最　終　報　告　書

（改訂版）

2-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-1105

作成日：2013 年 9 月 25 日

試験期間：2012 年 10 月 1 日-2013 年 3 月 28 日

試験施設
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

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

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

1. 目次

1. 目次 2
2. 試験実施概要 7
2.1 試験番号 7
2.2 試験表題 7
2.3 試験目的 7
2.4 試験委託者 7
2.5 試験受託者 7
2.6 試験実施施設 7
2.7 被験物質 7
2.8 試験日程 7
2.9 試験責任者 8
2.10 試験担当者 8
2.11 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 8
2.12 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 8
2.13 資料保存 9
2.14 試験責任者の記名・なつ印 9
3. 要約 10
3.1 反復投与毒性 10
3.2 生殖発生毒性 11
4. 緒言 12
4.1 GLP 12
4.2 毒性試験ガイドライン 12
4.3 動物の福祉 12
5. 試験材料及び方法 13
5.1 被験物質及び媒体 13
5.1.1 被験物質 13
5.1.2 媒体 14
5.2 投与液の調製及び保存方法 14
5.2.1 対照群投与液の採取 14
5.2.2 被験液の調製 15
5.2.3 投与液の保存 15
5.2.4 被験液の安定性 15
5.2.5 被験液の濃度確認 15
5.3 試験動物種及び系統の選択理由 16
5.4 試験動物 17

5.5 飼育条件 17
5.6 動物の識別 18
5.7 投与経路、投与期間及び投与回数並びに回復期間と
それらの選択理由 18
5.8 投与方法 18
5.9 投与量及び群構成 19
5.10 投与量の設定根拠 19
5.11 観察及び検査の方法 20
5.11.1 一般状態の観察 20
5.11.2 詳細な一般状態の観察、機能検査、握力及び自発運動量の測定 20
5.11.3 体重測定 21
5.11.4 摂餌量測定 21
5.11.5 膣垢検査 22
5.11.6 交配方法 22
5.11.7 分娩及び哺育観察 22
5.11.8 尿検査（摂水量測定を含む） 23
5.11.9 血液学検査 24
5.11.10 血液化学検査 25
5.11.11 血中ホルモン測定 26
5.11.12 病理学検査 26
5.12 統計解析 28
5.12.1 パラメータの算出 28
5.12.2 検定 28
6. 試験結果 30
6.1 死亡動物（Appendix 1-16、1-20、1-28~1-30、3-8、3-12、3-18、4-8、
4-12、4-18、9-97、9-100、9-105、9-106、9-110、9-112、9-114） 30
6.2 生存動物の一般状態（Table 1-1~1-11、Appendix 1-1~1-34） 30
6.3 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） 31
6.3.1 ホームケージ内観察（Table 2-1~2-23、Appendix 2-1~2-72） 31
6.3.2 手に持っての観察（Table 2-24~2-46、Appendix 2-73~2-144） 31
6.3.3 オープンフィールド内観察（Table 2-47~2-69、
Appendix 2-145~2-216） 32
6.3.4 機能検査（Table 2-70~2-74、Appendix 2-217~2-230） 32
6.3.5 握力（Table 2-75~2-79、Appendix 2-231~2-244） 32
6.3.6 自発運動量（Fig. 1~5、Table 2-80~2-84、
Appendix 2-245~2-258） 32
6.4 体重（Fig. 6~8、Table 3-1~3-7、Appendix 3-1~3-22） 33

