	794	14.8	41.6	52.4	18.6	35.5	2.2	76.8	12.7	15.5	249
3004	834	15.6	43.7	52.3	18.7	35.7	2.7	104.5	17.6	22.0	274
3005	845	15.9	44.6	52.8	18.8	35.5	1.8	89.1	13.1	17.6	257
Mean	839	15.3	43.3	51.6	18.3	35.4	2.2	96.5	13.9	18.0	265
S.D.	29	0.4	1.1	1.3	0.6	0.3	0.4	13.1	2.3	2.4	11

Appendix 6-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 100

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
3001	91.7	81.7	13.9	0.9	0.3	2.6	0.5	74.9	12.8	0.8	0.3	2.4	0.5
3002	76.1	68.1	25.6	1.6	0.3	3.5	0.9	51.8	19.5	1.2	0.2	2.7	0.7
3003	121.3	66.9	29.1	1.6	0.3	1.6	0.5	81.2	35.3	1.9	0.4	1.9	0.6
3004	123.8	78.3	18.9	0.6	0.3	1.4	0.5	96.8	23.4	0.8	0.4	1.7	0.6
3005	72.7	75.9	19.9	1.4	0.4	2.0	0.5	55.2	14.5	1.0	0.3	1.4	0.4
Mean	97.1	74.2	21.5	1.2	0.3	2.2	0.6	72.0	21.1	1.1	0.3	2.0	0.6
S.D.	24.3	6.5	6.0	0.4	0.0	0.8	0.2	18.7	9.0	0.5	0.1	0.5	0.1

LUC: Large unstained cells

Appendix 6-7

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 300

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
4001	866	15.4	44.1	50.9	17.8	34.9	2.0	103.7	13.0	16.8	239
4002	834	14.8	42.4	50.8	17.8	35.0	1.8	79.6	16.8	21.0	225
4003	844	15.2	43.0	51.0	18.0	35.3	2.1	91.9	14.3	19.0	217
4004	879	15.9	44.4	50.5	18.1	35.8	1.7	115.8	14.6	19.0	279
4005	844	15.4	43.3	51.3	18.2	35.5	1.7	99.9	17.1	20.3	243
Mean	853	15.3	43.4	50.9	18.0	35.3	1.9	98.2	15.2	19.2	241
S.D.	18	0.4	0.8	0.3	0.2	0.4	0.2	13.5	1.7	1.6	24

Appendix 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 300

Animal number	WBC 10E2/μL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/μL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4001	72.6	77.9	18.6	1.3	0.2	1.7	0.3	56.5	13.5	0.9	0.2	1.2	0.2
4002	73.2	59.9	34.8	1.0	0.2	3.1	1.0	43.8	25.4	0.7	0.2	2.2	0.7
4003	56.3	63.7	31.2	1.7	0.3	2.6	0.4	35.9	17.6	1.0	0.2	1.4	0.2
4004	66.7	62.8	33.6	0.8	0.2	2.1	0.5	41.9	22.4	0.5	0.1	1.4	0.3
4005	63.3	72.9	23.8	0.7	0.4	1.6	0.6	46.1	15.1	0.4	0.3	1.0	0.4
Mean	66.4	67.4	28.4	1.1	0.3	2.2	0.6	44.8	18.8	0.7	0.2	1.4	0.4
S.D.	7.0	7.6	6.9	0.4	0.1	0.6	0.3	7.5	5.0	0.3	0.1	0.5	0.2

LUC: Large unstained cells

Appendix 6-9

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
1101	670	12.9	37.0	55.3	19.2	34.7	5.9	176.6	10.9	14.2	267
1102	751	13.3	38.6	51.4	17.7	34.4	5.6	137.8	13.0	12.8	391
1106	763	14.1	40.2	52.7	18.5	35.0	5.6	128.9	12.4	18.1	218
1108	652	13.0	36.7	56.4	19.9	35.3	8.8	154.0	11.1	13.0	330
1112	717	14.0	39.9	55.6	19.5	35.0	6.0	133.1	12.0	15.7	317
Mean	711	13.5	38.5	54.3	19.0	34.9	6.4	146.1	11.9	14.8	305
S.D.	49	0.6	1.6	2.1	0.9	0.3	1.4	19.5	0.9	2.2	66

Appendix 6-10

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1101	129.3	43.5	52.1	0.7	0.2	2.8	0.6	56.2	67.4	0.9	0.2	3.7	0.8
1102	86.1	53.7	43.7	0.5	0.1	1.5	0.4	46.3	37.7	0.4	0.1	1.3	0.4
1106	100.0	66.6	28.0	1.9	0.2	2.7	0.7	66.6	28.0	1.9	0.2	2.7	0.7
1108	72.7	58.7	36.8	0.9	0.2	2.5	1.0	42.7	26.7	0.7	0.1	1.8	0.7
1112	105.6	62.3	32.3	0.9	0.4	2.6	1.6	65.8	34.1	0.9	0.4	2.7	1.7
Mean	98.7	57.0	38.6	1.0	0.2	2.4	0.9	55.5	38.8	1.0	0.2	2.4	0.9
S.D.	21.3	8.9	9.5	0.5	0.1	0.5	0.5	10.9	16.6	0.6	0.1	0.9	0.5

LUC: Large unstained cells

Appendix 6-11

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 30

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
2101	692	13.5	38.3	55.4	19.5	35.3	7.1	127.2	11.4	14.0	273
2102	733	14.0	39.9	54.4	19.0	35.0	4.7	95.0	12.4	18.9	366
2103	701	13.0	37.5	53.4	18.5	34.7	4.2	118.7	11.5	16.5	264
2104	718	13.6	38.3	53.3	18.9	35.4	5.2	108.9	12.2	13.7	374
2108	696	13.3	37.6	54.1	19.1	35.3	5.4	123.1	11.7	11.2	220
Mean	708	13.5	38.3	54.1	19.0	35.1	5.3	114.6	11.8	14.9	299
S.D.	17	0.4	1.0	0.9	0.4	0.3	1.1	12.9	0.4	2.9	68

Appendix 6-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 30

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
2101	159.9	49.6	45.7	0.6	0.2	3.5	0.4	79.3	73.1	0.9	0.4	5.5	0.7
2102	126.6	53.0	44.1	0.6	0.1	1.4	0.8	67.1	55.9	0.7	0.2	1.7	1.0
2103	97.0	51.5	43.5	0.9	0.2	3.1	1.0	49.9	42.1	0.9	0.2	3.0	0.9
2104	87.4	54.8	41.2	0.4	0.2	2.6	0.9	47.9	36.0	0.4	0.1	2.3	0.8
2108	123.3	64.8	31.3	0.4	0.4	2.3	0.8	79.9	38.6	0.5	0.5	2.8	1.0
Mean	118.8	54.7	41.2	0.6	0.2	2.6	0.8	64.8	49.1	0.7	0.3	3.1	0.9
S.D.	28.4	5.9	5.7	0.2	0.1	0.8	0.2	15.4	15.4	0.2	0.2	1.5	0.1

LUC: Large unstained cells

Appendix 6-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
3101	705	13.3	38.1	54.0	18.9	34.9	5.5	128.7	10.9	16.6	318
3102	735	13.3	38.0	51.7	18.0	34.9	4.8	131.5	12.4	14.3	363
3103	707	13.8	38.8	54.9	19.5	35.6	5.7	118.3	11.7	15.0	224
3104	707	13.3	38.3	54.2	18.9	34.8	3.6	122.2	11.4	13.5	254
3108	715	13.8	38.9	54.5	19.4	35.6	6.1	115.1	11.2	10.0*	268
3111a)	679Z	12.8Z	35.4Z	52.2Z	18.8Z	36.0Z	4.8Z	151.4Z	14.1Z	19.4Z	278Z
Mean	714	13.5	38.4	53.9	18.9	35.2	5.1	123.2	11.5	13.9	285
S.D.	12	0.3	0.4	1.3	0.6	0.4	1.0	6.9	0.6	2.5	55

a): Necropsied on lactation day 2 because all pups died.
*: Re-analyzed value
Z: Data was excluded from statistical analysis.

Appendix 6-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
3101	119.4	58.6	37.9	0.3	0.2	1.9	1.1	69.9	45.2	0.4	0.3	2.3	1.3
3102	151.7	42.9	54.5	0.5	0.2	1.5	0.5	65.0	82.7	0.7	0.3	2.2	0.8
3103	101.5	60.5	32.3	0.6	0.3	4.0	2.3	61.4	32.8	0.6	0.3	4.1	2.3
3104	149.8	54.4	41.1	0.5	0.2	2.4	1.4	81.5	61.5	0.8	0.3	3.6	2.0
3108	99.2	67.8	27.7	0.7	0.3	2.6	0.9	67.3	27.5	0.7	0.3	2.5	0.9
3111a)	101.5Z	66.3Z	29.0Z	1.4Z	0.3Z	2.3Z	0.7Z	67.3Z	29.4Z	1.4Z	0.3Z	2.4Z	0.7Z
Mean	124.3	56.8	38.7	0.5	0.2	2.5	1.2	69.0	49.9	0.6	0.3	2.9	1.5
S.D.	25.4	9.2	10.2	0.1	0.1	1.0	0.7	7.6	22.5	0.2	0.0	0.9	0.7

LUC: Large unstained cells
a): Necropsied on lactation day 2 because all pups died.
Z: Data was excluded from statistical analysis.

Appendix 6-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
4101	690	14.0	40.1	58.1	20.3	34.9	8.8	136.6	12.9	15.9	252
4103	734	13.8	39.1	53.3	18.9	35.4	5.1	121.2	12.2	16.4	319
4104	730	13.9	39.4	53.9	19.1	35.4	5.6	135.5	11.5	14.8	253
4109	718	13.8	39.8	55.4	19.2	34.7	6.9	147.7	13.6	16.8	260
4110	702	13.2	37.9	54.0	18.8	34.8	6.2	140.9	11.8	13.7	290
4111a)	492Z	8.9Z	25.2Z	51.2Z	18.2Z	35.5Z	4.2Z	208.8Z	9.9Z	9.0Z*	277Z
Mean	715	13.7	39.3	54.9	19.3	35.0	6.5	136.4	12.4	15.5	275
S.D.	19	0.3	0.9	1.9	0.6	0.3	1.4	9.7	0.9	1.3	29

a): Necropsied on lactation day 4 because all pups died.
*: Re-analyzed value
Z: Data was excluded from statistical analysis.

Appendix 6-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4101	82.6	56.2	40.3	0.7	0.1	2.2	0.5	46.4	33.3	0.5	0.1	1.8	0.4
4103	132.2	59.0	36.8	0.5	0.3	2.9	0.6	78.0	48.7	0.6	0.4	3.8	0.7
4104	130.3	60.1	36.0	0.2	0.2	2.8	0.6	78.3	46.9	0.3	0.3	3.7	0.8
4109	90.5	57.5	36.9	1.0	0.4	3.0	1.2	52.0	33.3	0.9	0.4	2.7	1.1
4110	121.1	60.6	35.0	0.4	0.3	2.6	1.1	73.3	42.4	0.5	0.4	3.1	1.3
4111a)	258.5Z	28.2Z	65.9Z	0.2Z	0.1Z	5.1Z	0.5Z	72.9Z	170.3Z	0.5Z	0.4Z	13.1Z	1.3Z
Mean	111.3	58.7	37.0	0.6	0.3	2.7	0.8	65.6	40.9	0.6	0.3	3.0	0.9
S.D.	23.2	1.8	2.0	0.3	0.1	0.3	0.3	15.2	7.3	0.2	0.1	0.8	0.4

LUC: Large unstained cells
a): Necropsied on lactation day 4 because all pups died.
Z: Data was excluded from statistical analysis.

Appendix 6-17

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
1113	836	15.9	44.1	52.8	19.0	36.0	2.3	121.2	12.3	15.2	182
1114	845	15.0	42.8	50.6	17.7	35.0	1.9	104.5	12.3	15.7	183
1115	860	15.8	43.7	50.8	18.4	36.2	2.2	116.4	10.8	10.6	191
1116	769	14.0	39.4	51.2	18.2	35.5	2.0	97.6	11.8	14.1	180
1117	816	15.2	42.0	51.5	18.7	36.3	1.9	116.3	11.1	14.6	161
Mean	825	15.2	42.4	51.4	18.4	35.8	2.1	111.2	11.7	14.0	179
S.D.	35	0.8	1.9	0.9	0.5	0.5	0.2	9.8	0.7	2.0	11

Appendix 6-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1113	63.5	59.6	35.6	2.1	0.2	2.0	0.3	37.9	22.6	1.3	0.1	1.3	0.2
1114	43.8	58.8	34.8	3.6	0.3	1.9	0.6	25.8	15.3	1.6	0.1	0.8	0.3
1115	45.7	71.0	24.4	2.6	0.5	1.3	0.3	32.5	11.2	1.2	0.2	0.6	0.1
1116	46.4	78.1	16.1	2.8	0.4	1.8	0.8	36.3	7.5	1.3	0.2	0.8	0.4
1117	40.4	68.9	24.2	3.3	0.2	2.8	0.4	27.9	9.8	1.3	0.1	1.1	0.2
Mean	48.0	67.3	27.0	2.9	0.3	2.0	0.5	32.1	13.3	1.3	0.1	0.9	0.2
S.D.	9.0	8.1	8.2	0.6	0.1	0.5	0.2	5.2	5.9	0.2	0.1	0.3	0.1

LUC: Large unstained cells

Appendix 6-19

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
4113	777	14.9	41.2	53.0	19.2	36.2	1.7	125.1	10.8	13.0	197
4114	746	14.4	40.1	53.8	19.2	35.8	2.7	114.3	10.6	13.6	187
4115	807	15.6	42.4	52.6	19.3	36.7	1.6	117.2	11.7	16.0	184
4116	757	14.1	39.0	51.5	18.6	36.2	2.8	104.5	12.2	12.6	177
4117	743	14.9	39.6	53.2	20.1	37.7	2.6	110.8	11.8	12.7	197
Mean	766	14.8	40.5	52.8	19.3	36.5	2.3	114.4	11.4	13.6	188
S.D.	27	0.6	1.4	0.9	0.5	0.7	0.6	7.6	0.7	1.4	9

Appendix 6-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4113	34.1	76.5	16.3	4.5	0.3	2.1	0.3	26.1	5.6	1.5	0.1	0.7	0.1
4114	79.0	83.8	11.5	1.5	0.3	2.1	0.8	66.1	9.1	1.2	0.2	1.7	0.6
4115	33.1	57.7	35.1	1.2	0.2	4.5	1.3	19.1	11.6	0.4	0.1	1.5	0.4
4116	33.1	79.0	15.6	1.6	0.1	3.4	0.4	26.1	5.2	0.5	0.0	1.1	0.1
4117	75.9	81.0	15.7	0.8	0.2	1.4	0.9	61.5	11.9	0.6	0.2	1.0	0.7
Mean	51.0	75.6	18.8	1.9	0.2	2.7	0.7	39.8	8.7	0.8	0.1	1.2	0.4
S.D.	24.1	10.4	9.3	1.5	0.1	1.2	0.4	22.2	3.2	0.5	0.1	0.4	0.3

LUC: Large unstained cells

Appendix 6-21

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
1008	904	15.6	46.0	50.9	17.3	34.0	2.3	97.2	15.9	20.6	280
1009	848	15.7	43.9	51.8	18.5	35.8	2.5	108.4	16.6	23.3	251
1010	929	15.6	44.8	48.2	16.8	34.9	1.9	102.3	16.8	19.5	255
1011	881	15.5	44.1	50.0	17.6	35.2	2.1	100.0	16.3	17.3	230
1012	888	15.6	43.1	48.6	17.6	36.3	1.6	97.2	16.4	22.8	246
Mean	890	15.6	44.4	49.9	17.6	35.2	2.1	101.0	16.4	20.7	252
S.D.	30	0.1	1.1	1.5	0.6	0.9	0.3	4.6	0.3	2.5	18

Appendix 6-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1008	116.0	82.4	12.0	1.2	0.3	3.0	1.1	95.6	13.9	1.4	0.4	3.5	1.3
1009	67.3	84.0	10.1	2.8	0.3	2.5	0.4	56.5	6.8	1.9	0.2	1.7	0.3
1010	77.0	73.2	21.2	1.6	0.3	3.3	0.4	56.4	16.3	1.2	0.2	2.6	0.3
1011	42.9	71.0	22.2	3.6	0.2	2.7	0.3	30.5	9.5	1.6	0.1	1.1	0.1
1012	44.6	71.3	20.6	2.4	0.3	3.9	1.5	31.8	9.2	1.1	0.1	1.7	0.6
Mean	69.6	76.4	17.2	2.3	0.3	3.1	0.7	54.2	11.1	1.4	0.2	2.1	0.5
S.D.	29.8	6.3	5.7	1.0	0.0	0.5	0.5	26.4	3.9	0.3	0.1	0.9	0.5

LUC: Large unstained cells

Appendix 6-23

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 300

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
4008	870	15.9	45.4	52.2	18.3	35.0	2.8	106.7	14.5	19.8	296
4009	896	16.7	47.7	53.2	18.7	35.1	1.9	106.3	13.2	17.0	258
4010	886	15.7	45.7	51.6	17.8	34.5	1.7	93.4	16.9	25.4	257
4011	859	15.4	43.7	50.8	18.0	35.4	1.9	96.3	13.5	21.5	210
4012	848	15.2	43.4	51.2	17.9	35.0	2.1	93.4	15.2	18.7	267
Mean	872	15.8	45.2	51.8	18.1	35.0	2.1	99.2	14.7	20.5	258
S.D.	19	0.6	1.7	0.9	0.4	0.3	0.4	6.8	1.5	3.2	31

Appendix 6-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 300

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4008	116.4	74.6	20.4	1.4	0.4	2.7	0.5	86.9	23.7	1.7	0.5	3.1	0.6
4009	85.7	83.9	11.8	1.2	0.4	1.8	0.8	71.9	10.1	1.1	0.3	1.6	0.7
4010	58.2	76.6	19.1	1.5	0.2	2.1	0.4	44.5	11.1	0.9	0.1	1.2	0.2
4011	44.5	82.8	12.6	1.5	0.4	2.1	0.7	36.8	5.6	0.6	0.2	0.9	0.3
4012	64.7	74.7	19.1	2.1	0.4	3.2	0.4	48.4	12.4	1.4	0.3	2.1	0.3
Mean	73.9	78.5	16.6	1.5	0.4	2.4	0.6	57.7	12.6	1.1	0.3	1.8	0.4
S.D.	28.0	4.5	4.1	0.3	0.1	0.6	0.2	20.9	6.7	0.4	0.1	0.9	0.2

LUC: Large unstained cells

Appendix 6-25

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	RBC 10E4/μL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/μL	PT s	APTT s	FIB mg/dL
1118	848	15.2	42.7	50.4	18.0	35.6	1.8	106.2	11.0	15.1	166
1119	794	14.5	40.8	51.4	18.3	35.6	2.1	104.4	10.9	13.3	177
1120	845	15.2	42.7	50.5	18.0	35.6	1.5	136.2	10.5	12.7	158
1121	765	15.4	42.8	56.0	20.1	35.9	2.9	93.8	11.0	16.3	161
1122	831	15.9	43.9	52.9	19.2	36.2	2.1	110.7	12.3	16.9	211
Mean	817	15.2	42.6	52.2	18.7	35.8	2.1	110.3	11.1	14.9	175
S.D.	36	0.5	1.1	2.3	0.9	0.3	0.5	15.8	0.7	1.8	22

Appendix 6-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	WBC 10E2/μL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/μL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
1118	66.2	82.4	13.4	1.8	0.4	1.3	0.6	54.5	8.9	1.2	0.2	0.9	0.4
1119	37.3	77.9	18.0	1.3	0.1	1.8	0.8	29.0	6.7	0.5	0.1	0.7	0.3
1120	83.7	71.5	22.9	0.9	0.5	3.5	0.8	59.8	19.2	0.8	0.4	2.9	0.7
1121	37.8	83.2	12.7	1.8	0.1	1.3	0.9	31.5	4.8	0.7	0.0	0.5	0.3
1122	41.3	66.8	26.0	1.5	0.3	4.3	1.2	27.6	10.7	0.6	0.1	1.8	0.5
Mean	53.3	76.4	18.6	1.5	0.3	2.4	0.9	40.5	10.1	0.8	0.2	1.4	0.4
S.D.	20.8	7.1	5.8	0.4	0.2	1.4	0.2	15.4	5.6	0.3	0.2	1.0	0.2

LUC: Large unstained cells

Appendix 6-27

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 300

Animal number	RBC 10E4/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	Retic %	PLT 10E4/µL	PT s	APTT s	FIB mg/dL
4118	840	15.6	43.9	52.3	18.5	35.5	2.3	119.9	11.6	17.5	165
4119	781	14.3	40.6	52.0	18.4	35.3	2.4	129.7	10.5	16.1	137
4120	760	13.9	39.4	51.8	18.3	35.4	2.6	114.2	11.0	12.4	180
4121	804	15.2	42.6	53.0	18.9	35.7	1.6	122.2	11.8	14.7	164
4122	835	15.8	43.5	52.1	18.9	36.2	1.6	97.4	12.7	17.5	186
Mean	804	15.0	42.0	52.2	18.6	35.6	2.1	116.7	11.5	15.6	166
S.D.	34	0.8	1.9	0.5	0.3	0.4	0.5	12.1	0.8	2.2	19

Appendix 6-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 300

Animal number	WBC 10E2/µL	Differential leukocyte ratio (%) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC	Differential leukocyte counts (10E2/µL) Lymph.	Neut.	Eosino.	Baso.	Mono.	LUC
4118	78.0	82.3	11.8	2.4	0.6	2.0	0.8	64.3	9.2	1.9	0.5	1.6	0.6
4119	38.6	83.2	11.2	1.5	0.2	3.0	0.8	32.1	4.3	0.6	0.1	1.2	0.3
4120	57.3	69.6	23.4	1.2	0.2	3.4	2.2	39.8	13.4	0.7	0.1	1.9	1.3
4121	71.4	71.5	22.5	1.3	0.4	3.6	0.6	51.1	16.1	0.9	0.3	2.6	0.4
4122	53.6	86.1	8.6	2.3	0.2	2.2	0.6	46.1	4.6	1.2	0.1	1.2	0.3
Mean	59.8	78.5	15.5	1.7	0.3	2.8	1.0	46.7	9.5	1.1	0.2	1.7	0.6
S.D.	15.5	7.5	6.9	0.6	0.2	0.7	0.7	12.1	5.2	0.5	0.2	0.6	0.4

LUC: Large unstained cells

Appendix 7-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1001	64*	36*	53*	0*	305*	32.7*	50*	45*	91*	0.1*	114*
1002	57*	26*	38*	0*	327*	12.8*	57*	46*	89*	0.1*	144*
1003	56*	30*	41*	0*	304*	8.9*	49*	19*	76*	0.0*	124*
1004	68*	29*	60*	0*	353*	6.1*	64*	34*	96*	0.1*	125*
1005	59*	24*	37*	0*	259*	6.6*	41*	21*	68*	0.1*	126*
Mean	61	29	46	0	310	13.4	52	33	84	0.1	127
S.D.	5	5	10	0	35	11.1	9	13	12	0.0	11

*: Re-analyzed value

Appendix 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1001	14*	0.26*	143*	4.7*	105*	9.9*	5.7*	6.0*	3.5*	1.40*
1002	12*	0.27*	142*	4.6*	106*	10.0*	6.2*	5.7*	3.2*	1.28*
1003	11*	0.25*	144*	4.3*	107*	9.9*	6.6*	5.9*	3.3*	1.27*
1004	12*	0.27*	145*	4.4*	107*	10.2*	7.2*	6.0*	3.2*	1.14*
1005	14*	0.31*	142*	4.4*	106*	9.8*	6.1*	6.0*	3.3*	1.22*
Mean	13	0.27	143	4.5	106	10.0	6.4	5.9	3.3	1.26
S.D.	1	0.02	1	0.2	1	0.2	0.6	0.1	0.1	0.09

*: Re-analyzed value

Appendix 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 30

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2001	62*	31*	63*	0*	389*	14.9*	54*	47*	96*	0.1*	144*
2002	65*	26*	48*	0*	252*	13.6*	53*	21*	77*	0.0*	118*
2003	60*	25*	60*	0*	307*	22.1*	64*	29*	88*	0.1*	129*
2004	52*	22*	39*	0*	409*	4.1*	74*	28*	97*	0.0*	136*
2005	55*	21*	39*	0*	179*	5.3*	55*	16*	77*	0.1*	106*
Mean	59	25	50	0	307	12.0	60	28	87	0.1	127
S.D.	5	4	11	0	96	7.4	9	12	10	0.1	15

*: Re-analyzed value

Appendix 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 30

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2001	12*	0.27*	141*	4.5*	104*	9.7*	6.5*	5.6*	3.2*	1.33*
2002	14*	0.33*	145*	4.5*	108*	10.0*	5.8*	5.9*	3.2*	1.19*
2003	15*	0.30*	145*	4.6*	105*	10.3*	6.8*	6.1*	3.2*	1.10*
2004	12*	0.22*	147*	4.5*	110*	10.3*	6.0*	5.8*	3.3*	1.32*
2005	11*	0.26*	144*	4.4*	105*	10.1*	7.0*	5.8*	3.2*	1.23*
Mean	13	0.28	144	4.5	106	10.1	6.4	5.8	3.2	1.23
S.D.	2	0.04	2	0.1	3	0.2	0.5	0.2	0.0	0.10

*: Re-analyzed value

Appendix 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 100

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3001	45*	20*	35*	0*	288*	7.3*	45*	43*	75*	0.0*	131*
3002	74*	32*	58*	1*	294*	14.7*	59*	29*	86*	0.0*	122*
3003	68*	27*	53*	0*	353*	4.4*	52*	38*	81*	0.0*	126*
3004	49*	23*	37*	0*	254*	4.0*	49*	17*	74*	0.0*	135*
3005	71*	34*	56*	1*	350*	24.7*	52*	42*	84*	0.1*	110*
Mean	61	27	48	0	308	11.0	51	34	80	0.0	125
S.D.	13	6	11	1	43	8.8	5	11	5	0.0	10

*: Re-analyzed value

Appendix 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 100

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3001	12*	0.29*	143*	4.8*	105*	10.3*	6.6*	6.3*	3.4*	1.17*
3002	14*	0.32*	145*	4.6*	105*	9.8*	5.9*	5.8*	3.0*	1.07*
3003	13*	0.29*	142*	5.0*	105*	10.2*	6.5*	5.5*	3.1*	1.29*
3004	13*	0.26*	142*	4.8*	106*	9.8*	6.3*	5.7*	3.2*	1.28*
3005	15*	0.34*	145*	4.5*	106*	10.3*	7.4*	6.0*	3.2*	1.14*
Mean	13	0.30	143	4.7	105	10.1	6.5	5.9	3.2	1.19
S.D.	1	0.03	2	0.2	1	0.3	0.6	0.3	0.1	0.09

*: Re-analyzed value

Appendix 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4001	61*	30*	60*	0*	349*	25.9*	67*	35*	94*	0.1*	152*
4002	53*	24*	38*	0*	269*	9.5*	69*	34*	103*	0.0*	116*
4003	60*	28*	45*	0*	229*	10.5*	69*	27*	100*	0.0*	122*
4004	71*	31*	59*	0*	323*	39.1*	68*	28*	93*	0.1*	106*
4005	72*	23*	37*	0*	319*	3.0*	37*	20*	60*	0.0*	112*
Mean	63	27	48	0	298	17.6	62	29	90	0.0	122
S.D.	8	4	11	0	48	14.7	14	6	17	0.1	18

*: Re-analyzed value

Appendix 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4001	11*	0.24*	145*	4.8*	106*	10.1*	5.9*	5.5*	3.2*	1.39*
4002	13*	0.32*	142*	4.9*	104*	9.7*	5.6*	5.8*	3.3*	1.32*
4003	14*	0.31*	144*	4.8*	105*	10.3*	6.1*	5.8*	3.2*	1.23*
4004	16*	0.35*	144*	4.3*	105*	10.1*	5.8*	6.0*	3.3*	1.22*
4005	13*	0.24*	146*	4.6*	107*	10.1*	6.5*	6.0*	3.3*	1.22*
Mean	13	0.29	144	4.7	105	10.1	6.0	5.8	3.3	1.28
S.D.	2	0.05	1	0.2	1	0.2	0.3	0.2	0.1	0.08

*: Re-analyzed value

Appendix 7-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1101	77*	51*	34*	0*	221*	11.9*	56*	28*	100*	0.1*	122*
1102	112*	70*	35*	1*	257*	71.3*	70*	37*	116*	0.1*	119*
1106	85*	48*	48*	1*	150*	7.3*	62*	34*	113*	0.0*	101*
1108	76*	48*	45*	1*	146*	32.8*	59*	32*	107*	0.1*	107*
1112	70*	38*	30*	0*	219*	20.5*	64*	40*	108*	0.1*	128*
Mean	84	51	38	1	199	28.8	62	34	109	0.1	115
S.D.	17	12	8	1	49	25.7	5	5	6	0.0	11

*: Re-analyzed value

Appendix 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1101	13*	0.40*	144*	3.5*	108*	10.0*	6.3*	5.9*	3.5*	1.46*
1102	13*	0.31*	142*	3.9*	106*	10.0*	6.4*	5.8*	3.4*	1.42*
1106	15*	0.32*	140*	4.1*	105*	10.1*	7.3*	6.2*	3.6*	1.38*
1108	13*	0.29*	142*	4.7*	105*	10.6*	7.4*	6.1*	3.4*	1.26*
1112	10*	0.26*	141*	5.0*	107*	10.2*	6.6*	5.6*	3.3*	1.43*
Mean	13	0.32	142	4.2	106	10.2	6.8	5.9	3.4	1.39
S.D.	2	0.05	1	0.6	1	0.2	0.5	0.2	0.1	0.08

*: Re-analyzed value

Appendix 7-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 30

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
2101	118*	73*	36*	0*	220*	8.1*	49*	72*	101*	0.0*	116*
2102	90*	52*	29*	1*	236*	17.5*	54*	39*	98*	0.0*	139*
2103	67*	50*	27*	0*	121*	14.0*	51*	29*	97*	0.0*	133*
2104	79*	46*	38*	1*	191*	34.8*	74*	37*	129*	0.1*	123*
2108	66*	40*	32*	1*	154*	5.2*	33*	54*	73*	0.1*	141*
Mean	84	52	32	1	184	15.9	52	46	100	0.0	130
S.D.	21	12	5	1	47	11.6	15	17	20	0.1	11

*: Re-analyzed value

Appendix 7-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 30

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
2101	11*	0.27*	141*	4.2*	102*	10.7*	7.9*	6.3*	3.6*	1.33*
2102	14*	0.35*	143*	3.5*	106*	10.3*	5.8*	5.8*	3.4*	1.42*
2103	12*	0.26*	139*	4.9*	106*	10.4*	7.1*	6.3*	3.5*	1.25*
2104	16*	0.34*	142*	3.9*	107*	10.4*	6.6*	6.0*	3.5*	1.40*
2108	13*	0.27*	141*	4.3*	107*	10.6*	7.2*	5.5*	3.3*	1.50*
Mean	13	0.30	141	4.2	106	10.5	6.9	6.0	3.5	1.38
S.D.	2	0.04	1	0.5	2	0.2	0.8	0.3	0.1	0.09

*: Re-analyzed value

Appendix 7-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
3101	78*	51*	35*	0*	209*	12.1*	55*	51*	100*	0.0*	156*
3102	105*	60*	37*	1*	268*	17.9*	66*	61*	117*	0.1*	120*
3103	56*	30*	28*	0*	226*	22.8*	48*	76*	94*	0.0*	131*
3104	70*	51*	33*	0*	365*	19.5*	68*	56*	125*	0.1*	115*
3108	61*	41*	29*	1*	290*	15.9*	59*	57*	109*	0.0*	124*
3111a)	56Z*	28Z*	66Z*	1Z*	266Z*	24.7Z*	66Z*	54Z*	137Z*	0.1Z*	134Z*
Mean	74	47	32	0	272	17.6	59	60	109	0.0	129
S.D.	19	11	4	1	61	4.0	8	10	13	0.1	16

a): Necropsied on lactation day 2 because all pups died.
*: Re-analyzed value
Z: Data was excluded from statistical analysis.

Appendix 7-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 100

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
3101	7*	0.24*	141*	4.4*	106*	10.2*	6.9*	6.0*	3.4*	1.31*
3102	12*	0.33*	143*	3.3*	105*	10.7*	6.3*	5.9*	3.4*	1.36*
3103	14*	0.30*	139*	4.4*	103*	10.4*	7.8*	5.8*	3.3*	1.32*
3104	10*	0.28*	141*	4.4*	102*	10.4*	7.1*	6.4*	3.6*	1.29*
3108	12*	0.26*	140*	4.7*	105*	10.6*	8.2*	6.3*	3.5*	1.25*
3111a)	25Z*	0.30Z*	141Z*	4.2Z*	101Z*	12.1Z*	6.6Z*	7.8Z*	4.5Z*	1.36Z*
Mean	11	0.28	141	4.2	104	10.5	7.3	6.1	3.4	1.31
S.D.	3	0.03	1	0.5	2	0.2	0.8	0.3	0.1	0.04

a): Necropsied on lactation day 2 because all pups died.
*: Re-analyzed value
Z: Data was excluded from statistical analysis.

Appendix 7-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4101	62*	27*	39*	0*	162*	14.5*	68*	29*	109*	0.1*	132*
4103	56*	41*	34*	0*	286*	8.6*	65*	56*	115*	0.1*	115*
4104	72*	46*	26*	1*	260*	22.4*	43*	54*	79*	0.0*	112*
4109	70*	38*	41*	0*	172*	8.2*	42*	22*	78*	0.0*	145*
4110	78*	51*	36*	0*	182*	10.9*	63*	51*	113*	0.1*	136*
4111a)	58Z*	32Z*	63Z*	1Z*	220Z*	16.9Z*	78Z*	111Z*	125Z*	0.0Z*	134Z*
Mean	68	41	35	0	212	12.9	56	42	99	0.1	128
S.D.	9	9	6	0	57	5.9	13	16	19	0.1	14

a): Necropsied on lactation day 4 because all pups died.
*: Re-analyzed value
Z: Data was excluded from statistical analysis.

Appendix 7-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4101	12*	0.33*	143*	4.1*	108*	9.9*	6.2*	5.8*	3.4*	1.42*
4103	17*	0.38*	141*	3.8*	105*	10.4*	6.1*	6.1*	3.5*	1.35*
4104	13*	0.30*	140*	4.4*	103*	10.4*	8.1*	5.8*	3.2*	1.23*
4109	12*	0.30*	143*	4.0*	108*	10.0*	6.0*	5.9*	3.3*	1.27*
4110	12*	0.26*	141*	5.1*	104*	10.5*	7.4*	5.7*	3.2*	1.28*
4111a)	81Z*	0.69Z*	144Z*	4.1Z*	108Z*	11.9Z*	8.0Z*	5.8Z*	3.4Z*	1.42Z*
Mean	13	0.31	142	4.3	106	10.2	6.8	5.9	3.3	1.31
S.D.	2	0.04	1	0.5	2	0.3	0.9	0.2	0.1	0.08

a): Necropsied on lactation day 4 because all pups died.
*: Re-analyzed value
Z: Data was excluded from statistical analysis.