6.5 摂餌量（Fig. 9~11、Table 4-1~4-7、Appendix 4-1~4-22） 33
6.6 尿検査（摂水量測定を含む）（Table 5-1~5-16、Appendix 5-1~5-30） 34
6.7 血液学検査（Table 6-1~6-10、Appendix 6-1~6-28） 34
6.8 血液化学検査（Table 7-1~7-10、Appendix 7-1~7-28） 34
6.9 血中ホルモン測定（Table 7-11~7-15、Appendix 7-29~7-42） 35
6.10 器官重量（Table 8-1~8-10、Appendix 8-1~8-48） 35
6.11 剖検所見（Table 9-1~9-6、Appendix 9-1~9-116） 36
6.12 病理組織学検査（Table 10-1~10-16、Appendix 9-1~9-116） 37
6.13 性周期（Table 11、Appendix 10-1~10-4） 40
6.14 交配成績（Table 12、Appendix 11-1~11-5） 41
6.15 分娩成績（Table 13、Appendix 12-1~12-4）並びに分娩及び哺育状態（Table 1-3 及び 1-4、Appendix 1-9~1-16） 41
6.16 出生児の生存率（Table 14、Appendix 13-1~13-4） 41
6.17 出生児の性比（Table 15、Appendix 14-1~14-4） 41
6.18 出生児の体重（Table 16、Appendix 15-1~15-4） 41
6.19 死亡児の肉眼観察所見（Table 17、Appendix 16-1~16-4） 41
6.20 出生児の生後 4 日肉眼観察所見（Table 18、Appendix 17-1~17-4） 41
7. 考察 42
7.1 反復投与毒性 42
7.2 生殖発生毒性 44
8. 文献 45

添付資料

添付資料 1 試験成績書（2-tert-ブチルシクロヘキサン-1-イル=アセタートの特性） 46
添付資料 2 試験成績書（2-tert-ブチルシクロヘキサン-1-イル=アセタートの安定性） 47
添付資料 3 試験成績書（被験液中 2-tert-ブチルシクロヘキサン-1-イル=アセタートの安定性） 49
添付資料 4 被験液中の被験物質濃度分析結果（初回投与） 50
添付資料 5 被験液中の被験物質濃度分析結果（投与 6 週） 51
添付資料 6 2-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 52

図

Fig. 1~5 自発運動量 53
Fig. 6~8 体重 58
Fig. 9~11 摂餌量 61

表

Table 1-1~1-11 一般状態 64
Table 2-1~2-23 ホームケージ内観察 75
Table 2-24~2-46 手に持っての観察 98
Table 2-47~2-69 オープンフィールド内観察 121
Table 2-70~2-74 機能検査 144
Table 2-75~2-79 握力 149
Table 2-80~2-84 自発運動量 154
Table 3-1~3-7 体重 159
Table 4-1~4-7 摂餌量 166
Table 5-1~5-16 尿検査（含、摂水量） 173
Table 6-1~6-10 血液学検査 189
Table 7-1~7-10 血液化学検査 199
Table 7-11~7-15 血中ホルモン測定 209
Table 8-1~8-10 器官重量 214
Table 9-1~9-8 剖検所見 224
Table 10-1~10-21 病理組織学検査 232
Table 11 性周期 253
Table 12 交配成績 254
Table 13 分娩成績 255
Table 14 出生児の生存率 256
Table 15 出生児の性比 257
Table 16 出生児の体重 258
Table 17 死亡児の肉眼観察所見 259
Table 18 出生児の生後 4 日肉眼観察所見 260

個体別表

Appendix 1-1~1-34 一般状態 261
Appendix 2-1~2-72 ホームケージ内観察 295
Appendix 2-73~2-144 手に持っての観察 367
Appendix 2-145~2-216 オープンフィールド内観察 439
Appendix 2-217~2-230 機能検査 511
Appendix 2-231~2-244 握力 525

Appendix 2-245~2-258　自発運動量.....539
Appendix 3-1~3-22　体重.....553
Appendix 4-1~4-22　摂餌量.....575
Appendix 5-1~5-30　尿検査（含、摂水量）.....597
Appendix 6-1~6-28　血液学検査.....627
Appendix 7-1~7-28　血液化学検査.....655
Appendix 7-29~7-42　血中ホルモン測定.....683
Appendix 8-1~8-48　器官重量.....697
Appendix 9-1~9-116　剖検所見及び病理組織学検査.....745
Appendix 10-1~10-4　性周期.....861
Appendix 11-1~11-4　交配成績.....865
Appendix 12-1~12-4　分娩成績.....869
Appendix 13-1~13-4　出生児の生存率.....873
Appendix 14-1~14-4　出生児の性比.....877
Appendix 15-1~15-4　出生児の体重.....881
Appendix 16-1~16-4　死亡児の肉眼観察所見.....885
Appendix 17-1~17-4　出生児の生後 4 日肉眼観察所見.....889