Appendix 7-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1113	54*	23*	41*	0*	132*	9.9*	42*	12*	83*	0.1*	125*
1114	62*	21*	37*	0*	276*	9.9*	46*	15*	85*	0.0*	132*
1115	58*	22*	39*	1*	269*	11.1*	58*	20*	103*	0.0*	140*
1116	48*	18*	23*	0*	186*	13.9*	75*	22*	144*	0.1*	140*
1117	54*	34*	26*	1*	153*	6.4*	87*	19*	148*	0.0*	146*
Mean	55	24	33	0	203	10.2	62	18	113	0.0	137
S.D.	5	6	8	1	66	2.7	19	4	32	0.1	8

*: Re-analyzed value

Appendix 7-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1113	17*	0.39*	142*	4.5*	108*	10.1*	4.3*	6.4*	3.8*	1.46*
1114	15*	0.32*	143*	4.2*	109*	9.7*	4.7*	6.0*	3.3*	1.22*
1115	16*	0.37*	143*	4.3*	109*	9.9*	3.7*	6.2*	3.7*	1.48*
1116	15*	0.36*	144*	4.0*	109*	10.5*	4.6*	6.4*	4.1*	1.78*
1117	15*	0.35*	142*	4.1*	108*	10.7*	3.6*	7.2*	4.5*	1.67*
Mean	16	0.36	143	4.2	109	10.2	4.2	6.4	3.9	1.52
S.D.	1	0.03	1	0.2	1	0.4	0.5	0.5	0.4	0.22

*: Re-analyzed value

Appendix 7-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4113	48*	21*	32*	0*	120*	8.6*	66*	17*	125*	0.1*	129*
4114	58*	23*	44*	0*	221*	6.9*	76*	24*	134*	0.0*	120*
4115	50*	20*	42*	0*	166*	12.9*	73*	18*	134*	0.0*	128*
4116	42*	19*	28*	0*	119*	10.0*	83*	23*	146*	0.1*	115*
4117	45*	22*	26*	0*	113*	5.8*	69*	27*	120*	0.0*	101*
Mean	49	21	34	0	148	8.8	73	22	132	0.0	119
S.D.	6	2	8	0	46	2.8	7	4	10	0.1	11

*: Re-analyzed value

Appendix 7-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4113	14*	0.37*	141*	4.7*	106*	10.8*	4.0*	6.9*	4.3*	1.65*
4114	16*	0.38*	142*	4.8*	106*	10.5*	5.4*	6.1*	3.7*	1.54*
4115	15*	0.32*	143*	4.6*	107*	10.6*	4.4*	7.0*	4.1*	1.41*
4116	14*	0.28*	144*	4.5*	109*	10.6*	5.0*	6.5*	3.9*	1.50*
4117	15*	0.32*	144*	4.4*	106*	10.6*	6.8*	6.7*	4.0*	1.48*
Mean	15	0.33	143	4.6	107	10.6	5.1	6.6	4.0	1.52
S.D.	1	0.04	1	0.2	1	0.1	1.1	0.4	0.2	0.09

*: Re-analyzed value

Appendix 7-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1008	68*	29*	44*	0*	245*	12.9*	57*	25*	85*	0.0*	135*
1009	63*	27*	41*	0*	245*	15.8*	58*	25*	85*	0.1*	144*
1010	62*	24*	50*	0*	249*	10.3*	48*	16*	78*	0.0*	127*
1011	56*	25*	39*	1*	243*	9.8*	39*	27*	67*	0.0*	149*
1012	68*	30*	48*	0*	228*	7.6*	51*	33*	84*	0.1*	120*
Mean	63	27	44	0	242	11.3	51	25	80	0.0	135
S.D.	5	3	5	0	8	3.2	8	6	8	0.1	12

*: Re-analyzed value

Appendix 7-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1008	17*	0.33*	143*	4.8*	105*	9.5*	6.0*	6.1*	3.2*	1.10*
1009	18*	0.34*	140*	4.7*	105*	9.8*	6.1*	5.8*	3.4*	1.42*
1010	18*	0.31*	141*	4.7*	106*	9.8*	5.9*	6.1*	3.2*	1.10*
1011	16*	0.30*	142*	4.6*	107*	9.4*	4.7*	5.7*	3.3*	1.38*
1012	16*	0.35*	144*	4.5*	106*	10.2*	5.6*	6.3*	3.4*	1.17*
Mean	17	0.33	142	4.7	106	9.7	5.7	6.0	3.3	1.23
S.D.	1	0.02	2	0.1	1	0.3	0.6	0.2	0.1	0.15

*: Re-analyzed value

Appendix 7-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4008	83*	36*	68*	1*	309*	23.2*	76*	45*	107*	0.1*	141*
4009	55*	25*	34*	0*	178*	5.2*	67*	49*	96*	0.1*	153*
4010	54*	27*	37*	0*	268*	7.4*	69*	48*	100*	0.0*	156*
4011	73*	31*	50*	0*	250*	14.5*	58*	18*	82*	0.1*	129*
4012	64*	30*	57*	0*	297*	15.8*	59*	21*	84*	0.1*	150*
Mean	66	30	49	0	260	13.2	66	36	94	0.1	146
S.D.	12	4	14	0	52	7.2	7	15	11	0.0	11

*: Re-analyzed value

Appendix 7-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4008	19*	0.41*	142*	4.6*	104*	9.7*	6.3*	5.9*	3.2*	1.19*
4009	20*	0.34*	144*	4.5*	109*	9.6*	5.5*	5.4*	3.1*	1.35*
4010	15*	0.28*	145*	4.5*	108*	9.6*	5.5*	5.9*	3.3*	1.27*
4011	17*	0.33*	143*	4.5*	108*	9.6*	6.0*	5.7*	3.1*	1.19*
4012	16*	0.29*	142*	3.9*	106*	9.7*	5.3*	6.0*	3.3*	1.22*
Mean	17	0.33	143	4.4	107	9.6	5.7	5.8	3.2	1.24
S.D.	2	0.05	1	0.3	2	0.1	0.4	0.2	0.1	0.07

*: Re-analyzed value

Appendix 7-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
1118	119*	40*	72*	1*	129*	39.5*	84*	16*	142*	0.1*	120*
1119	55*	19*	47*	1*	132*	7.4*	42*	12*	86*	0.1*	144*
1120	165*	142*	56*	1*	114*	12.1*	73*	18*	129*	0.1*	114*
1121	101*	69*	72*	0*	83*	20.5*	133*	21*	220*	0.1*	145*
1122	54*	19*	32*	1*	117*	15.4*	48*	11*	96*	0.1*	140*
Mean	99	58	56	1	115	19.0	76	16	135	0.1	133
S.D.	47	51	17	0	19	12.4	36	4	53	0.0	15

*: Re-analyzed value

Appendix 7-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
1118	19*	0.37*	143*	4.2*	108*	10.5*	4.8*	6.7*	4.0*	1.48*
1119	16*	0.34*	142*	4.0*	108*	10.1*	4.8*	6.3*	3.6*	1.33*
1120	19*	0.32*	143*	3.9*	108*	10.9*	5.5*	7.1*	4.4*	1.63*
1121	16*	0.31*	144*	3.8*	107*	10.9*	6.1*	7.4*	4.5*	1.55*
1122	17*	0.36*	143*	4.5*	109*	9.8*	4.7*	6.3*	3.8*	1.52*
Mean	17	0.34	143	4.1	108	10.4	5.2	6.8	4.1	1.50
S.D.	2	0.03	1	0.3	1	0.5	0.6	0.5	0.4	0.11

*: Re-analyzed value

Appendix 7-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 300

Animal number	AST IU/L	ALT IU/L	LDH IU/L	r-GTP IU/L	ALP IU/L	TBA µmol/L	T-CHO mg/dL	TG mg/dL	PL mg/dL	T-BIL mg/dL	GLU mg/dL
4118	76*	40*	38*	1*	173*	16.2*	51*	17*	93*	0.1*	125*
4119	78*	41*	54*	0*	65*	17.9*	105*	59*	191*	0.1*	152*
4120	67*	26*	31*	0*	184*	6.1*	80*	19*	136*	0.1*	122*
4121	64*	30*	36*	0*	114*	5.4*	44*	20*	88*	0.1*	100*
4122	77*	36*	52*	1*	145*	14.8*	73*	12*	128*	0.1*	117*
Mean	72	35	42	0	136	12.1	71	25	127	0.1	123
S.D.	6	6	10	1	48	5.9	24	19	41	0.0	19

*: Re-analyzed value

Appendix 7-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 300

Animal number	BUN mg/dL	CRNN mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mg/dL	P mg/dL	TP g/dL	ALB g/dL	A/G
4118	16*	0.35*	142*	4.3*	105*	10.0*	6.1*	6.1*	3.5*	1.35*
4119	18*	0.30*	142*	3.9*	105*	10.6*	4.7*	7.2*	4.4*	1.57*
4120	23*	0.39*	142*	4.2*	109*	10.3*	5.7*	6.5*	3.8*	1.41*
4121	27*	0.45*	142*	4.7*	108*	10.0*	6.0*	6.4*	3.6*	1.29*
4122	20*	0.40*	145*	4.4*	111*	10.2*	4.9*	6.5*	3.8*	1.41*
Mean	21	0.38	143	4.3	108	10.2	5.5	6.5	3.8	1.41
S.D.	4	0.06	1	0.3	3	0.2	0.6	0.4	0.3	0.10

*: Re-analyzed value

Appendix 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1001	488	2.18	12.3	13.5	9.0	22.5	248
	1002	529	2.15	10.7	10.4	10.7	21.1	282
	1003	509	2.22	12.3	11.0	11.1	22.1	387
	1004	542	2.29	13.8	8.6	9.3	17.9	285
	1005	524	2.21	13.3	12.4	10.2	22.6	298
	1006	526	2.29	13.4	11.7	10.2	21.9	269
	1007	575	2.08	16.6	17.9	12.2	30.1	445
	Mean	528	2.20	13.2	12.2	10.4	22.6	316
	S.D.	27	0.08	1.8	2.9	1.1	3.7	72
Relative	1001		0.45	2.5	2.8	1.8	4.6	51
	1002		0.41	2.0	2.0	2.0	4.0	53
	1003		0.44	2.4	2.2	2.2	4.3	76
	1004		0.42	2.5	1.6	1.7	3.3	53
	1005		0.42	2.5	2.4	1.9	4.3	57
	1006		0.44	2.5	2.2	1.9	4.2	51
	1007		0.36	2.9	3.1	2.1	5.2	77
	Mean		0.42	2.5	2.3	1.9	4.3	60
	S.D.		0.03	0.3	0.5	0.2	0.6	12

Appendix 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1001	1.69	12.80	0.68	1.86	1.84	3.70
	1002	1.49	14.98	0.75	1.65	1.67	3.32
	1003	1.66	13.64	0.77	1.52	1.67	3.19
	1004	1.62	13.96	0.78	1.75	1.88	3.63
	1005	1.40	12.50	0.71	1.48	1.56	3.04
	1006	1.40	13.26	0.83	1.64	1.59	3.23
	1007	1.56	16.15	0.74	1.87	1.97	3.84
	Mean	1.55	13.90	0.75	1.68	1.74	3.42
	S.D.	0.12	1.28	0.05	0.15	0.16	0.30
Relative	1001	0.35	2.62	0.14	0.38	0.38	0.76
	1002	0.28	2.83	0.14	0.31	0.32	0.63
	1003	0.33	2.68	0.15	0.30	0.33	0.63
	1004	0.30	2.58	0.14	0.32	0.35	0.67
	1005	0.27	2.39	0.14	0.28	0.30	0.58
	1006	0.27	2.52	0.16	0.31	0.30	0.61
	1007	0.27	2.81	0.13	0.33	0.34	0.67
	Mean	0.30	2.63	0.14	0.32	0.33	0.65
	S.D.	0.03	0.16	0.01	0.03	0.03	0.06

Appendix 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	1001	46	55	101	1.71	1.73	3.44
	1002	26	28	54	1.62	1.68	3.30
	1003	34	38	72	1.78	1.84	3.62
	1004	36	35	71	2.01	1.96	3.97
	1005	25	27	52	1.70	1.67	3.37
	1006	29	29	58	1.75	1.65	3.40
	1007	36	41	77	1.72	1.72	3.44
	Mean	33	36	69	1.76	1.75	3.51
	S.D.	7	10	17	0.12	0.11	0.23
Relative	1001	9	11	21	0.35	0.35	0.70
	1002	5	5	10	0.31	0.32	0.62
	1003	7	7	14	0.35	0.36	0.71
	1004	7	6	13	0.37	0.36	0.73
	1005	5	5	10	0.32	0.32	0.64
	1006	6	6	11	0.33	0.31	0.65
	1007	6	7	13	0.30	0.30	0.60
	Mean	6	7	13	0.33	0.33	0.66
	S.D.	1	2	4	0.02	0.02	0.05

Appendix 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 0

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	1001	663	685	1348	2.23	1.40
	1002	689	678	1367	1.37	1.09
	1003	603	635	1238	2.04	1.50
	1004	731	732	1463	2.10	1.61
	1005	680	666	1346	2.29	1.73
	1006	693	676	1369	1.83	1.08
	1007	748	793	1541	1.96	1.77
	Mean	687	695	1382	1.97	1.45
	S.D.	47	52	96	0.31	0.28
Relative	1001	136	140	276	0.46	0.29
	1002	130	128	258	0.26	0.21
	1003	118	125	243	0.40	0.29
	1004	135	135	270	0.39	0.30
	1005	130	127	257	0.44	0.33
	1006	132	129	260	0.35	0.21
	1007	130	138	268	0.34	0.31
	Mean	130	132	262	0.38	0.28
	S.D.	6	6	11	0.07	0.05

Appendix 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 30

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
	2001	554	2.14	13.6	11.4	9.0	20.4	349
	2002	563	2.15	12.6	12.6	11.7	24.3	228
	2003	563	2.28	13.8	11.4	14.1	25.5	291
	2004	574	2.25	13.4	9.1	10.7	19.8	183
	2005	576	2.20	17.3	10.9	8.5	19.4	254
	2006	531	2.17	12.6	9.3	10.0	19.3	332
	2007	495	2.18	11.9	15.1	10.4	25.5	195
Absolute	2008	534	2.07	14.1	14.0	11.2	25.2	249
	2009	532	2.15	11.9	14.2	15.0	29.2	286
	2010	519	2.17	14.0	11.7	15.9	27.6	269
	2011	520	2.06	13.2	14.1	11.5	25.6	252
	2012	508	2.13	16.3	17.4	16.7	34.1	283
	Mean	539	2.16	13.7	12.6	12.1	24.7	264
	S.D.	27	0.06	1.6	2.4	2.7	4.5	49
	2001		0.39	2.5	2.1	1.6	3.7	63
	2002		0.38	2.2	2.2	2.1	4.3	40
	2003		0.40	2.5	2.0	2.5	4.5	52
	2004		0.39	2.3	1.6	1.9	3.4	32
	2005		0.38	3.0	1.9	1.5	3.4	44
	2006		0.41	2.4	1.8	1.9	3.6	63
	2007		0.44	2.4	3.1	2.1	5.2	39
Relative	2008		0.39	2.6	2.6	2.1	4.7	47
	2009		0.40	2.2	2.7	2.8	5.5	54
	2010		0.42	2.7	2.3	3.1	5.3	52
	2011		0.40	2.5	2.7	2.2	4.9	48
	2012		0.42	3.2	3.4	3.3	6.7	56
	Mean		0.40	2.5	2.4	2.3	4.6	49
	S.D.		0.02	0.3	0.5	0.6	1.0	9

Appendix 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 30

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	2001	1.85	14.24	0.60	1.95	2.08	4.03
	2002	1.38	15.26	0.80	1.87	1.94	3.81
	2003	1.53	16.25	0.88	1.86	1.80	3.66
	2004	1.52	16.14	0.73	2.15	2.20	4.35
	2005	1.52	14.00	0.88	1.99	2.20	4.19
	2006	1.59	12.36	0.69	1.89	1.86	3.75
	2007	1.40	13.51	0.47	1.82	1.81	3.63
	2008	1.57	13.79	0.65	2.05	2.08	4.13
	2009	1.45	14.02	0.85	1.67	1.71	3.38
	2010	1.42	13.68	0.75	1.74	1.83	3.57
	2011	1.46	13.51	0.65	1.80	1.90	3.70
	2012	1.60	13.45	0.78	1.87	1.80	3.67
	Mean	1.52	14.18	0.73	1.89	1.93	3.82
	S.D.	0.13	1.15	0.12	0.13	0.17	0.29
Relative	2001	0.33	2.57	0.11	0.35	0.38	0.73
	2002	0.25	2.71	0.14	0.33	0.34	0.68
	2003	0.27	2.89	0.16	0.33	0.32	0.65
	2004	0.26	2.81	0.13	0.37	0.38	0.76
	2005	0.26	2.43	0.15	0.35	0.38	0.73
	2006	0.30	2.33	0.13	0.36	0.35	0.71
	2007	0.28	2.73	0.09	0.37	0.37	0.73
	2008	0.29	2.58	0.12	0.38	0.39	0.77
	2009	0.27	2.64	0.16	0.31	0.32	0.64
	2010	0.27	2.64	0.14	0.34	0.35	0.69
	2011	0.28	2.60	0.13	0.35	0.37	0.71
	2012	0.31	2.65	0.15	0.37	0.35	0.72
	Mean	0.28	2.63	0.13	0.35	0.36	0.71
	S.D.	0.02	0.15	0.02	0.02	0.02	0.04

Appendix 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 30

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
	2001	33	31	64	1.43	1.45	2.88
	2002	34	39	73	1.84	1.89	3.73
	2003	30	32	62	1.93	1.93	3.86
	2004	37	39	76	1.77	1.71	3.48
	2005	36	41	77	2.11	2.14	4.25
	2006	29	29	58	1.88	1.93	3.81
	2007	30	28	58	1.71	1.78	3.49
Absolute	2008	26	30	56	1.88	1.83	3.71
	2009	35	37	72	1.79	1.78	3.57
	2010	32	34	66	1.45	1.39	2.84
	2011	44	49	93	1.57	1.55	3.12
	2012	33	33	66	2.07	2.03	4.10
	Mean	33	35	68	1.79	1.78	3.57
	S.D.	5	6	11	0.22	0.23	0.44
	2001	6	6	12	0.26	0.26	0.52
	2002	6	7	13	0.33	0.34	0.66
	2003	5	6	11	0.34	0.34	0.69
	2004	6	7	13	0.31	0.30	0.61
	2005	6	7	13	0.37	0.37	0.74
	2006	5	5	11	0.35	0.36	0.72
	2007	6	6	12	0.35	0.36	0.71
Relative	2008	5	6	10	0.35	0.34	0.69
	2009	7	7	14	0.34	0.33	0.67
	2010	6	7	13	0.28	0.27	0.55
	2011	8	9	18	0.30	0.30	0.60
	2012	6	6	13	0.41	0.40	0.81
	Mean	6	7	13	0.33	0.33	0.66
	S.D.	1	1	2	0.04	0.04	0.08