2.　試験実施概要

2.1　試験番号

R-1105

2.2　試験表題

2-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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats）

2.3　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。

2.4　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

2.5　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

2.6　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

2.7　被験物質

製造者	:	Sigma-Aldrich Co.
名称	:	2-tert-ブチルシクロヘキサン-1-イル=アセタート
英名	:	2-tert-Butylcyclohexan-1-yl acetate
CAS 番号	:	88-41-5
官報公示整理番号	:	3-2356、3-2311、3-2345
入手日	:	2012 年 7 月 17 日

2.8　試験日程

試験開始日	:	2012 年 10 月　1 日
被験物質出庫日	:	2012 年 10 月 16 日

動物入荷日　　：　2012 年 10 月　3 日
実験開始日（投与開始日）
　　：　2012 年 10 月 23 日
交配開始日　　：　2012 年 11 月　6 日
分娩開始日　　：　2012 年 11 月 28 日
母動物剖検開始日　：　2012 年 12 月　3 日
投与終了剖検日　　：　2012 年 12 月　4 日　（雄及び非交配群雌）
回復開始日　　：　2012 年 12 月　4 日
回復終了剖検日　　：　2012 年 12 月 18 日
動物試験終了日　　：　2012 年 12 月 18 日
実験終了日（病理組織学検査終了日）
　　：　2013 年　2 月 20 日
試験終了日　　：　2013 年　3 月 28 日

2.9　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

■ ■　■

2.10　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　　：　■ ■ ■ ■

2.11　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

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

2.12　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)　交配

50 及び 500 mg/kg 投与群の各 1 例（動物番号 2104 及び 4107）の交尾確認において、腟栓形成あるいは腟垢中の精子が確認できなかったため交尾不成立とした。しかし、投与 37 日に腹部が膨らみ、妊娠が確認された（妊娠 20 日に相当）。交配期間中の性周期から 2 例とも交配 2 日を妊娠 0 日として、妊娠 20 日以降の観察、測定及び検査を実施した。これら 2 例の交配期間から分娩前のデータは参考値とし、統計解析から除外した。交尾が確認できなかった動物は 50 及び 500 mg/kg 投与群の雌各 1 例であり、

他の動物で十分評価が可能な例数を確保できていることから、試験の信頼性に及ぼす影響はないと判断した。

2) 一般状態の観察

投与 12 日の投与後の一般状態観察において、50 及び 500 mg/kg 投与群の観察を試験計画書の規定時間（投与 1~3 時間後）より 4 及び 7 分早く開始してしまった。しかし、観察時間のずれによる一般状態変化の見落としはなかったので、試験の信頼性に及ぼす影響はないと判断した。

3) 病理組織学検査

動物番号 3107 で上皮小体（両側）が標本上確認できず、欠臓器となった。しかし、高用量群の上皮小体に異常がみられなかったことから、中及び低用量群は検査対象外であり、試験の評価上問題はなかった。従って、試験の信頼性に及ぼす影響はないと判断した。

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。

2.13 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、試験計画書原本（試験計画書変更書を含む）、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 日出生児については、出生率及び生後 4 日生存率に被験物質投与の影響が認められなかったため試験終了までに廃棄した。

2.14 試験責任者の記名・なつ印

[redacted]　　2013 年 9 月 25 日 [redacted]

3. 要約

2-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希釈し、50、150 及び 500 mg/kg の投与量で Sprague-Dawley 系 SPF ラットの雄（12 匹/群）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（12 匹/群）には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌（対照群及び 1000 mg/kg：10 匹/群）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、対照群及び 500 mg/kg 群の一部の動物（交配群雄各 5 匹と非交配群雌 5 及び 3 匹）については、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。

3.1 反復投与毒性

500 mg/kg 投与群の交配群雌 4 例と非交配群雌 3 例が急死した。生存動物では、500 mg/kg 投与群の雌雄で流涎及びあるいは間代性痙攣がみられた。500 mg/kg 投与群の雄で体重増加の抑制傾向、交配群雌で妊娠期間中に体重増加の抑制、雌雄の 500 mg/kg 投与群で投与初期に摂餌量の低値、雄の 500 mg/kg 投与群で摂水量及び尿量の高値傾向に伴い尿浸透圧の低値傾向、ナトリウム及びカリウム排泄量の高値傾向並びに塩素排出量の高値、グルコースの低値、非交配群雌の 500 mg/kg 投与群で赤血球数の低値、雄及び非交配群雌の 500 mg/kg 投与群で総胆汁酸の低値が認められた。肝臓で雄の 50 mg/kg 以上の投与群で絶対及び相対重量の高値、交配群雌の 150 mg/kg 投与群で相対重量の高値、交配群雌及び非交配群雌の 500 mg/kg 投与群で絶対及び相対重量の高値が認められ、雄の 150 mg/kg 投与群で大型化、雄と交配群雌の 150 mg/kg 以上の投与群及び非交配群雌の 500 mg/kg 投与群で小葉中心性の肝細胞肥大がみられた。甲状腺で非交配群雌の 500 mg/kg 投与群で絶対及び相対重量の高値、雄の 150 mg/kg 以上の投与群及び交配群雌と非交配群雌の 500 mg/kg 投与群でろ胞上皮細胞の肥大がみられた。腎臓で雄の 50 及び 150 mg/kg 投与群で相対重量の高値、500 mg/kg 投与群で絶対及び相対重量の高値が認められ、雄の 150 mg/kg 以上の投与群で大型化、雄の 50 mg/kg 以上の投与群で尿細管上皮細胞の好酸性小体、150 mg/kg 以上の投与群で再生尿細管、500 mg/kg 投与群で尿細管の拡張、顆粒円柱及び間質の細胞浸潤がみられた。なお、交配群雌の 150 mg/kg 以上の投与群で腎臓の相対重量の高値が認められたが、組織学的に異常はなかった。副腎で交配群雌の 150 mg/kg 以上の投与群で相対重量の高値、500 mg/kg 投与群で絶対及び相対重量の高値、交配群雌及び非交配群雌の 500 mg/kg 投与群で皮質細胞の空胞化がみられた。胸腺で交配群雌及び非交配群雌の 500 mg/kg 投与群で絶対及び相対重量の低値が認められた。

これら変化のうち、腎臓の再生尿細管、顆粒円柱、尿量の高値と塩素排出量の高値を除き 14 日間の回復により減弱又は消失し、回復性が認められた。

3.2　生殖発生毒性

雌雄動物に被験物質投与の影響は認められなかったが、500 mg/kg 投与群で出生児の生後 0~4 日の体重増加量に低値傾向がみられた。

これらの結果から、50 mg/kg 以上の投与群で肝臓（雄）及び腎臓（雄）、150 mg/kg 以上の投与群で肝臓（雌）、腎臓（雌）、甲状腺（雄）、副腎（雌）がみられたことから、反復投与毒性に対する無影響量及び無毒性量は雄で 50 mg/kg 未満、雌で 50 mg/kg と判断した。親動物には被験物質投与による影響は認められなかったが、500 mg/kg 投与群で児の生後 0~4 日の体重増加量に低値傾向がみられことから、雌雄親動物の生殖能力に対する無影響量及び無毒性量は雌雄で 500 mg/kg、児動物における無影響量及び無毒性量はいずれも 150 mg/kg と判断した。

4.　緒言

厚生労働省　医薬食品局　審査管理課　化学物質安全対策室の委託により、2-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、本試験は動物実験委員会の承認を受けている。

4.1　GLP

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

4.2　毒性試験ガイドライン

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

4.3　動物の福祉

- 「動物の愛護及び管理に関する法律」
  （昭和 48 年 10 月 1 日法律第 105 号、最終改正：平成 23 年 8 月 30 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）