Appendix 8-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 30

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	2001	642	628	1270	1.98	1.34
	2002	719	729	1448	2.10	1.54
	2003	782	749	1531	1.81	1.39
	2004	734	675	1409	2.22	1.38
	2005	733	714	1447	1.76	1.33
	2006	684	710	1394	1.71	1.54
	2007	715	691	1406	1.94	1.33
	2008	618	637	1255	1.61	1.40
	2009	726	725	1451	2.21	0.92
	2010	531	550	1081	1.59	1.39
	2011	683	654	1337	1.59	0.92
	2012	761	736	1497	1.53	1.35
	Mean	694	683	1377	1.84	1.32
	S.D.	69	58	125	0.25	0.20
Relative	2001	116	113	229	0.36	0.24
	2002	128	129	257	0.37	0.27
	2003	139	133	272	0.32	0.25
	2004	128	118	245	0.39	0.24
	2005	127	124	251	0.31	0.23
	2006	129	134	263	0.32	0.29
	2007	144	140	284	0.39	0.27
	2008	116	119	235	0.30	0.26
	2009	136	136	273	0.42	0.17
	2010	102	106	208	0.31	0.27
	2011	131	126	257	0.31	0.18
	2012	150	145	295	0.30	0.27
	Mean	129	127	256	0.34	0.25
	S.D.	13	12	24	0.04	0.04

Appendix 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	3001	522	2.18	10.5	10.7	8.2	18.9	203
	3002	544	2.14	13.4	13.5	12.8	26.3	187
	3003	542	2.31	13.1	15.8	15.9	31.7	340
	3004	512	2.12	15.0	12.7	11.3	24.0	300
	3005	549	2.08	13.0	13.1	12.8	25.9	241
	3006	533	2.15	12.0	8.7	10.1	18.8	245
	3007	602	2.19	15.7	14.6	15.6	30.2	353
	3008	529	2.32	14.5	10.3	11.2	21.5	259
	3009	517	2.15	10.7	10.8	10.3	21.1	319
	3010	523	2.13	15.5	13.3	11.6	24.9	267
	3011	503	2.09	13.5	10.9	13.7	24.6	353
	3012	550	2.24	11.9	13.7	15.8	29.5	299
	Mean	536	2.18	13.2	12.3	12.4	24.8	281
	S.D.	26	0.08	1.7	2.1	2.5	4.2	56
Relative	3001		0.42	2.0	2.0	1.6	3.6	39
	3002		0.39	2.5	2.5	2.4	4.8	34
	3003		0.43	2.4	2.9	2.9	5.8	63
	3004		0.41	2.9	2.5	2.2	4.7	59
	3005		0.38	2.4	2.4	2.3	4.7	44
	3006		0.40	2.3	1.6	1.9	3.5	46
	3007		0.36	2.6	2.4	2.6	5.0	59
	3008		0.44	2.7	1.9	2.1	4.1	49
	3009		0.42	2.1	2.1	2.0	4.1	62
	3010		0.41	3.0	2.5	2.2	4.8	51
	3011		0.42	2.7	2.2	2.7	4.9	70
	3012		0.41	2.2	2.5	2.9	5.4	54
	Mean		0.41	2.5	2.3	2.3	4.6	53
	S.D.		0.02	0.3	0.3	0.4	0.7	11

Appendix 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	3001	1.73	14.15	0.85	1.59	1.82	3.41
	3002	1.57	15.29	0.70	1.86	1.92	3.78
	3003	1.36	15.05	1.08	1.82	1.98	3.80
	3004	1.66	13.35	0.91	1.94	2.04	3.98
	3005	1.59	14.64	0.79	1.86	1.93	3.79
	3006	1.53	15.19	0.79	2.20	2.07	4.27
	3007	1.58	17.44	0.72	2.37	2.35	4.72
	3008	1.59	13.58	0.74	2.34	2.25	4.59
	3009	1.56	14.00	0.66	2.06	1.96	4.02
	3010	1.43	14.43	0.67	2.12	2.11	4.23
	3011	1.93	13.19	0.81	1.98	2.03	4.01
	3012	1.56	14.58	0.79	2.17	2.13	4.30
	Mean	1.59	14.57	0.79	2.03	2.05	4.08
	S.D.	0.14	1.14	0.12	0.23	0.15	0.37
Relative	3001	0.33	2.71	0.16	0.30	0.35	0.65
	3002	0.29	2.81	0.13	0.34	0.35	0.69
	3003	0.25	2.78	0.20	0.34	0.37	0.70
	3004	0.32	2.61	0.18	0.38	0.40	0.78
	3005	0.29	2.67	0.14	0.34	0.35	0.69
	3006	0.29	2.85	0.15	0.41	0.39	0.80
	3007	0.26	2.90	0.12	0.39	0.39	0.78
	3008	0.30	2.57	0.14	0.44	0.43	0.87
	3009	0.30	2.71	0.13	0.40	0.38	0.78
	3010	0.27	2.76	0.13	0.41	0.40	0.81
	3011	0.38	2.62	0.16	0.39	0.40	0.80
	3012	0.28	2.65	0.14	0.39	0.39	0.78
	Mean	0.30	2.72	0.15	0.38	0.38	0.76
	S.D.	0.03	0.10	0.02	0.04	0.02	0.06

Appendix 8-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
	3001	27	30	57	1.86	1.89	3.75
	3002	41	42	83	1.54	1.55	3.09
	3003	27	32	59	1.65	1.59	3.24
	3004	28	31	59	1.67	1.66	3.33
	3005	36	37	73	1.61	1.64	3.25
	3006	34	32	66	1.74	1.79	3.53
	3007	34	35	69	2.02	2.02	4.04
Absolute	3008	40	43	83	1.71	1.77	3.48
	3009	30	30	60	1.68	1.66	3.34
	3010	30	35	65	1.63	1.67	3.30
	3011	30	33	63	1.77	1.81	3.58
	3012	38	39	77	2.10	2.12	4.22
	Mean	33	35	68	1.75	1.76	3.51
	S.D.	5	4	9	0.17	0.17	0.34
	3001	5	6	11	0.36	0.36	0.72
	3002	8	8	15	0.28	0.28	0.57
	3003	5	6	11	0.30	0.29	0.60
	3004	5	6	12	0.33	0.32	0.65
	3005	7	7	13	0.29	0.30	0.59
	3006	6	6	12	0.33	0.34	0.66
	3007	6	6	11	0.34	0.34	0.67
Relative	3008	8	8	16	0.32	0.33	0.66
	3009	6	6	12	0.32	0.32	0.65
	3010	6	7	12	0.31	0.32	0.63
	3011	6	7	13	0.35	0.36	0.71
	3012	7	7	14	0.38	0.39	0.77
	Mean	6	7	13	0.33	0.33	0.66
	S.D.	1	1	2	0.03	0.03	0.06

Appendix 8-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 100

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	3001	679	643	1322	1.95	1.34
	3002	700	706	1406	1.52	1.41
	3003	832	814	1646	2.09	1.18
	3004	699	677	1376	1.59	1.20
	3005	779	808	1587	1.55	1.34
	3006	645	714	1359	1.21	0.99
	3007	715	714	1429	1.82	1.26
	3008	773	827	1600	2.04	1.35
	3009	610	585	1195	1.67	1.27
	3010	725	678	1403	1.53	1.43
	3011	730	709	1439	1.60	1.13
	3012	773	739	1512	2.03	1.77
	Mean	722	718	1440	1.72	1.31
	S.D.	62	72	129	0.27	0.19
Relative	3001	130	123	253	0.37	0.26
	3002	129	130	258	0.28	0.26
	3003	154	150	304	0.39	0.22
	3004	137	132	269	0.31	0.23
	3005	142	147	289	0.28	0.24
	3006	121	134	255	0.23	0.19
	3007	119	119	237	0.30	0.21
	3008	146	156	302	0.39	0.26
	3009	118	113	231	0.32	0.25
	3010	139	130	268	0.29	0.27
	3011	145	141	286	0.32	0.22
	3012	141	134	275	0.37	0.32
	Mean	135	134	269	0.32	0.24
	S.D.	12	13	24	0.05	0.03

Appendix 8-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4001	562	2.18	14.4	12.4	14.3	26.7	331
	4002	516	2.25	12.4	9.4	8.8	18.2	296
	4003	505	2.15	13.3	11.0	10.2	21.2	275
	4004	520	2.19	13.3	11.4	10.8	22.2	251
	4005	504	2.04	13.8	11.6	11.8	23.4	205
	4006	500	2.17	12.5	10.4	9.4	19.8	282
	4007	561	2.25	13.0	11.5	10.5	22.0	362
	Mean	524	2.18	13.2	11.1	10.8	21.9	286
	S.D.	27	0.07	0.7	1.0	1.8	2.7	51
Relative	4001		0.39	2.6	2.2	2.5	4.8	59
	4002		0.44	2.4	1.8	1.7	3.5	57
	4003		0.43	2.6	2.2	2.0	4.2	54
	4004		0.42	2.6	2.2	2.1	4.3	48
	4005		0.40	2.7	2.3	2.3	4.6	41
	4006		0.43	2.5	2.1	1.9	4.0	56
	4007		0.40	2.3	2.0	1.9	3.9	65
	Mean		0.42	2.5	2.1	2.1	4.2	54
	S.D.		0.02	0.1	0.2	0.3	0.4	8

Appendix 8-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4001	1.68	17.16	0.88	2.32	2.43	4.75
	4002	1.51	14.10	0.75	1.98	2.08	4.06
	4003	1.39	14.86	0.67	1.66	1.78	3.44
	4004	1.47	15.28	0.70	2.03	2.03	4.06
	4005	1.57	14.93	0.88	2.09	2.15	4.24
	4006	1.43	14.23	0.81	2.11	2.10	4.21
	4007	1.54	15.49	0.75	1.94	2.11	4.05
	Mean	1.51	15.15	0.78	2.02	2.10	4.12
	S.D.	0.10	1.02	0.08	0.20	0.19	0.39
Relative	4001	0.30	3.05	0.16	0.41	0.43	0.85
	4002	0.29	2.73	0.15	0.38	0.40	0.79
	4003	0.28	2.94	0.13	0.33	0.35	0.68
	4004	0.28	2.94	0.13	0.39	0.39	0.78
	4005	0.31	2.96	0.17	0.41	0.43	0.84
	4006	0.29	2.85	0.16	0.42	0.42	0.84
	4007	0.27	2.76	0.13	0.35	0.38	0.72
	Mean	0.29	2.89	0.15	0.38	0.40	0.79
	S.D.	0.01	0.12	0.02	0.03	0.03	0.07

Appendix 8-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	4001	36	36	72	1.77	1.83	3.60
	4002	33	34	67	1.76	1.76	3.52
	4003	31	32	63	1.74	1.72	3.46
	4004	31	32	63	1.67	1.72	3.39
	4005	34	38	72	1.91	1.92	3.83
	4006	38	41	79	1.71	1.67	3.38
	4007	30	31	61	1.80	1.87	3.67
	Mean	33	35	68	1.77	1.78	3.55
	S.D.	3	4	6	0.08	0.09	0.16
Relative	4001	6	6	13	0.31	0.33	0.64
	4002	6	7	13	0.34	0.34	0.68
	4003	6	6	12	0.34	0.34	0.69
	4004	6	6	12	0.32	0.33	0.65
	4005	7	8	14	0.38	0.38	0.76
	4006	8	8	16	0.34	0.33	0.68
	4007	5	6	11	0.32	0.33	0.65
	Mean	6	7	13	0.34	0.34	0.68
	S.D.	1	1	2	0.02	0.02	0.04

Appendix 8-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 300

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	4001	730	740	1470	2.15	1.85
	4002	715	721	1436	1.79	1.12
	4003	613	587	1200	2.01	1.11
	4004	741	744	1485	1.77	1.54
	4005	780	794	1574	1.74	1.03
	4006	766	735	1501	1.54	1.54
	4007	752	779	1531	1.67	1.27
	Mean	728	729	1457	1.81	1.35
	S.D.	55	67	121	0.21	0.30
Relative	4001	130	132	262	0.38	0.33
	4002	139	140	278	0.35	0.22
	4003	121	116	238	0.40	0.22
	4004	143	143	286	0.34	0.30
	4005	155	158	312	0.35	0.20
	4006	153	147	300	0.31	0.31
	4007	134	139	273	0.30	0.23
	Mean	139	139	278	0.35	0.26
	S.D.	12	13	24	0.04	0.05

Appendix 8-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
	1101	336	2.13	18.9	8.0	9.8	17.8	184
	1102	317	2.10	11.2	9.4	8.5	17.9	204
	1103	345	1.89	18.6	9.3	8.6	17.9	239
	1104	355	2.04	19.5	7.9	9.9	17.8	155
	1105	316	2.03	21.8	8.7	8.9	17.6	132
	1106	339	1.99	18.4	8.0	7.9	15.9	324
	1107	338	2.04	17.8	11.2	10.3	21.5	154
Absolute	1108	350	2.01	18.0	9.5	9.0	18.5	200
	1109	324	1.97	20.9	8.1	4.8	12.9	210
	1110	305	2.01	15.6	6.1	10.0	16.1	133
	1111	358	1.96	18.5	7.7	4.7	12.4	150
	1112	377	2.05	20.6	12.4	10.8	23.2	278
	Mean	338	2.02	18.3	8.9	8.6	17.5	197
	S.D.	20	0.06	2.8	1.7	2.0	3.0	60
	1101		0.63	5.6	2.4	2.9	5.3	55
	1102		0.66	3.5	3.0	2.7	5.6	64
	1103		0.55	5.4	2.7	2.5	5.2	69
	1104		0.57	5.5	2.2	2.8	5.0	44
	1105		0.64	6.9	2.8	2.8	5.6	42
	1106		0.59	5.4	2.4	2.3	4.7	96
	1107		0.60	5.3	3.3	3.0	6.4	46
Relative	1108		0.57	5.1	2.7	2.6	5.3	57
	1109		0.61	6.5	2.5	1.5	4.0	65
	1110		0.66	5.1	2.0	3.3	5.3	44
	1111		0.55	5.2	2.2	1.3	3.5	42
	1112		0.54	5.5	3.3	2.9	6.2	74
	Mean		0.60	5.4	2.6	2.6	5.2	58
	S.D.		0.04	0.8	0.4	0.6	0.8	16

Appendix 8-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1101	1.01	9.93	0.58	1.07	1.01	2.08
	1102	0.96	9.46	0.65	1.10	1.10	2.20
	1103	1.26	11.98	0.98	1.12	1.11	2.23
	1104	1.13	11.34	0.70	1.14	1.21	2.35
	1105	1.09	10.51	0.86	1.13	1.05	2.18
	1106	1.07	11.08	0.63	1.05	1.12	2.17
	1107	1.00	11.90	0.67	1.08	1.02	2.10
	1108	1.04	10.30	0.86	1.06	1.09	2.15
	1109	1.09	11.68	0.55	1.12	1.09	2.21
	1110	1.08	9.74	0.71	1.15	1.11	2.26
	1111	1.17	11.12	0.67	1.38	1.27	2.65
	1112	1.07	11.31	0.77	1.24	1.31	2.55
	Mean	1.08	10.86	0.72	1.14	1.12	2.26
	S.D.	0.08	0.86	0.13	0.09	0.09	0.17
Relative	1101	0.30	2.96	0.17	0.32	0.30	0.62
	1102	0.30	2.98	0.21	0.35	0.35	0.69
	1103	0.37	3.47	0.28	0.32	0.32	0.65
	1104	0.32	3.19	0.20	0.32	0.34	0.66
	1105	0.34	3.33	0.27	0.36	0.33	0.69
	1106	0.32	3.27	0.19	0.31	0.33	0.64
	1107	0.30	3.52	0.20	0.32	0.30	0.62
	1108	0.30	2.94	0.25	0.30	0.31	0.61
	1109	0.34	3.60	0.17	0.35	0.34	0.68
	1110	0.35	3.19	0.23	0.38	0.36	0.74
	1111	0.33	3.11	0.19	0.39	0.35	0.74
	1112	0.28	3.00	0.20	0.33	0.35	0.68
	Mean	0.32	3.21	0.21	0.34	0.33	0.67
	S.D.	0.03	0.23	0.04	0.03	0.02	0.04

Appendix 8-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
	1101	40	46	86	51.8	57.4	109.2	735
	1102	36	40	76	58.2	51.0	109.2	705
	1103	39	41	80	66.3	61.2	127.5	668
	1104	40	41	81	66.4	62.5	128.9	737
	1105	51	53	104	50.1	65.5	115.6	807
	1106	41	49	90	38.3	60.3	98.6	710
	1107	46	52	98	66.0	68.0	134.0	764
Absolute	1108	51	54	105	47.3	66.3	113.6	804
	1109	39	44	83	64.9	73.2	138.1	633
	1110	33	37	70	70.8	47.8	118.6	663
	1111	40	41	81	77.0	55.3	132.3	729
	1112	45	48	93	76.5	46.5	123.0	728
	Mean	42	46	87	61.1	59.6	120.7	724
	S.D.	6	6	11	12.1	8.3	11.9	53
	1101	12	14	26	15.4	17.1	32.5	219
	1102	11	13	24	18.4	16.1	34.4	222
	1103	11	12	23	19.2	17.7	37.0	194
	1104	11	12	23	18.7	17.6	36.3	208
	1105	16	17	33	15.9	20.7	36.6	255
	1106	12	14	27	11.3	17.8	29.1	209
	1107	14	15	29	19.5	20.1	39.6	226
Relative	1108	15	15	30	13.5	18.9	32.5	230
	1109	12	14	26	20.0	22.6	42.6	195
	1110	11	12	23	23.2	15.7	38.9	217
	1111	11	11	23	21.5	15.4	37.0	204
	1112	12	13	25	20.3	12.3	32.6	193
	Mean	12	14	26	18.1	17.7	35.8	214
	S.D.	2	2	3	3.4	2.7	3.7	18