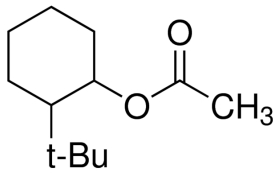
5. 試験材料及び方法

5.1 被験物質及び媒体

5.1.1 被験物質

2-tert-ブチルシクロヘキサン-1-イル=アセタートは[redacted]から以下の情報とともに購入した。また、試験開始前に赤外吸収スペクトルの測定により特性が確認されている（試験番号：A-2516、添付資料 1）。

製造者	:	[redacted]
名称	:	2-tert-ブチルシクロヘキサン-1-イル=アセタート
英名	:	2-tert-Butylcyclohexan-1-yl acetate
製品名	:	o-tert-酢酸ブチルシクロヘキシル、異性体混合物
製品名（英名）	:	o-tert-Butylcyclohexyl acetate, mixture of isomers
CAS 番号	:	88-41-5
官報公示整理番号	:	3-2356、3-2311、3-2345
構造式又は示性式	:	



分子式	:	$(CH_3)_3CC_6H_{10}OC(O)CH_3$
分子量	:	198.30
常温における性状（外観）	:	無色透明液体
沸点	:	221°C*
引火点	:	90°C*
ロット番号	:	02404AA-209
純度（異性体混合物）（GC）	:	99.4%
組成比	:	不明
酸価	:	0.1 mL
ヒ素	:	1 ppm
カドミウム	:	1 ppm
水銀	:	1 ppm
鉛	:	1 ppm
比重	:	0.940 g/cm^3
屈折率（20°C）	:	1.453
赤外線スペクトル	:	適合

入手量	:	2 kg（関連試験を含む）
保存条件	:	密栓、冷所
保存方法	:	気密容器に入れ冷蔵庫内（許容値：1~10°C、実測値：2~8°C）に保存した。
保存場所	:	御殿場研究所被験物質保存室、第 3 研究棟 2 階被験物質調製室及び生化学部標準物質保存場所
安定性	:	投与期間終了後に株式会社ボゾリサーチセンター御殿場研究所において、残余被験物質の赤外吸収スペクトルを確認した結果、実験実施前に確認した参照スペクトルとほぼ同様であり安定性に問題はなかった（添付資料 2）。
取扱い上の注意	:	作業場の換気を十分に行い、マスク、保護眼鏡、保護手袋等の適切な保護具を着用し、直接の接触を防ぐ。取り扱い後は、手、顔等を良く洗い、うがいをする。
残余被験物質の処理	:	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。

*：製造元のシグマアルドリッチジャパン株式会社発行の製品安全データシートに基づく

5.1.2 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	:	WEN1861 及び LAE4488
有効期限	:	WEN1861；2017 年 5 月 10 日、6 月 12 日、8 月 6 日 LAE4488；2017 年 2 月 9 日、8 月 6 日
保存方法	:	室温
保存場所	:	御殿場研究所第 3 研究棟 2 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-2516）[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。

5.2 投与液の調製及び保存方法

5.2.1 対照群投与液の採取

対照群投与液は、被験液調製当日の被験物質を取り扱う前に必要量の媒体を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。

5.2.2　被験液の調製

被験液の調製は先ず、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。次に、媒体をメスシリンダーに加え規定量にメスアップし、10、30 及び 100 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。

5.2.3　投与液の保存

投与液は、褐色ガラス瓶に入れて冷所（冷蔵庫内、許容値 : 1~10°C、実測値 : 3~7°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。

5.2.4　被験液の安定性

本被験物質の 1 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、その後室温で 24 時間安定であることが株式会社ボゾリサーチセンターで確認されている（試験番号：A-2516、添付資料 3）[1]。

5.2.5　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 101.0~106.0%であり、いずれも許容範囲内（濃度：表示値に対する割合；100.0±10.0%）であった（添付資料 4、5）ことから、被験液の調製に問題はなかったと考えられた。なお、GC を用いた被験液中濃度測定法バリデーションは株式会社ボゾリサーチセンター御殿場研究所（試験番号：A-2516）[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	:	2-tert-ブチルシクロヘキサン-1-イル＝アセタート
ロット番号	:	02404AA-209
保存方法	:	冷所（冷蔵庫内；許容値 : 1~10°C、実測値 : 3~8°C）、密栓
保存場所	:	御殿場研究所被験物質保存室、第 3 研究棟 2 階被験物質調製室及び生化学部標準物質保存場所

[測定実測試料の調製]

被験液の任意の場所から n=1 で採取し、以下の表に従い、測定実測試料を用時調製した。

被験液濃度 (mg/mL)	溶解		希釈		希釈率
	採取量 (mL)	定容量 (mL)	採取量 (mL)	定容量 (mL)	
10	1	20	2	20	200
30	1	30	2.5	50	600
100	1	100	2.5	50	2000

溶媒：アセトン

[GC システム]

GC : HP6890N（Agilent Technologies Inc.）
インジェクタ : G2613A（Agilent Technologies Inc.）
オートサンプラトレイ
: G2614A（Agilent Technologies Inc.）
データ処理ソフト : GC ChemStation G2070AJ（Agilent Technologies Inc.）

[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
H2 流量 : 45 mL/min
Air 流量 : 450 mL/min
メイクアップガス（N2）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

5.3 試験動物種及び系統の選択理由

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

であることから選択した。

5.4　試験動物

Sprague-Dawley 系 SPF ラット〔Crl:CD(SD)、日本チャールス・リバー株式会社、厚木飼育センター〕の雄 62 匹及び雌 83 匹をそれぞれ 8 週齢で入手[注]し、入荷日を馴化 1 日と起算して、3 日間の検疫期間を含む 20 日間の馴化飼育を行った。その間に一般状態の観察（1 回/日）、体重測定（馴化 1、3、8、13 及び 20 日の 5 回）、詳細な一般状態の観察（群分け 4 日前の馴化 16 日に 1 回）を行った。更に、雄は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行った。また、雌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 4 例（耳標番号：268、272、312 及び 321）にみられ、背部の掻創（外傷）が雄 1 例（耳標番号：133）、粗毛が雌 1 例（耳標番号：268）にみられた。それらの異常例を除き、検疫・馴化期間中の一般状態、詳細な一般状態、体重推移、精巣の触診結果及び性周期に異常がなく、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 匹と雌 79 匹中 68 匹を選択し、それぞれ 10 週齢で投与に使用した。投与開始時（10 週齢）の体重の変動範囲は雄で 353~465 g（平均体重：391g）、雌で 226~280g（平均体重：251g）であり、雌雄それぞれ平均体重の±20%以内であった。

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

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

5.5　飼育条件

動物は、温度 23±3°C（実測値：22~23°C）、相対湿度 50±20%（実測値：41~61%）、換気回数 12~17 回/時間、照明 12 時間/日（07:00~19:00）の動物飼育室（飼育室番号：3112 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）に個別に収容した。なお、交配中は雌雄各 1 匹収容した。また、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：2012-2）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：

120815）をステンレス製給餌器により自由に摂取させた。

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

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

5.6　動物の識別

動物は番号（雄：101~162、雌：248~330）が刻印された耳標を入荷時に装着し、個体識別を行った。群分け後は、1000 の位は群（対照群、低、中及び高用量の順）、100 の位は性別（0 番を雄、1 番を雌）、10 と 1 の位は個体番号を示す 4 桁の動物番号を設定した。各飼育ケージに投与量（群）ごとに色分けしたケージラベルを付け、試験番号、投与経路、投与量、性別、動物番号、耳標番号、剖検予定日（雄及び非交配群雌）、交尾成立日（交配群の雌雄）及び分娩日（交配群雌）を明記した。