Appendix 8-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 30

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	2101	318	1.95	17.8	8.1	7.1	15.2	214
	2102	346	1.88	15.1	8.1	6.9	15.0	251
	2103	359	2.17	21.8	7.0	5.7	12.7	175
	2104	360	2.10	19.2	12.0	10.8	22.8	205
	2105	338	2.02	18.0	10.6	8.8	19.4	195
	2106	332	2.03	20.1	8.9	9.6	18.5	215
	2107	322	1.98	15.7	10.0	9.0	19.0	178
	2108	315	1.83	16.7	9.0	9.2	18.2	177
	2109	379	2.08	20.6	9.8	8.2	18.0	141
	2110	360	1.95	13.5	6.6	6.7	13.3	233
	2111	355	1.92	18.8	10.5	8.0	18.5	186
	2112	335	2.03	20.6	9.3	9.7	19.0	193
	Mean	343	2.00	18.2	9.2	8.3	17.5	197
	S.D.	20	0.10	2.5	1.6	1.5	2.9	29
Relative	2101		0.61	5.6	2.5	2.2	4.8	67
	2102		0.54	4.4	2.3	2.0	4.3	73
	2103		0.60	6.1	1.9	1.6	3.5	49
	2104		0.58	5.3	3.3	3.0	6.3	57
	2105		0.60	5.3	3.1	2.6	5.7	58
	2106		0.61	6.1	2.7	2.9	5.6	65
	2107		0.61	4.9	3.1	2.8	5.9	55
	2108		0.58	5.3	2.9	2.9	5.8	56
	2109		0.55	5.4	2.6	2.2	4.7	37
	2110		0.54	3.8	1.8	1.9	3.7	65
	2111		0.54	5.3	3.0	2.3	5.2	52
	2112		0.61	6.1	2.8	2.9	5.7	58
	Mean		0.58	5.3	2.7	2.4	5.1	58
	S.D.		0.03	0.7	0.5	0.5	0.9	9

Appendix 8-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 30

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	2101	1.07	10.84	0.58	1.24	1.27	2.51
	2102	1.04	10.84	0.75	1.12	1.13	2.25
	2103	1.08	11.23	0.75	1.15	1.24	2.39
	2104	1.04	11.85	0.73	1.05	1.19	2.24
	2105	1.02	11.68	0.68	1.19	1.25	2.44
	2106	1.11	11.14	0.66	1.16	1.15	2.31
	2107	1.08	10.23	0.59	1.05	1.02	2.07
	2108	0.99	10.15	0.62	1.05	1.00	2.05
	2109	1.13	11.26	0.68	1.15	1.11	2.26
	2110	1.17	11.02	0.65	1.20	1.15	2.35
	2111	1.03	11.67	0.72	1.20	1.18	2.38
	2112	0.98	11.67	0.65	1.23	1.21	2.44
	Mean	1.06	11.13	0.67	1.15	1.16	2.31
	S.D.	0.06	0.55	0.06	0.07	0.08	0.14
Relative	2101	0.34	3.41	0.18	0.39	0.40	0.79
	2102	0.30	3.13	0.22	0.32	0.33	0.65
	2103	0.30	3.13	0.21	0.32	0.35	0.67
	2104	0.29	3.29	0.20	0.29	0.33	0.62
	2105	0.30	3.46	0.20	0.35	0.37	0.72
	2106	0.33	3.36	0.20	0.35	0.35	0.70
	2107	0.34	3.18	0.18	0.33	0.32	0.64
	2108	0.31	3.22	0.20	0.33	0.32	0.65
	2109	0.30	2.97	0.18	0.30	0.29	0.60
	2110	0.33	3.06	0.18	0.33	0.32	0.65
	2111	0.29	3.29	0.20	0.34	0.33	0.67
	2112	0.29	3.48	0.19	0.37	0.36	0.73
	Mean	0.31	3.25	0.20	0.34	0.34	0.67
	S.D.	0.02	0.16	0.01	0.03	0.03	0.05

Appendix 8-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 30

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
	2101	55	56	111	45.1	52.2	97.3	590
	2102	33	40	73	52.1	47.3	99.4	658
	2103	41	42	83	52.2	47.8	100.0	630
	2104	42	46	88	60.9	38.2	99.1	715
	2105	49	49	98	60.6	52.2	112.8	633
	2106	41	43	84	56.9	55.4	112.3	657
	2107	38	45	83	53.7	55.5	109.2	642
Absolute	2108	47	51	98	48.5	58.6	107.1	669
	2109	41	43	84	68.0	59.4	127.4	763
	2110	36	42	78	60.3	55.3	115.6	643
	2111	41	47	88	68.8	66.6	135.4	696
	2112	44	46	90	60.9	66.0	126.9	720
	Mean	42	46	88	57.3	54.5	111.9	668
	S.D.	6	4	10	7.3	7.9	12.6	48
	2101	17	18	35	14.2	16.4	30.6	186
	2102	10	12	21	15.1	13.7	28.7	190
	2103	11	12	23	14.5	13.3	27.9	175
	2104	12	13	24	16.9	10.6	27.5	199
	2105	14	14	29	17.9	15.4	33.4	187
	2106	12	13	25	17.1	16.7	33.8	198
	2107	12	14	26	16.7	17.2	33.9	199
Relative	2108	15	16	31	15.4	18.6	34.0	212
	2109	11	11	22	17.9	15.7	33.6	201
	2110	10	12	22	16.8	15.4	32.1	179
	2111	12	13	25	19.4	18.8	38.1	196
	2112	13	14	27	18.2	19.7	37.9	215
	Mean	12	14	26	16.7	16.0	32.6	195
	S.D.	2	2	4	1.6	2.6	3.5	12

Appendix 8-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 100

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	3101	313	2.10	15.7	6.9	6.4	13.3	186
	3102	351	2.03	14.9	9.0	8.1	17.1	286
	3103	337	1.87	17.5	9.0	9.0	18.0	282
	3104	360	2.02	20.3	9.0	8.5	17.5	244
	3105	339	2.11	17.5	8.6	8.4	17.0	181
	3106	351	2.17	18.6	10.2	10.2	20.4	239
	3107	319	2.09	19.3	11.6	8.9	20.5	133
	3108	303	2.03	15.1	9.3	8.2	17.5	217
	3109	311	1.95	18.0	12.6	10.3	22.9	138
	3110	342	1.91	16.0	10.0	9.9	19.9	190
	3111a)	370Z	2.03Z	17.1Z	10.0Z	8.5Z	18.5Z	274Z
	3112	304	1.99	17.3	9.3	6.8	16.1	249
	Mean	330	2.02	17.3	9.6	8.6	18.2	213
	S.D.	21	0.09	1.7	1.5	1.3	2.6	52
Relative	3101		0.67	5.0	2.2	2.0	4.2	59
	3102		0.58	4.2	2.6	2.3	4.9	81
	3103		0.55	5.2	2.7	2.7	5.3	84
	3104		0.56	5.6	2.5	2.4	4.9	68
	3105		0.62	5.2	2.5	2.5	5.0	53
	3106		0.62	5.3	2.9	2.9	5.8	68
	3107		0.66	6.1	3.6	2.8	6.4	42
	3108		0.67	5.0	3.1	2.7	5.8	72
	3109		0.63	5.8	4.1	3.3	7.4	44
	3110		0.56	4.7	2.9	2.9	5.8	56
	3111a)		0.55Z	4.6Z	2.7Z	2.3Z	5.0Z	74Z
	3112		0.65	5.7	3.1	2.2	5.3	82
	Mean		0.62	5.3	2.9	2.6	5.5	64
	S.D.		0.05	0.5	0.5	0.4	0.9	15

a): Necropsied on lactation day 2 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 100

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	3101	0.95	10.79	0.53	1.14	1.28	2.42
	3102	1.00	11.80	0.61	1.12	1.13	2.25
	3103	0.96	11.15	0.57	1.17	1.22	2.39
	3104	1.04	11.78	0.75	1.18	1.24	2.42
	3105	1.12	12.87	0.85	1.01	1.04	2.05
	3106	1.05	12.16	0.84	1.24	1.16	2.40
	3107	1.02	10.45	0.74	1.13	1.10	2.23
	3108	1.03	10.43	0.66	1.09	1.15	2.24
	3109	0.94	10.80	0.60	1.26	1.17	2.43
	3110	1.10	11.12	0.60	1.13	1.07	2.20
	3111a)	1.04Z	14.71Z	0.69Z	1.27Z	1.27Z	2.54Z
	3112	0.87	9.20	0.57	1.00	0.96	1.96
	Mean	1.01	11.14	0.67	1.13	1.14	2.27
	S.D.	0.07	0.99	0.11	0.08	0.09	0.16
Relative	3101	0.30	3.45	0.17	0.36	0.41	0.77
	3102	0.28	3.36	0.17	0.32	0.32	0.64
	3103	0.28	3.31	0.17	0.35	0.36	0.71
	3104	0.29	3.27	0.21	0.33	0.34	0.67
	3105	0.33	3.80	0.25	0.30	0.31	0.60
	3106	0.30	3.46	0.24	0.35	0.33	0.68
	3107	0.32	3.28	0.23	0.35	0.34	0.70
	3108	0.34	3.44	0.22	0.36	0.38	0.74
	3109	0.30	3.47	0.19	0.41	0.38	0.78
	3110	0.32	3.25	0.18	0.33	0.31	0.64
	3111a)	0.28Z	3.98Z	0.19Z	0.34Z	0.34Z	0.69Z
	3112	0.29	3.03	0.19	0.33	0.32	0.64
	Mean	0.30	3.37	0.20	0.34	0.35	0.69
	S.D.	0.02	0.19	0.03	0.03	0.03	0.06

a): Necropsied on lactation day 2 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 100

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	3101	45	50	95	45.5	51.2	96.7	660
	3102	40	46	86	63.4	50.6	114.0	636
	3103	48	51	99	59.4	51.3	110.7	647
	3104	49	51	100	53.8	48.5	102.3	623
	3105	39	40	79	67.9	57.4	125.3	824
	3106	36	46	82	79.1	57.6	136.7	787
	3107	43	47	90	57.0	46.7	103.7	664
	3108	41	45	86	49.1	55.8	104.9	745
	3109	45	48	93	57.0	60.4	117.4	821
	3110	42	42	84	68.3	72.5	140.8	640
	3111a)	38Z	39Z	77Z	54.8Z	50.0Z	104.8Z	1706Z
	3112	28	34	62	47.5	60.8	108.3	779
	Mean	41	45	87	58.9	55.7	114.6	711
	S.D.	6	5	11	10.2	7.3	14.3	80
Relative	3101	14	16	30	14.5	16.4	30.9	211
	3102	11	13	25	18.1	14.4	32.5	181
	3103	14	15	29	17.6	15.2	32.8	192
	3104	14	14	28	14.9	13.5	28.4	173
	3105	12	12	23	20.0	16.9	37.0	243
	3106	10	13	23	22.5	16.4	38.9	224
	3107	13	15	28	17.9	14.6	32.5	208
	3108	14	15	28	16.2	18.4	34.6	246
	3109	14	15	30	18.3	19.4	37.7	264
	3110	12	12	25	20.0	21.2	41.2	187
	3111a)	10Z	11Z	21Z	14.8Z	13.5Z	28.3Z	461Z
	3112	9	11	20	15.6	20.0	35.6	256
	Mean	12	14	26	17.8	16.9	34.7	217
	S.D.	2	2	3	2.4	2.5	3.8	32

a): Necropsied on lactation day 2 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4101	322	2.08	16.0	8.0	7.8	15.8	240
	4102	286	2.00	15.1	8.3	9.0	17.3	172
	4103	312	2.00	16.3	8.6	8.8	17.4	164
	4104	327	2.03	19.0	6.3	7.0	13.3	137
	4105	335	2.08	18.3	11.6	9.9	21.5	172
	4106	313	2.08	19.5	12.4	10.2	22.6	238
	4107	329	2.10	19.9	10.1	6.9	17.0	161
	4108	297	1.93	17.7	6.9	9.8	16.7	152
	4109	324	2.03	19.9	10.1	8.1	18.2	257
	4110	337	2.00	18.7	9.7	9.3	19.0	164
	4111a)	278Z	1.93Z	13.7Z	8.6Z	8.5Z	17.1Z	59Z
	4112	332	1.98	22.4	6.7	6.8	13.5	104
	Mean	319	2.03	18.4	9.0	8.5	17.5	178
	S.D.	16	0.05	2.1	2.0	1.3	2.9	47
Relative	4101		0.65	5.0	2.5	2.4	4.9	75
	4102		0.70	5.3	2.9	3.1	6.0	60
	4103		0.64	5.2	2.8	2.8	5.6	53
	4104		0.62	5.8	1.9	2.1	4.1	42
	4105		0.62	5.5	3.5	3.0	6.4	51
	4106		0.66	6.2	4.0	3.3	7.2	76
	4107		0.64	6.0	3.1	2.1	5.2	49
	4108		0.65	6.0	2.3	3.3	5.6	51
	4109		0.63	6.1	3.1	2.5	5.6	79
	4110		0.59	5.5	2.9	2.8	5.6	49
	4111a)		0.69Z	4.9Z	3.1Z	3.1Z	6.2Z	21Z
	4112		0.60	6.7	2.0	2.0	4.1	31
	Mean		0.64	5.8	2.8	2.7	5.5	56
	S.D.		0.03	0.5	0.6	0.5	0.9	15

a): Necropsied on lactation day 4 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4101	1.07	11.02	0.66	1.08	1.08	2.16
	4102	0.83	10.22	0.59	1.09	1.06	2.15
	4103	1.00	12.46	0.60	1.09	1.12	2.21
	4104	1.04	11.27	0.57	1.07	1.09	2.16
	4105	1.00	10.80	0.52	1.18	1.17	2.35
	4106	1.07	9.34	0.48	1.18	1.25	2.43
	4107	1.00	12.82	0.68	1.31	1.36	2.67
	4108	0.94	10.77	0.53	1.13	1.12	2.25
	4109	0.99	10.95	0.72	1.23	1.17	2.40
	4110	1.09	12.78	0.76	1.21	1.17	2.38
	4111a)	0.80Z	11.24Z	0.63Z	1.47Z	1.40Z	2.87Z
	4112	0.99	11.57	0.71	1.22	1.14	2.36
	Mean	1.00	11.27	0.62	1.16	1.16	2.32
	S.D.	0.07	1.08	0.09	0.08	0.09	0.16
Relative	4101	0.33	3.42	0.20	0.34	0.34	0.67
	4102	0.29	3.57	0.21	0.38	0.37	0.75
	4103	0.32	3.99	0.19	0.35	0.36	0.71
	4104	0.32	3.45	0.17	0.33	0.33	0.66
	4105	0.30	3.22	0.16	0.35	0.35	0.70
	4106	0.34	2.98	0.15	0.38	0.40	0.78
	4107	0.30	3.90	0.21	0.40	0.41	0.81
	4108	0.32	3.63	0.18	0.38	0.38	0.76
	4109	0.31	3.38	0.22	0.38	0.36	0.74
	4110	0.32	3.79	0.23	0.36	0.35	0.71
	4111a)	0.29Z	4.04Z	0.23Z	0.53Z	0.50Z	1.03Z
	4112	0.30	3.48	0.21	0.37	0.34	0.71
	Mean	0.31	3.53	0.19	0.37	0.36	0.73
	S.D.	0.02	0.29	0.03	0.02	0.03	0.05

a): Necropsied on lactation day 4 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4101	53	53	106	56.1	40.9	97.0	632
	4102	44	48	92	51.1	36.9	88.0	599
	4103	48	55	103	57.3	63.4	120.7	538
	4104	52	57	109	66.5	55.1	121.6	529
	4105	43	44	87	49.8	76.2	126.0	651
	4106	44	42	86	58.0	59.2	117.2	690
	4107	48	54	102	68.2	71.2	139.4	824
	4108	48	50	98	63.6	72.0	135.6	662
	4109	41	42	83	58.1	55.0	113.1	814
	4110	47	49	96	67.1	54.8	121.9	716
	4111a)	55Z	61Z	116Z	70.4Z	75.8Z	146.2Z	981Z
	4112	44	46	90	53.2	55.1	108.3	583
	Mean	47	49	96	59.0	58.2	117.2	658
	S.D.	4	5	9	6.5	12.3	15.2	99
Relative	4101	16	16	33	17.4	12.7	30.1	196
	4102	15	17	32	17.9	12.9	30.8	209
	4103	15	18	33	18.4	20.3	38.7	172
	4104	16	17	33	20.3	16.9	37.2	162
	4105	13	13	26	14.9	22.7	37.6	194
	4106	14	13	27	18.5	18.9	37.4	220
	4107	15	16	31	20.7	21.6	42.4	250
	4108	16	17	33	21.4	24.2	45.7	223
	4109	13	13	26	17.9	17.0	34.9	251
	4110	14	15	28	19.9	16.3	36.2	212
	4111a)	20Z	22Z	42Z	25.3Z	27.3Z	52.6Z	353Z
	4112	13	14	27	16.0	16.6	32.6	176
	Mean	15	15	30	18.5	18.2	36.7	206
	S.D.	1	2	3	2.0	3.7	4.7	30

a): Necropsied on lactation day 4 because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1113	287	2.00	13.2	5.9	4.3	10.2	304
	1114	281	1.98	16.8	10.0	7.7	17.7	244
	1115	307	1.93	14.8	7.8	8.3	16.1	380
	1116	348	2.04	19.6	12.3	9.9	22.2	523
	1117	309	1.95	24.2	8.7	8.0	16.7	337
	Mean	306	1.98	17.7	8.9	7.6	16.6	358
	S.D.	26	0.04	4.3	2.4	2.1	4.3	105
Relative	1113		0.70	4.6	2.1	1.5	3.6	106
	1114		0.70	6.0	3.6	2.7	6.3	87
	1115		0.63	4.8	2.5	2.7	5.2	124
	1116		0.59	5.6	3.5	2.8	6.4	150
	1117		0.63	7.8	2.8	2.6	5.4	109
	Mean		0.65	5.8	2.9	2.5	5.4	115
	S.D.		0.05	1.3	0.6	0.5	1.1	23

Appendix 8-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1113	0.94	7.60	0.51	0.91	0.92	1.83
	1114	0.89	7.25	0.50	1.03	1.01	2.04
	1115	0.92	7.31	0.53	0.99	0.97	1.96
	1116	1.00	9.34	0.51	1.10	1.08	2.18
	1117	1.05	8.59	0.44	1.00	1.02	2.02
	Mean	0.96	8.02	0.50	1.01	1.00	2.01
	S.D.	0.06	0.91	0.03	0.07	0.06	0.13
Relative	1113	0.33	2.65	0.18	0.32	0.32	0.64
	1114	0.32	2.58	0.18	0.37	0.36	0.73
	1115	0.30	2.38	0.17	0.32	0.32	0.64
	1116	0.29	2.68	0.15	0.32	0.31	0.63
	1117	0.34	2.78	0.14	0.32	0.33	0.65
	Mean	0.32	2.61	0.16	0.33	0.33	0.66
	S.D.	0.02	0.15	0.02	0.02	0.02	0.04