5.7　投与経路、投与期間及び投与回数並びに回復期間とそれらの選択理由

投与経路は毒性試験法ガイドラインに準じ、経口投与を選択した。投与期間は交配群雌雄ともに交配前 14 日、更に、雄は交配開始後 28 日（計 42 日）、交配群雌は交配期間及び妊娠期間を通して授乳 4 日まで（計 41~46 日）、非交配群雌は 42 日、不妊であった 25 日未分娩動物（動物番号 1106）は 40 日であった。投与回数は反復投与試験で一般的に行われている 1 日 1 回とした。回復動物は 42 日の投与期間終了後、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。

5.8　投与方法

投与方法はげっ歯類の経口投与に際して一般的な強制経口投与とした。投与容量は 5 mL/kg 体重とし、胃ゾンデを用いて投与液を 08:51~12:28 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、14:24~15:43 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。

5.9　投与量及び群構成

投与量は 50、150 及び 500 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 番以降の各 5 匹並びに非交配群雌の群内番号 18 番以降の各 5 匹（高用量群は投与期間中に 2 匹が死亡し、3 匹となった）は、最終投与終了日以降回復動物とした。群構成を表 1-1.及び 1-2.に示した。

表 1-1.群構成表（雄）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群	
				動物数	動物番号
対照群	0	0	5	12	1001~1012 注 1
低用量群	50	10	5	12	2001~2012
中用量群	150	30	5	12	3001~3012
高用量群	500	100	5	12	4001~4012 注 1

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

表 1-2.群構成表（雌）

試験群	投与量 (mg/kg)	被験液濃度 (mg/mL)	投与容量 (mL/kg)	交配群		非交配群	
				動物数	動物番号	動物数	動物番号
対照群	0	0	5	12	1101~1112	10	1113~1122 注 2
低用量群	50	10	5	12	2101~2112	−	−
中用量群	150	30	5	12	3101~3112	−	−
高用量群	500	100	5	12	4101~4112	10	4113~4122 注 2

注 2：群内番号 18 番以降の 5 あるいは 3 匹（高用量群で投与期間中に死亡発現による）は、最終投与終了日以降回復動物とした。

5.10　投与量の設定根拠

本試験の投与量は、先に実施した「2-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-R036、投与量：250、500 及び 1000 mg/kg/day」[2]の結果（添付資料 6）を参考に設定した。投与量設定試験では、1000 mg/kg 投与群で雌全例が死亡し、雄で糞量の減少及び流涎、投与初期に体重の減少及び摂餌量の低値、体重増加の抑制、総たん白質の高値、肝臓及び腎臓の絶対及び相対重量の高値が認められた。500 mg/kg 投与群では、雌で強直性痙攣、流涎あるいは糞量の減少、雌雄で投与初期に摂餌量の低値、雄で投与期間中に体重増加の抑制、雌で投与初期に体重増加の抑制、また、雄で肝臓の相対重量の高値、腎臓の絶対及び相対重量の高値、雌でヘモグロビン量の低値、肝臓、副腎の絶対及び相対重量の高値、甲状腺の相対重量の高値が認められた。250 mg/kg 投与群では、雌で投与初期に摂餌量の低値、雄で肝臓の相対重量の高値が認められた。これらのことから、本試験では明らかな毒性兆候が予想される 500 mg/kg を高用量とし、以下公比約 3 で除して 150 及び 50 mg/kg をそれぞれ中及び低用量に設定した。

5.11　観察及び検査の方法

試験日の起算は投与開始日を投与 1 日、投与 1 日から 7 日を投与 1 週、回復開始日（投与 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。

死亡動物は、発見後体重を測定し、速やかに病理学検査に供した。

5.11.1　一般状態の観察

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

5.11.2　詳細な一般状態の観察、機能検査、握力及び自発運動量の測定

詳細な一般状態の観察は全個体について、投与開始前（馴化期間中）に 1 回行った。また、雄及び非交配群雌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、分娩動物は授乳 4 日）にそれぞれ行った。

なお、交尾が成立していた動物番号 2104 及び 4107 は交尾確認時に腟栓形成あるいは腟垢中に精子を確認できず、未交尾動物と判断していたため、交配開始後 7（実施は観察もれのため 1 日遅延）及び 13 日に詳細な一般状態観察を実施した。また、妊娠期間中は妊娠 21 日のみ同検査を実施した。これらの値はいずれも参考データとした。