Appendix 8-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1113	40	43	83	72.2	57.3	129.5	502
	1114	42	44	86	42.0	40.7	82.7	739
	1115	32	36	68	37.2	43.3	80.5	742
	1116	45	50	95	64.3	53.5	117.8	753
	1117	32	36	68	24.2	30.6	54.8	672
	Mean	38	42	80	48.0	45.1	93.1	682
	S.D.	6	6	12	19.8	10.6	30.3	105
Relative	1113	14	15	29	25.2	20.0	45.1	175
	1114	15	16	31	14.9	14.5	29.4	263
	1115	10	12	22	12.1	14.1	26.2	242
	1116	13	14	27	18.5	15.4	33.9	216
	1117	10	12	22	7.8	9.9	17.7	217
	Mean	12	14	26	15.7	14.8	30.5	223
	S.D.	2	2	4	6.6	3.6	10.1	33

Appendix 8-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4113	290	1.99	17.7	10.3	6.8	17.1	261
	4114	305	2.02	18.0	8.3	9.7	18.0	365
	4115	272	1.93	22.1	8.2	7.0	15.2	206
	4116	299	2.08	17.4	8.1	10.0	18.1	324
	4117	280	1.99	19.1	10.0	7.9	17.9	255
	Mean	289	2.00	18.9	9.0	8.3	17.3	282
	S.D.	13	0.05	1.9	1.1	1.5	1.2	62
Relative	4113		0.69	6.1	3.6	2.3	5.9	90
	4114		0.66	5.9	2.7	3.2	5.9	120
	4115		0.71	8.1	3.0	2.6	5.6	76
	4116		0.70	5.8	2.7	3.3	6.1	108
	4117		0.71	6.8	3.6	2.8	6.4	91
	Mean		0.69	6.5	3.1	2.8	6.0	97
	S.D.		0.02	1.0	0.5	0.4	0.3	17

Appendix 8-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4113	0.90	8.43	0.46	0.92	0.95	1.87
	4114	0.93	9.08	0.65	1.06	1.08	2.14
	4115	0.87	7.87	0.42	0.97	1.01	1.98
	4116	0.99	9.81	0.59	1.34	1.29	2.63
	4117	0.82	8.26	0.46	0.99	1.04	2.03
	Mean	0.90	8.69	0.52	1.06	1.07	2.13
	S.D.	0.06	0.76	0.10	0.17	0.13	0.30
Relative	4113	0.31	2.91	0.16	0.32	0.33	0.64
	4114	0.30	2.98	0.21	0.35	0.35	0.70
	4115	0.32	2.89	0.15	0.36	0.37	0.73
	4116	0.33	3.28	0.20	0.45	0.43	0.88
	4117	0.29	2.95	0.16	0.35	0.37	0.73
	Mean	0.31	3.00	0.18	0.37	0.37	0.74
	S.D.	0.02	0.16	0.03	0.05	0.04	0.09

Appendix 8-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4113	33	36	69	51.4	57.3	108.7	403
	4114	43	52	95	66.5	64.5	131.0	577
	4115	45	47	92	49.1	39.4	88.5	677
	4116	53	56	109	55.6	60.1	115.7	875
	4117	38	44	82	62.0	53.2	115.2	644
	Mean	42	47	89	56.9	54.9	111.8	635
	S.D.	8	8	15	7.3	9.6	15.4	171
Relative	4113	11	12	24	17.7	19.8	37.5	139
	4114	14	17	31	21.8	21.1	43.0	189
	4115	17	17	34	18.1	14.5	32.5	249
	4116	18	19	36	18.6	20.1	38.7	293
	4117	14	16	29	22.1	19.0	41.1	230
	Mean	15	16	31	19.7	18.9	38.6	220
	S.D.	3	3	5	2.1	2.6	4.0	59

Appendix 8-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1008	535	2.16	15.1	11.3	10.7	22.0	395
	1009	500	2.11	13.0	10.7	7.5	18.2	336
	1010	564	2.49	13.8	10.5	10.8	21.3	309
	1011	528	2.19	12.7	9.9	8.2	18.1	247
	1012	564	2.25	14.8	9.3	14.1	23.4	155
	Mean	538	2.24	13.9	10.3	10.3	20.6	288
	S.D.	27	0.15	1.1	0.8	2.6	2.4	92
Relative	1008		0.40	2.8	2.1	2.0	4.1	74
	1009		0.42	2.6	2.1	1.5	3.6	67
	1010		0.44	2.4	1.9	1.9	3.8	55
	1011		0.41	2.4	1.9	1.6	3.4	47
	1012		0.40	2.6	1.6	2.5	4.1	27
	Mean		0.41	2.6	1.9	1.9	3.8	54
	S.D.		0.02	0.2	0.2	0.4	0.3	18

Appendix 8-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1008	1.60	13.32	0.81	1.73	1.88	3.61
	1009	1.32	12.45	0.63	1.64	1.59	3.23
	1010	1.62	13.62	0.75	1.84	1.93	3.77
	1011	1.37	11.95	0.57	1.66	1.83	3.49
	1012	1.46	13.65	0.62	1.62	1.97	3.59
	Mean	1.47	13.00	0.68	1.70	1.84	3.54
	S.D.	0.13	0.76	0.10	0.09	0.15	0.20
Relative	1008	0.30	2.49	0.15	0.32	0.35	0.67
	1009	0.26	2.49	0.13	0.33	0.32	0.65
	1010	0.29	2.41	0.13	0.33	0.34	0.67
	1011	0.26	2.26	0.11	0.31	0.35	0.66
	1012	0.26	2.42	0.11	0.29	0.35	0.64
	Mean	0.27	2.41	0.13	0.32	0.34	0.66
	S.D.	0.02	0.09	0.02	0.02	0.01	0.01

Appendix 8-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	1008	23	25	48	1.93	1.94	3.87
	1009	28	31	59	1.43	1.45	2.88
	1010	40	46	86	1.86	1.86	3.72
	1011	29	35	64	1.90	1.92	3.82
	1012	28	33	61	1.68	0.83	2.51
	Mean	30	34	64	1.76	1.60	3.36
	S.D.	6	8	14	0.21	0.47	0.62
Relative	1008	4	5	9	0.36	0.36	0.72
	1009	6	6	12	0.29	0.29	0.58
	1010	7	8	15	0.33	0.33	0.66
	1011	5	7	12	0.36	0.36	0.72
	1012	5	6	11	0.30	0.15	0.45
	Mean	5	6	12	0.33	0.30	0.63
	S.D.	1	1	2	0.03	0.09	0.11

Appendix 8-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	1008	754	801	1555	2.10	1.19
	1009	600	623	1223	1.56	1.20
	1010	643	730	1373	1.76	1.18
	1011	741	770	1511	1.81	1.40
	1012	735	304	1039	1.57	1.10
	Mean	695	646	1340	1.76	1.21
	S.D.	69	202	213	0.22	0.11
Relative	1008	141	150	291	0.39	0.22
	1009	120	125	245	0.31	0.24
	1010	114	129	243	0.31	0.21
	1011	140	146	286	0.34	0.27
	1012	130	54	184	0.28	0.20
	Mean	129	121	250	0.33	0.23
	S.D.	12	39	43	0.04	0.03

Appendix 8-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4008	544	2.20	12.0	9.9	10.9	20.8	269
	4009	504	2.19	12.1	11.8	10.0	21.8	292
	4010	566	2.17	14.4	12.6	12.6	25.2	227
	4011	538	2.24	17.0	10.5	7.6	18.1	225
	4012	518	2.11	12.9	13.1	14.8	27.9	280
	Mean	534	2.18	13.7	11.6	11.2	22.8	259
	S.D.	24	0.05	2.1	1.4	2.7	3.8	31
Relative	4008		0.40	2.2	1.8	2.0	3.8	49
	4009		0.43	2.4	2.3	2.0	4.3	58
	4010		0.38	2.5	2.2	2.2	4.5	40
	4011		0.42	3.2	2.0	1.4	3.4	42
	4012		0.41	2.5	2.5	2.9	5.4	54
	Mean		0.41	2.6	2.2	2.1	4.3	49
	S.D.		0.02	0.4	0.3	0.5	0.8	8

Appendix 8-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4008	1.41	13.65	0.75	1.66	1.61	3.27
	4009	1.44	11.95	0.77	1.50	1.63	3.13
	4010	1.45	15.75	0.77	2.05	2.19	4.24
	4011	1.30	12.55	0.60	1.72	1.75	3.47
	4012	1.38	13.31	0.74	1.75	1.79	3.54
	Mean	1.40	13.44	0.73	1.74	1.79	3.53
	S.D.	0.06	1.45	0.07	0.20	0.23	0.43
Relative	4008	0.26	2.51	0.14	0.31	0.30	0.60
	4009	0.29	2.37	0.15	0.30	0.32	0.62
	4010	0.26	2.78	0.14	0.36	0.39	0.75
	4011	0.24	2.33	0.11	0.32	0.33	0.64
	4012	0.27	2.57	0.14	0.34	0.35	0.68
	Mean	0.26	2.51	0.14	0.33	0.34	0.66
	S.D.	0.02	0.18	0.02	0.02	0.03	0.06

Appendix 8-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Testis (R) g(g/100g BW)	Testis (L) g(g/100g BW)	Testis (R+L) g(g/100g BW)
Absolute	4008	27	28	55	1.79	1.79	3.58
	4009	34	34	68	1.93	1.97	3.90
	4010	32	33	65	1.69	1.75	3.44
	4011	29	33	62	1.83	1.77	3.60
	4012	32	33	65	1.96	1.98	3.94
	Mean	31	32	63	1.84	1.85	3.69
	S.D.	3	2	5	0.11	0.11	0.22
Relative	4008	5	5	10	0.33	0.33	0.66
	4009	7	7	13	0.38	0.39	0.77
	4010	6	6	11	0.30	0.31	0.61
	4011	5	6	12	0.34	0.33	0.67
	4012	6	6	13	0.38	0.38	0.76
	Mean	6	6	12	0.35	0.35	0.69
	S.D.	1	1	1	0.03	0.03	0.07

Appendix 8-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Epididymis (R) mg(mg/100g BW)	Epididymis (L) mg(mg/100g BW)	Epididymis (R+L) mg(mg/100g BW)	Seminal vesicle g(g/100g BW)	Prostate g(g/100g BW)
Absolute	4008	683	686	1369	1.39	1.07
	4009	670	719	1389	1.59	1.00
	4010	752	788	1540	2.06	1.47
	4011	675	693	1368	1.64	1.32
	4012	724	774	1498	1.71	1.18
	Mean	701	732	1433	1.68	1.21
	S.D.	36	47	81	0.24	0.19
Relative	4008	126	126	252	0.26	0.20
	4009	133	143	276	0.32	0.20
	4010	133	139	272	0.36	0.26
	4011	125	129	254	0.30	0.25
	4012	140	149	289	0.33	0.23
	Mean	131	137	269	0.31	0.23
	S.D.	6	10	16	0.04	0.03

Appendix 8-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	1118	331	2.04	15.6	9.5	7.0	16.5	265
	1119	288	1.95	20.6	7.0	6.6	13.6	208
	1120	309	2.03	18.0	9.7	10.9	20.6	193
	1121	305	2.04	20.2	8.8	8.7	17.5	249
	1122	301	1.98	14.6	8.8	8.7	17.5	265
	Mean	307	2.01	17.8	8.8	8.4	17.1	236
	S.D.	16	0.04	2.7	1.1	1.7	2.5	33
Relative	1118		0.62	4.7	2.9	2.1	5.0	80
	1119		0.68	7.2	2.4	2.3	4.7	72
	1120		0.66	5.8	3.1	3.5	6.7	62
	1121		0.67	6.6	2.9	2.9	5.7	82
	1122		0.66	4.9	2.9	2.9	5.8	88
	Mean		0.66	5.8	2.8	2.7	5.6	77
	S.D.		0.02	1.1	0.3	0.6	0.8	10

Appendix 8-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	1118	0.93	7.27	0.66	0.99	1.02	2.01
	1119	0.87	6.71	0.52	1.00	1.04	2.04
	1120	0.95	8.33	0.60	1.12	1.12	2.24
	1121	0.91	8.84	0.55	1.12	1.17	2.29
	1122	0.88	7.39	0.46	1.04	1.07	2.11
	Mean	0.91	7.71	0.56	1.05	1.08	2.14
	S.D.	0.03	0.86	0.08	0.06	0.06	0.12
Relative	1118	0.28	2.20	0.20	0.30	0.31	0.61
	1119	0.30	2.33	0.18	0.35	0.36	0.71
	1120	0.31	2.70	0.19	0.36	0.36	0.72
	1121	0.30	2.90	0.18	0.37	0.38	0.75
	1122	0.29	2.46	0.15	0.35	0.36	0.70
	Mean	0.30	2.52	0.18	0.35	0.35	0.70
	S.D.	0.01	0.28	0.02	0.03	0.03	0.05

Appendix 8-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 0

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	1118	32	36	68	52.0	57.7	109.7	770
	1119	31	31	62	57.3	46.2	103.5	486
	1120	41	44	85	63.0	58.8	121.8	496
	1121	39	43	82	43.9	51.3	95.2	851
	1122	40	43	83	61.3	58.4	119.7	666
	Mean	37	39	76	55.5	54.5	110.0	654
	S.D.	5	6	10	7.7	5.5	11.1	162
Relative	1118	10	11	21	15.7	17.4	33.1	233
	1119	11	11	22	19.9	16.0	35.9	169
	1120	13	14	28	20.4	19.0	39.4	161
	1121	13	14	27	14.4	16.8	31.2	279
	1122	13	14	28	20.4	19.4	39.8	221
	Mean	12	13	25	18.2	17.7	35.9	213
	S.D.	1	2	3	2.9	1.4	3.8	49

Appendix 8-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Body weight g	Brain g(g/100g BW)	Pituitary mg(mg/100g BW)	Thyroid (R) mg(mg/100g BW)	Thyroid (L) mg(mg/100g BW)	Thyroid (R+L) mg(mg/100g BW)	Thymus mg(mg/100g BW)
Absolute	4118	298	2.24	16.6	9.4	11.4	20.8	210
	4119	302	2.07	23.2	8.7	8.3	17.0	298
	4120	316	2.06	16.6	10.4	10.0	20.4	287
	4121	314	2.13	14.6	8.0	8.5	16.5	233
	4122	321	2.04	17.4	9.8	11.7	21.5	364
	Mean	310	2.11	17.7	9.3	10.0	19.2	278
	S.D.	10	0.08	3.3	0.9	1.6	2.3	60
Relative	4118		0.75	5.6	3.2	3.8	7.0	70
	4119		0.69	7.7	2.9	2.7	5.6	99
	4120		0.65	5.3	3.3	3.2	6.5	91
	4121		0.68	4.6	2.5	2.7	5.3	74
	4122		0.64	5.4	3.1	3.6	6.7	113
	Mean		0.68	5.7	3.0	3.2	6.2	89
	S.D.		0.04	1.2	0.3	0.5	0.7	18

Appendix 8-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Heart g(g/100g BW)	Liver g(g/100g BW)	Spleen g(g/100g BW)	Kidney (R) g(g/100g BW)	Kidney (L) g(g/100g BW)	Kidney (R+L) g(g/100g BW)
Absolute	4118	0.98	7.38	0.63	0.99	1.09	2.08
	4119	1.12	9.36	0.50	1.11	1.17	2.28
	4120	0.95	8.73	0.70	1.09	1.13	2.22
	4121	0.94	7.62	0.58	1.05	1.06	2.11
	4122	1.01	7.96	0.58	1.19	1.14	2.33
	Mean	1.00	8.21	0.60	1.09	1.12	2.20
	S.D.	0.07	0.82	0.07	0.07	0.04	0.11
Relative	4118	0.33	2.48	0.21	0.33	0.37	0.70
	4119	0.37	3.10	0.17	0.37	0.39	0.75
	4120	0.30	2.76	0.22	0.34	0.36	0.70
	4121	0.30	2.43	0.18	0.33	0.34	0.67
	4122	0.31	2.48	0.18	0.37	0.36	0.73
	Mean	0.32	2.65	0.19	0.35	0.36	0.71
	S.D.	0.03	0.28	0.02	0.02	0.02	0.03

Appendix 8-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 300

	Animal number	Adrenal (R) mg(mg/100g BW)	Adrenal (L) mg(mg/100g BW)	Adrenal (R+L) mg(mg/100g BW)	Ovary (R) mg(mg/100g BW)	Ovary (L) mg(mg/100g BW)	Ovary (R+L) mg(mg/100g BW)	Uterus mg(mg/100g BW)
Absolute	4118	42	41	83	69.2	60.0	129.2	716
	4119	41	46	87	32.0	26.2	58.2	723
	4120	43	42	85	41.3	46.7	88.0	471
	4121	36	42	78	58.6	59.8	118.4	498
	4122	42	45	87	46.4	43.6	90.0	524
	Mean	41	43	84	49.5	47.3	96.8	586
	S.D.	3	2	4	14.6	13.9	28.0	123
Relative	4118	14	14	28	23.2	20.1	43.4	240
	4119	14	15	29	10.6	8.7	19.3	239
	4120	14	13	27	13.1	14.8	27.8	149
	4121	11	13	25	18.7	19.0	37.7	159
	4122	13	14	27	14.5	13.6	28.0	163
	Mean	13	14	27	16.0	15.2	31.2	190
	S.D.	1	1	1	5.0	4.6	9.4	45

Appendix 9-1(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1001 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Mammary gland,inguinal
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-2(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1002 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-3(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1003 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Pituitary	Cyst,pars distalis: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Parathyroid, Pancreas, Prostate
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Seminal vesicle(Coagulating gland), Spinal cord,thoracic, Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-4(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1004 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Epididymis	Nodule: 1 present cauda,2x2x2mm
Other tissues	Not remarkable

Histopathology:

Epididymis	Granuloma,spermatic: mild, unilateral
Heart	Cell infiltration: minimal, focal, mononuclear
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, mononuclear ventral and dorsolateral
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-5(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1005 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Parathyroid
Pancreas, Pituitary, Prostate, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-6(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1006 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-7(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1007 Male 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-8(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1008 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney

Appendix 9-9(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1009 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney

Appendix 9-10(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1010 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney

Appendix 9-11(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1011 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal

Appendix 9-12(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1012 Male 0 mg/kg Day 57 End of recovery period

Gross pathology:

Epididymis	Small: mild, left
Testis	Small: mild, left
Other tissues	Not remarkable

Histopathology:

Following tissues : Not remarkable

Kidney

Appendix 9-13(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2001 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Eosinophilic body,tubular cell: mild, proximal

Appendix 9-14(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2002 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Eosinophilic body,tubular cell: mild, proximal Hyperplasia,transitional,focal: minimal

Appendix 9-15(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2003 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Eosinophilic body,tubular cell: mild, proximal

Appendix 9-16(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2004 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Eosinophilic body,tubular cell: minimal, proximal

Appendix 9-17(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2005 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Eosinophilic body,tubular cell: minimal, proximal

Appendix 9-18(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2006 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-19(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2007 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-20(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2008 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-21(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2009 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-22(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2010 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-23(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2011 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-24(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2012 Male 30 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-25(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3001 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Eosinophilic body,tubular cell: minimal, proximal

Appendix 9-26(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3002 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: mild, proximal

Appendix 9-27(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3003 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Eosinophilic body,tubular cell: mild, proximal

Appendix 9-28(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3004 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: mild, proximal

Appendix 9-29(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3005 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Eosinophilic body,tubular cell: mild, proximal

Appendix 9-30(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3006 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-31(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3007 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Dilatation,pelvic: mild, right
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-32(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3008 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-33(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3009 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-34(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3010 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-35(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3011 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-36(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3012 Male 100 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-37(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4001 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney(alpha2u globulin)	Alpha2u globulin immunohistochemistry positive
Kidney	Regeneration,tubular: minimal Eosinophilic body,tubular cell: moderate, proximal
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Mammary gland,inguinal, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-38(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4002 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney(alpha2u globulin)	Alpha2u globulin immunohistochemistry positive
Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: mild, proximal
Liver	Microgranuloma: minimal
Parathyroid	No sample
Prostate	Cell infiltration: mild, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-39(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4003 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: mild, proximal
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Mammary gland,inguinal, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Seminal vesicle(Coagulating gland), Spinal cord,thoracic
Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-40(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4004 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Urinary cast,granular: minimal Eosinophilic body,tubular cell: moderate, proximal
Prostate	Cell infiltration: minimal, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Mammary gland,inguinal
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-41(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4005 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: moderate, proximal
Liver	Microgranuloma: minimal
Prostate	Cell infiltration: minimal, mononuclear ventral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Mammary gland,inguinal, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(Coagulating gland)
Spinal cord,thoracic, Testis, Thymus, Trachea, Thyroid, Urinary bladder

Appendix 9-42(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4006 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-43(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4007 Male 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-44(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4008 Male 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild

Appendix 9-45(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4009 Male 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal Hyperplasia,transitional,focal: minimal

Appendix 9-46(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4010 Male 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild

Appendix 9-47(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4011 Male 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild

Appendix 9-48(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4012 Male 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: minimal

Appendix 9-49(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Mammary gland,inguinal
Ovary, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Sciatic nerve, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-50(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1102 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Parathyroid	No sample
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Ovary, Pancreas, Pituitary, Salivary gland,submandibular
Sciatic nerve, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-51(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1103 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-52(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 52 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-53(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1105 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-54(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Mammary gland,inguinal
Ovary, Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Sciatic nerve, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-55(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-56(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Mammary gland,inguinal, Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-57(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-58(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-59(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-60(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-61(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1113 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-62(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1114 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-63(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1115 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-64(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1116 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Parathyroid	No sample

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Mammary gland,inguinal, Ovary, Pancreas, Pituitary, Salivary gland,submandibular
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-65(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1117 Female 0 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Ovary	Atrophy: moderate, bilateral
Parathyroid	No sample

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Pancreas, Pituitary, Salivary gland,submandibular
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-66(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1118 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-67(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1119 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-68(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1120 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-69(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1121 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-70(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1122 Female 0 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-71(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2101 Female 30 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-72(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2102 Female 30 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-73(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2103 Female 30 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-74(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2104 Female 30 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-75(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2105 Female 30 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-76(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2106 Female 30 mg/kg Day 50 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-77(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2107 Female 30 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-78(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2108 Female 30 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-79(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2109 Female 30 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-80(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2110 Female 30 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-81(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2111 Female 30 mg/kg Day 46 End of administration period (L4)

Gross pathology:

Lung(bronchus)	Focus,dark red: 1 present 5x7mm
Stomach	Focus,dark red,glandular stomach: 1 present 0.5x0.5mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-82(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2112 Female 30 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-83(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3101 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole, zona fasciculata: minimal
Liver	Microgranuloma: minimal

Appendix 9-84(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3102 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-85(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3103 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-86(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3104 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-87(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3105 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-88(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3106 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-89(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3107 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-90(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3108 Female 100 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: minimal

Following tissues : Not remarkable

Liver

Appendix 9-91(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3109 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-92(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3110 Female 100 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-93(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3111 Female 100 mg/kg Day 42 All littermates died

Gross pathology:

All tissues	Not remarkable

Histopathology:

Mammary gland,inguinal	Decreased lactation: moderate
Ovary	Decreased large corpus luteum: moderate, bilateral
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Lung(bronchus)
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-94(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3112 Female 100 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 3x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-95(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4101 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: mild
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-96(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4102 Female 300 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-97(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4103 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: mild
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Mammary gland,inguinal, Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-98(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4104 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: mild
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-99(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4105 Female 300 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-100(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4106 Female 300 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-101(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4107 Female 300 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-102(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4108 Female 300 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-103(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4109 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: minimal
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-104(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4110 Female 300 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: mild
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Stomach, Skeletal muscle,femoral
Spinal cord,thoracic, Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-105(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4111 Female 300 mg/kg Day 44 All littermates died

Gross pathology:

General descriptions	Fracture,incisor
Mammary gland,inguinal	Undeveloped
Stomach	Focus,white,forestomach: many less than 2x2mm
Other tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: moderate
Intestine,colon	Atrophy,goblet cell: minimal
Kidney	Dilatation,tubular: mild collecting duct and distal tubule Vacuolation,tubular cell: moderate proximal Necrosis,tubular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Mammary gland,inguinal	Decreased lactation: mild
Salivary gland,submandibular	Decreased granule,granular duct: minimal
Stomach	Ulcer,forestomach: minimal Hyperplasia,squamous,forestomach: mild
Thymus	Atrophy: moderate

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Ovary, Parathyroid, Pancreas, Pituitary
Sciatic nerve, Spleen, Skeletal muscle,femoral, Spinal cord,thoracic, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-106(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4112 Female 300 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-107(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4113 Female 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-108(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4114 Female 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Mammary gland,inguinal, Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular, Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-109(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4115 Female 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Increased vacuole,zona fasciculata: mild
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-110(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4116 Female 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-111(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4117 Female 300 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(Pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus)
Mammary gland,inguinal, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Sciatic nerve, Spleen, Stomach
Skeletal muscle,femoral, Spinal cord,thoracic, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-112(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4118 Female 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-113(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4119 Female 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 9-114(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4120 Female 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-115(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4121 Female 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal

Appendix 9-116(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4122 Female 300 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver

Appendix 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 0

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
1101	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1102c)	D	P	E	M	D	P	E	E	M	D	D	P	E	M	D	3	5.0	
1103	M	D	P	E	M	D	D	P	E	M	D	P	E	M	D	3	4.5	
1104	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1105	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1106	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
1107	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1108	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1109	E	M	D	P	E	M	D	P	E	M	D	D	P	E	M	4	4.3	
1110	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
1111	D	P	E	E	M	D	P	E	E	M	D	P	E	E	M	3	5.0	
1112	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
Total(%)b)																		1/12(8.3)
Mean																3.6	4.2	
S.D.																0.5	0.4	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100
c): Abnormal estrous cycle

Appendix 10-2

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 30

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
2101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2102	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2103	E	M	D	D	P	E	M	D	D	P	E	M	D	D	P	3	5.0	
2104	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2105	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2106	M	D	P	E	M	D	D	P	E	M	D	P	E	M	D	3	4.5	
2107	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
2109	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2110	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
2111	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
2112	D	P	E	M	D	D	P	E	M	D	P	E	E	M	D	3	4.5	
Total(%)b)																		0/12(0.0)
Mean																3.6	4.2	
S.D.																0.5	0.3	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 10-3

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 100

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
3101	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3102	M	D	P	E	M	D	D	P	E	M	D	P	E	M	D	3	4.5	
3103	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3104	E	E	M	D	P	E	E	M	D	P	E	E	M	D	P	3	5.0	
3105	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
3106	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3107	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3108	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
3110	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
3111	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
3112	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
Total(%)b)																		0/12(0.0)
Mean																3.6	4.1	
S.D.																0.5	0.3	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 10-4

Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual estrous cycle in female rats during the pre-mating period (Main group)
Dose (mg/kg): 300

Animal number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15a)	Count of estrus	Mean duration of cycles	Index of animals with abnormal estrous cycle (%)
4101	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
4102	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
4103	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
4104	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
4105	P	E	E	M	D	P	E	E	M	D	P	E	E	M	D	3	5.0	
4106	D	P	E	M	D	P	E	E	M	D	P	E	M	D	P	3	4.5	
4107	P	E	M	D	P	E	E	M	D	P	E	M	D	P	E	4	4.3	
4108	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4110	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
4111	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4112	P	E	M	D	P	E	E	M	D	P	E	E	M	D	P	3	4.5	
Total(%)b)																		0/12(0.0)
Mean																3.7	4.2	
S.D.																0.5	0.3	

P: Proestrus E: Estrus M: Metestrus D: Diestrus
a): Day of sampling
b): (No. of animals with abnormal estrous cycle / No. of animals examined)×100

Appendix 11-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 0

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
1001	1101	C	2	P
1002	1102	C	2	P
1003	1103	C	2	P
1004	1104	C	10	P
1005	1105	C	2	P
1006	1106	C	1	P
1007	1107	C	3	P
1008	1108	C	2	P
1009	1109	C	3	P
1010	1110	C	4	P
1011	1111	C	4	P
1012	1112	C	1	P

C: Copulated P: Pregnant

Appendix 11-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 30

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
2001	2101	C	1	P
2002	2102	C	2	P
2003	2103	C	1	P
2004	2104	C	2	P
2005	2105	C	2	P
2006	2106	C	8	P
2007	2107	C	3	P
2008	2108	C	1	P
2009	2109	C	2	P
2010	2110	C	4	P
2011	2111	C	4	P
2012	2112	C	2	P

C: Copulated P: Pregnant

Appendix 11-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 100

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
3001	3101	C	1	P
3002	3102	C	2	P
3003	3103	C	1	P
3004	3104	C	1	P
3005	3105	C	3	P
3006	3106	C	2	P
3007	3107	C	2	P
3008	3108	C	1	P
3009	3109	C	3	P
3010	3110	C	2	P
3011	3111	C	3	P
3012	3112	C	3	P

C: Copulated P: Pregnant

Appendix 11-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 300

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
4001	4101	C	2	P
4002	4102	C	4	P
4003	4103	C	2	P
4004	4104	C	1	P
4005	4105	C	3	P
4006	4106	C	3	P
4007	4107	C	4	P
4008	4108	C	3	P
4009	4109	C	3	P
4010	4110	C	1	P
4011	4111	C	3	P
4012	4112	C	2	P

C: Copulated P: Pregnant

Appendix 12-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual delivery data on dams
Dose (mg/kg): 0

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
1101	22	15	15	100.0	100.0	0(0.0)	15	0(0.0)
1102	22	15	15	100.0	93.3	1(7.1)	13	0(0.0)
1103	22	17	16	94.1	93.8	0(0.0)	15	0(0.0)
1104	22	18	18	100.0	100.0	0(0.0)	18	0(0.0)
1105	22	17	16	94.1	100.0	0(0.0)	16	0(0.0)
1106	22	17	16	94.1	100.0	1(6.3)	15	0(0.0)
1107	22	16	15	93.8	93.3	0(0.0)	14	0(0.0)
1108	21	17	16	94.1	100.0	0(0.0)	16	0(0.0)
1109	23	19	18	94.7	83.3	0(0.0)	15	0(0.0)
1110	22	16	16	100.0	100.0	0(0.0)	16	0(0.0)
1111	22	20	20	100.0	95.0	0(0.0)	19	0(0.0)
1112	22	17	16	94.1	93.8	0(0.0)	15	0(0.0)
Total		204	197			2	187	0
Mean	22.0	17.0	16.4	96.6	96.0	(1.1)	15.6	(0.0)
S.D.	0.4	1.5	1.5	3.0	5.1	(2.6)	1.6	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 12-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual delivery data on dams
Dose (mg/kg): 30

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
2101	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
2102	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
2103	22	15	15	100.0	93.3	0(0.0)	14	0(0.0)
2104	22	17	16	94.1	100.0	1(6.3)	15	0(0.0)
2105	22	17	15	88.2	93.3	0(0.0)	14	0(0.0)
2106	22	16	15	93.8	86.7	0(0.0)	13	0(0.0)
2107	22	17	15	88.2	93.3	0(0.0)	14	0(0.0)
2108	22	15	15	100.0	100.0	0(0.0)	15	0(0.0)
2109	22	20	19	95.0	100.0	0(0.0)	19	0(0.0)
2110	22	19	18	94.7	94.4	0(0.0)	17	0(0.0)
2111	22	18	18	100.0	88.9	0(0.0)	16	0(0.0)
2112	22	19	18	94.7	100.0	1(5.6)	17	0(0.0)
Total		205	195			2	184	0
Mean	22.0	17.1	16.3	95.2	95.3	(1.0)	15.3	(0.0)
S.D.	0.0	1.6	1.5	4.2	4.7	(2.3)	1.7	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 12-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual delivery data on dams
Dose (mg/kg): 100

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
3101	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
3102	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
3103	22	14	14	100.0	100.0	0(0.0)	14	0(0.0)
3104	22	15	15	100.0	100.0	0(0.0)	15	0(0.0)
3105	22	18	18	100.0	88.9	0(0.0)	16	0(0.0)
3106	22	16	16	100.0	75.0	0(0.0)	12	0(0.0)
3107	22	16	16	100.0	87.5	0(0.0)	14	0(0.0)
3108	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
3109	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
3110	22	19	18	94.7	94.4	0(0.0)	17	0(0.0)
3111	22	17	16	94.1	93.8	0(0.0)	15	0(0.0)
3112	22	15	15	100.0	93.3	0(0.0)	14	0(0.0)
Total		197	195			0	180	0
Mean	22.0	16.4	16.3	99.1	92.4	(0.0)	15.0	(0.0)
S.D.	0.0	1.4	1.2	2.2	6.6	(0.0)	1.3	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 12-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual delivery data on dams
Dose (mg/kg): 300

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
4101	22	14	8	57.1	100.0	0(0.0)	8	0(0.0)
4102	22	14	14	100.0	100.0	1(7.1)	13	0(0.0)
4103	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
4104	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
4105	22	18	18	100.0	77.8	0(0.0)	14	0(0.0)
4106	22	12	12	100.0	91.7	0(0.0)	11	0(0.0)
4107	22	17	17	100.0	100.0	0(0.0)	17	0(0.0)
4108	22	18	17	94.4	100.0	0(0.0)	17	0(0.0)
4109	21	15	15	100.0	100.0	0(0.0)	15	0(0.0)
4110	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
4111	22	18	18	100.0	94.4	0(0.0)	17	0(0.0)
4112	22	15	14	93.3	100.0	0(0.0)	14	0(0.0)
Total		191	183			1	173	0
Mean	21.9	15.9	15.3	95.4	95.5	(0.6)	14.4	(0.0)
S.D.	0.3	1.9	2.9	12.3	6.4	(2.0)	2.7	(0.0)

a): (No. of implantation sites / No. of corpora lutea)×100
b): (No. of delivered pups / No. of implantation sites)×100
c): (No. of stillborns / No. of delivered pups)×100
d): No. of delivered pups with external abnormalities
e): (No. of delivered pups with external abnormalities / No. of delivered pups)×100

Appendix 13-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 0

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
1101	15	15	100.0	15	15	100.0
1102	13	14	92.9	13	13	100.0
1103	15	15	100.0	15	15	100.0
1104	18	18	100.0	18	15	83.3
1105	16	16	100.0	16	16	100.0
1106	15	16	93.8	15	14	93.3
1107	14	14	100.0	14	14	100.0
1108	16	16	100.0	16	14	87.5
1109	15	15	100.0	15	15	100.0
1110	16	16	100.0	16	15	93.8
1111	19	19	100.0	19	19	100.0
1112	15	15	100.0	15	15	100.0
Total	187	189		187	180	
Mean	15.6	15.8	98.9	15.6	15.0	96.5
S.D.	1.6	1.5	2.6	1.6	1.5	5.8

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 13-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 30

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
2101	15	15	100.0	15	15	100.0
2102	15	15	100.0	15	15	100.0
2103	14	14	100.0	14	14	100.0
2104	15	16	93.8	15	15	100.0
2105	14	14	100.0	14	14	100.0
2106	13	13	100.0	13	13	100.0
2107	14	14	100.0	14	14	100.0
2108	15	15	100.0	15	15	100.0
2109	19	19	100.0	19	18	94.7
2110	17	17	100.0	17	15	88.2
2111	16	16	100.0	16	16	100.0
2112	17	18	94.4	17	16	94.1
Total	184	186		184	180	
Mean	15.3	15.5	99.0	15.3	15.0	98.1
S.D.	1.7	1.8	2.3	1.7	1.3	3.8

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 13-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 100

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
3101	16	16	100.0	16	16	100.0
3102	16	16	100.0	16	16	100.0
3103	14	14	100.0	14	14	100.0
3104	15	15	100.0	15	15	100.0
3105	16	16	100.0	16	16	100.0
3106	12	12	100.0	12	12	100.0
3107	14	14	100.0	14	14	100.0
3108	15	15	100.0	15	15	100.0
3109	16	16	100.0	16	16	100.0
3110	17	17	100.0	17	16	94.1
3111	15	15	100.0	15	0	0.0
3112	14	14	100.0	14	14	100.0
Total	180	180		180	164	
Mean	15.0	15.0	100.0	15.0	13.7	91.2
S.D.	1.3	1.3	0.0	1.3	4.5	28.8

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 13-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 300

Dam number	No. of live-borns	No. of delivered pups	Live birth index % a)	No. of live pups Day 0	No. of live pups Day 4	Viability index on postnatal day 4 % b)
4101	8	8	100.0	8	8	100.0
4102	13	14	92.9	13	13	100.0
4103	16	16	100.0	16	16	100.0
4104	15	15	100.0	15	15	100.0
4105	14	14	100.0	14	13	92.9
4106	11	11	100.0	11	11	100.0
4107	17	17	100.0	17	16	94.1
4108	17	17	100.0	17	16	94.1
4109	15	15	100.0	15	7	46.7
4110	16	16	100.0	16	16	100.0
4111	17	17	100.0	17	0	0.0
4112	14	14	100.0	14	14	100.0
Total	173	174		173	145	
Mean	14.4	14.5	99.4	14.4	12.1	85.7
S.D.	2.7	2.7	2.0	2.7	4.9	30.9

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100

Appendix 14-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 0

Dam number	Liveborns No. of males	Liveborns No. of females	Stillborns No. of males	Stillborns No. of females	Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4 No. of males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
1101	7	8	0	0	0.47	0.47	7	8	0.47
1102	3	10	0	1	0.21	0.23	3	10	0.23
1103	9	6	0	0	0.60	0.60	9	6	0.60
1104	10	8	0	0	0.56	0.56	7	8	0.47
1105	9	7	0	0	0.56	0.56	9	7	0.56
1106	11	4	0	1	0.69	0.73	11	3	0.79
1107	9	5	0	0	0.64	0.64	9	5	0.64
1108	11	5	0	0	0.69	0.69	10	4	0.71
1109	4	11	0	0	0.27	0.27	4	11	0.27
1110	8	8	0	0	0.50	0.50	7	8	0.47
1111	11	8	0	0	0.58	0.58	11	8	0.58
1112	8	7	0	0	0.53	0.53	8	7	0.53
Total	100	87	0	2			95	85	
Mean	8.3	7.3	0.0	0.2	0.53	0.53	7.9	7.1	0.53
S.D.	2.6	2.1	0.0	0.4	0.15	0.15	2.5	2.3	0.16

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 30

Dam number	Liveborns		Stillborns		Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4		Sex ratio of live pups on day 4 c)
	No. of males	No. of females	No. of males	No. of females			No. of males	No. of females	
2101	12	3	0	0	0.80	0.80	12	3	0.80
2102	7	8	0	0	0.47	0.47	7	8	0.47
2103	8	6	0	0	0.57	0.57	8	6	0.57
2104	7	8	0	1	0.44	0.47	7	8	0.47
2105	5	9	0	0	0.36	0.36	5	9	0.36
2106	8	5	0	0	0.62	0.62	8	5	0.62
2107	7	7	0	0	0.50	0.50	7	7	0.50
2108	8	7	0	0	0.53	0.53	8	7	0.53
2109	7	12	0	0	0.37	0.37	7	11	0.39
2110	5	12	0	0	0.29	0.29	3	12	0.20
2111	10	6	0	0	0.63	0.63	10	6	0.63
2112	14	3	0	1	0.78	0.82	13	3	0.81
Total	98	86	0	2			95	85	
Mean	8.2	7.2	0.0	0.2	0.53	0.54	7.9	7.1	0.53
S.D.	2.7	2.9	0.0	0.4	0.16	0.16	2.7	2.8	0.17

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4

Appendix 14-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 100

Dam number	Liveborns No. of males	Liveborns No. of females	Stillborns No. of males	Stillborns No. of females	Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4 No. of males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
3101	11	5	0	0	0.69	0.69	11	5	0.69
3102	6	10	0	0	0.38	0.38	6	10	0.38
3103	8	6	0	0	0.57	0.57	8	6	0.57
3104	3	12	0	0	0.20	0.20	3	12	0.20
3105	5	11	0	0	0.31	0.31	5	11	0.31
3106	4	8	0	0	0.33	0.33	4	8	0.33
3107	5	9	0	0	0.36	0.36	5	9	0.36
3108	8	7	0	0	0.53	0.53	8	7	0.53
3109	8	8	0	0	0.50	0.50	8	8	0.50
3110	7	10	0	0	0.41	0.41	7	9	0.44
3111d)	10	5	0	0	0.67	0.67			
3112	8	6	0	0	0.57	0.57	8	6	0.57
Total	83	97	0	0			73	91	
Mean	6.9	8.1	0.0	0.0	0.46	0.46	6.6	8.3	0.44
S.D.	2.4	2.4	0.0	0.0	0.15	0.15	2.3	2.2	0.14

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4
d): All pups died by postnatal day 2.

Appendix 14-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 300

Dam number	Liveborns No. of males	Liveborns No. of females	Stillborns No. of males	Stillborns No. of females	Sex ratio of delivered pups a)	Sex ratio of liveborns b)	Postnatal day 4 No. of males	Postnatal day 4 No. of females	Sex ratio of live pups on day 4 c)
4101	4	4	0	0	0.50	0.50	4	4	0.50
4102	8	5	0	1	0.57	0.62	8	5	0.62
4103	6	10	0	0	0.38	0.38	6	10	0.38
4104	5	10	0	0	0.33	0.33	5	10	0.33
4105	6	8	0	0	0.43	0.43	5	8	0.38
4106	7	4	0	0	0.64	0.64	7	4	0.64
4107	6	11	0	0	0.35	0.35	6	10	0.38
4108	9	8	0	0	0.53	0.53	9	7	0.56
4109	7	8	0	0	0.47	0.47	1	6	0.14
4110	11	5	0	0	0.69	0.69	11	5	0.69
4111d)	10	7	0	0	0.59	0.59			
4112	7	7	0	0	0.50	0.50	7	7	0.50
Total	86	87	0	1			69	76	
Mean	7.2	7.3	0.0	0.1	0.50	0.50	6.3	6.9	0.47
S.D.	2.0	2.4	0.0	0.3	0.11	0.12	2.6	2.3	0.16

a): No. of delivered males / No. of delivered pups
b): No. of liveborn males / No. of liveborns
c): No. of live males on day 4 / No. of live pups on day 4
d): All pups died by postnatal day 4.

Appendix 15-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 0

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
1101	6.9	10.8	3.9	6.6	10.2	3.6
1102	7.3	10.5	3.2	6.7	10.0	3.3
1103	7.3	11.6	4.3	6.3	10.1	3.8
1104	6.2	9.9	3.7	5.9	9.2	3.3
1105	6.4	9.8	3.4	6.4	9.6	3.2
1106	6.3	10.8	4.5	5.7	10.5	4.8
1107	7.0	10.0	3.0	6.7	9.7	3.0
1108	5.3	8.8	3.5	5.0	8.3	3.3
1109	7.6	12.5	4.9	7.2	11.5	4.3
1110	6.6	9.7	3.1	6.3	9.2	2.9
1111	6.1	9.4	3.3	5.7	8.4	2.7
1112	7.1	10.9	3.8	6.7	10.5	3.8
Mean	6.7	10.4	3.7	6.3	9.8	3.5
S.D.	0.6	1.0	0.6	0.6	0.9	0.6

Unit: g
a): Postnatal day

Appendix 15-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 30

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
2101	6.6	11.3	4.7	6.2	10.9	4.7
2102	6.2	9.7	3.5	6.1	9.5	3.4
2103	6.8	11.4	4.6	6.4	10.5	4.1
2104	6.6	10.5	3.9	6.3	10.5	4.2
2105	7.2	11.1	3.9	6.8	10.4	3.6
2106	6.5	11.2	4.7	6.4	10.3	3.9
2107	7.1	10.4	3.3	6.4	10.1	3.7
2108	6.7	10.6	3.9	6.5	10.6	4.1
2109	6.3	9.2	2.9	5.9	9.0	3.1
2110	5.7	9.5	3.8	6.2	9.6	3.4
2111	6.4	10.7	4.3	6.3	10.0	3.7
2112	6.1	9.2	3.1	6.0	9.2	3.2
Mean	6.5	10.4	3.9	6.3	10.1	3.8
S.D.	0.4	0.8	0.6	0.2	0.6	0.5

Unit: g
a): Postnatal day

Appendix 15-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 100

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
3101	6.3	8.7	2.4	5.9	8.9	3.0
3102	7.0	10.9	3.9	6.3	9.5	3.2
3103	6.7	10.1	3.4	6.3	9.0	2.7
3104	6.8	11.1	4.3	6.7	11.6	4.9
3105	6.6	10.1	3.5	6.5	9.6	3.1
3106	7.5	10.3	2.8	7.3	10.4	3.1
3107	7.3	10.3	3.0	6.9	9.4	2.5
3108	6.9	10.7	3.8	5.9	9.5	3.6
3109	6.4	8.7	2.3	6.2	8.9	2.7
3110	6.3	9.3	3.0	6.1	9.2	3.1
3111b)	5.8			5.6		
3112	6.5	10.7	4.2	6.3	10.3	4.0
Mean	6.7	10.1	3.3	6.3	9.7	3.3
S.D.	0.5	0.8	0.7	0.5	0.8	0.7

Unit: g
a): Postnatal day
b): All pups died by postnatal day 2.

Appendix 15-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 300

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
4101	7.9	13.3	5.4	7.5	12.2	4.7
4102	6.5	10.0	3.5	6.1	9.3	3.2
4103	6.5	9.2	2.7	6.1	8.7	2.6
4104	6.7	11.0	4.3	6.1	10.1	4.0
4105	6.9	11.4	4.5	6.3	10.3	4.0
4106	7.2	11.8	4.6	6.8	11.4	4.6
4107	6.6	10.5	3.9	5.9	9.5	3.6
4108	6.4	9.9	3.5	6.0	9.1	3.1
4109	6.0	9.7	3.7	5.7	9.2	3.5
4110	6.9	10.0	3.1	6.3	9.0	2.7
4111b)	6.0			5.8		
4112	6.4	11.0	4.6	6.1	10.4	4.3
Mean	6.7	10.7	4.0	6.2	9.9	3.7
S.D.	0.5	1.2	0.8	0.5	1.1	0.7

Unit: g
a): Postnatal day
b): All pups died by postnatal day 4.

Appendix 16-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 0

Dam number	No. of pups examined Total (Male + Female)	Findings
1101	0	
1102	1 (0 + 1)	NAF
1103	0	
1104	3 (3 + 0)	NAF
1105	0	
1106	1 (0 + 1)	NAF
1107	0	
1108	0	
1109	0	
1110	1 (1 + 0)	NAF
1111	0	
1112	0	

NAF: No abnormal findings

Appendix 16-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 30

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	0	
2102	0	
2103	0	
2104	1 (0 + 1)	NAF
2105	0	
2106	0	
2107	0	
2108	0	
2109	0	
2110	1 (1 + 0)	NAF
2111	0	
2112	2 (1 + 1)	NAF

NAF: No abnormal findings

Appendix 16-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 100

Dam number	No. of pups examined Total (Male + Female)	Findings
3101	0	
3102	0	
3103	0	
3104	0	
3105	0	
3106	0	
3107	0	
3108	0	
3109	0	
3110	0	
3111	7 (3 + 4)	NAF
3112	0	

NAF: No abnormal findings

Appendix 16-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 300

Dam number	No. of pups examined Total (Male + Female)	Findings
4101	0	
4102	1 (0 + 1)	NAF
4103	0	
4104	0	
4105	1 (1 + 0)	NAF
4106	0	
4107	1 (0 + 1)	NAF
4108	0	
4109	1 (1 + 0)	NAF
4110	0	
4111	13 (7 + 6)	NAF
4112	0	

NAF: No abnormal findings

Appendix 17-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 0

Dam number	No. of pups examined Total (Male + Female)	Findings
1101	15 (7 + 8)	NAF
1102	13 (3 + 10)	NAF
1103	15 (9 + 6)	NAF
1104	15 (7 + 8)	NAF
1105	16 (9 + 7)	NAF
1106	14 (11 + 3)	NAF
1107	14 (9 + 5)	NAF
1108	14 (10 + 4)	NAF
1109	15 (4 + 11)	NAF
1110	15 (7 + 8)	NAF
1111	19 (11 + 8)	NAF
1112	15 (8 + 7)	NAF

NAF: No abnormal findings

Appendix 17-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 30

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	15 (12 + 3)	NAF
2102	15 (7 + 8)	NAF
2103	14 (8 + 6)	NAF
2104	15 (7 + 8)	NAF
2105	14 (5 + 9)	NAF
2106	13 (8 + 5)	NAF
2107	14 (7 + 7)	NAF
2108	15 (8 + 7)	NAF
2109	18 (7 + 11)	NAF
2110	15 (3 + 12)	NAF
2111	16 (10 + 6)	NAF
2112	16 (13 + 3)	NAF

NAF: No abnormal findings

Appendix 17-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 100

Dam number	No. of pups examined Total (Male + Female)	Findings
3101	16 (11 + 5)	NAF
3102	16 (6 + 10)	NAF
3103	14 (8 + 6)	NAF
3104	15 (3 + 12)	NAF
3105	16 (5 + 11)	NAF
3106	12 (4 + 8)	NAF
3107	14 (5 + 9)	NAF
3108	15 (8 + 7)	NAF
3109	16 (8 + 8)	NAF
3110	16 (7 + 9)	NAF
3111a)		
3112	14 (8 + 6)	NAF

NAF: No abnormal findings
a): All pups died by postnatal day 2.

Appendix 17-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 4-tert-butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 300

Dam number	No. of pups examined Total (Male + Female)	Findings
4101	8 (4 + 4)	NAF
4102	13 (8 + 5)	NAF
4103	16 (6 + 10)	NAF
4104	15 (5 + 10)	NAF
4105	13 (5 + 8)	NAF
4106	11 (7 + 4)	NAF
4107	16 (6 + 10)	NAF
4108	16 (9 + 7)	NAF
4109	7 (1 + 6)	NAF
4110	16 (11 + 5)	NAF
4111a)		
4112	14 (7 + 7)	NAF

NAF: No abnormal findings
a): All pups died by postnatal day 4.

信頼性保証書（1/3）

試験番号　：　R-1135

試験表題　：　4-tert-ブチルシクロヘキサン-1-イル=アセタートのラットを用いた経口投与による反復投与毒性・生殖発生毒性併合試験

本試験は以下に示す基準を遵守して実施されたことを保証致します。

- 「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成23年3月31日：薬食発0331第8号、平成23･03･29製局第6号、環保企発第110331010号）

なお、調査は下記の通り実施致しました。

2014年3月28日
株式会社ボゾリサーチセンター
信頼性保証部門 [redacted]

試験における調査

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
試験計画書	[redacted]	2013年　8月30日	2013年　8月30日
作業予定表・コンピュータプロトコール		2013年　9月18日	2013年　9月19日
改善確認		2013年　9月20日	2013年　9月20日
調製・保存（被験物質）		2013年　9月20日	2013年　9月20日
改善確認		2013年　9月24日	2013年　9月24日
被験液の濃度確認		2013年　9月20日	2013年　9月20日
検疫・馴化・群分け		2013年　9月23日	2013年　9月24日

信頼性保証書（2/3）

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
体重・摂餌量測定・投与・一般状態の観察・膣垢検査	[redacted]	2013年　9月24日	2013年　9月24日
詳細な一般状態の観察		2013年　9月25日	2013年　9月25日
試験計画書変更書（1）		2013年 10月　7日	2013年 10月　7日
交配		2013年 10月　9日	2013年 10月　9日
機能検査・握力測定・自発運動量測定		2013年 10月30日	2013年 10月30日
分娩・哺育観察・体重測定		2013年 10月31日	2013年 11月　1日
尿検査（尿量・色調・定性・沈渣）		2013年 11月　1日	2013年 11月　1日
摂水量測定		2013年 11月　2日	2013年 11月　5日
採血・剖検		2013年 11月　5日	2013年 11月　5日
病理組織学検査（切り出し）		2013年 11月12日	2013年 11月13日
被験物質の安定性		2013年 11月25日	2013年 11月25日
試験計画書変更書（2）		2013年 12月18日	2013年 12月18日
免疫組織化学染色標本の作製		2013年 12月18日	2013年 12月18日
生データ（動物の記録、被験物質調製記録、被験液の濃度確認、被験物質の安定性、投与及び一般状態、体重・摂餌量、尿検査（水含む）、膣垢検査、交配、分娩、哺育観察）		2014年　1月22日 2014年　1月23日 2014年　1月28日	2014年　1月29日
改善確認		2014年　1月29日	2014年　1月29日
測定レポート（被験液の濃度確認、被験物質の安定性：案）		2014年　1月28日	2014年　1月29日
最終報告書草案・図・表・付表		2014年　1月24日 2014年　1月25日 2014年　1月27日 2014年　1月28日	2014年　1月29日
改善確認		2014年　1月29日	2014年　1月29日

信頼性保証書（3/3）

項　目	担当者	調　査　日	試験責任者及び運営管理者への報告日
測定レポート（被験液の濃度確認、被験物質の安定性）	[redacted]	2014年　1月29日	2014年　1月29日
生データ（詳細な一般状態の観察記録、機能検査、握力及び自発運動量の測定記録）		2014年　2月24日 2014年　2月25日 2014年　2月26日 2014年　3月20日	2014年　3月20日
改善確認		2014年　3月25日	2014年　3月25日
生データ（被験物質関係、血液・血液化学検査、飼育関係、剖検・病理）		2014年　3月24日 2014年　3月25日	2014年　3月25日
最終報告書		2014年　3月28日	2014年　3月28日

プロセス調査

項　目	試験番号	担当者	調　査　日	試験責任者及び運営管理者への報告日
動物入荷	B-7496	[redacted]	2013年　8月　5日	2013年　8月　5日
検疫	B-7496		2013年　8月　5日	2013年　8月　5日
尿検査（浸透圧・電解質）	R-1114		2013年 10月 17日	2013年 10月 17日
血液学検査・血液化学検査	B-7433		2013年 10月 22日	2013年 10月 23日
病理組織学検査（包埋・薄切・染色）	B-7437		2013年 10月　7日	2013年 10月　7日
	B-7437		2013年 10月　8日	2013年 10月　8日
	B-7014		2013年 10月 11日	2013年 10月 11日