機能検査、握力測定及び自発運動量の測定は、各群の 5 匹[注1]（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2]、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雌で授乳 4 日（投与 41~44 日）に、その他は投与 6 週（投与 38 日）に、回復期間中は回復 2 週（回復 10 日）に行った。

上記の観察、検査及び測定は、動物をランダムに配置し、観察者に対して投与量などの情報を制限（ブラインド化）した状態で行った。ただし、自発運動量の測定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 1：　投与期間中に非交配群雌の高用量群で 2 匹が死亡し、検査動物数は 3 匹であった。
注 2：　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、1103、1105、1111
低用量群	2104、2105、2106、2108、2111
中用量群	3104、3105、3106、3110、3111
高用量群	4102、4104、4105、4107、4108

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。

5.11.3 体重測定

全個体について、馴化 1、3、8、13 及び 20 日に体重を測定した。雄及び非交配群雌は投与 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、交配群雌は投与 1、8、15、22 日（投与 22 日は動物番号 2104 及び 4107 のみ）、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（13:36~17:23 の間）を除き、体重測定は測定日の 08:00~11:07 の間（投与期間中は投与前）に行った。剖検日は前日から約 16 時間絶食させた後、相対器官重量算出に備えて体重を 07:54~08:51 の間に測定した。また、搬出前に測定した不妊であった妊娠 25 日未分娩動物の体重､死亡動物及び全哺育児が死亡した母動物の剖検日体重は、いずれも統計解析から除外した。

5.11.4 摂餌量測定

雄及び非交配群雌は投与 2、8、15、30、36 及び 42 日に、回復動物は更に回復 1、8 及び 14 日に、交配群雌は投与 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 08:21~11:19 の間（投与期間中は投与前）に行った。ただし、交配期間中は測定を行わなかった。

5.11.5　腟垢検査

馴化期間中は雌全個体について、検疫期間終了後から群分け日まで毎日（午前）腟垢を採取し、性周期異常を調べ、性周期異常動物は群分けから除外した。

交配群雌の投与期間中は全個体について、投与開始日から交尾成立まで毎日（午前）腟垢を採取した。交配前投与期間中の標本は、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。交配期間中の標本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。

非交配群雌は、投与期間終了時及び回復期間終了時の剖検 6 日前から剖検日まで毎日（午前）腟垢を採取し、鏡検した。鏡検結果は、剖検時における性周期ステージの判別のための参考データとした。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。

5.11.6　交配方法

交配前投与期間終了後、交配群の同じ投与群の雌雄を 1:1 で終夜同居させ、翌朝、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 5 日間[注]であった。なお、高用量群の雌 1 匹（動物番号 4112）が投与 10 日に死亡したため、高用量群の雄 1 匹（動物番号 4012）は無処置動物（耳標番号 249）と同居させた。無処置動物の雌より得られたデータは雄の交尾率及び授精率の算出に用いた。なお、低及び高用量群の雌各 1 匹（動物番号 2104 及び 4107）は交尾確認時に腟栓形成あるいは腟垢中に精子を確認できず、未交尾動物と判断していたため、交配期間終了日を妊娠 0 日と仮定して一般状態の観察、体重・摂餌量測定及び投与を継続した。これら動物の妊娠期間中のデータは統計解析から除外した。

注：交尾が確認できなかった動物番号 2104 及び 4107 を除く。

5.11.7　分娩及び哺育観察

1)　母動物の観察

交尾の確認された雌動物は、妊娠 21 日から妊娠 25 日の午前まで 1 日 2 回（午前・午後、妊娠 25 日は午前に 1 回）分娩の有無並びにその終了を確認するとともに分娩状態の異常の有無（胎盤及び羊膜の処理の有無など）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、哺育状態（児集め、営巣及び授乳など）を観察し、授乳 5 日に病理学検査に供した。なお、妊娠 25 日の午前までに分娩が終了しなかった対照群の 1 例（動物番号 1106）は、イソフルラン麻酔下で採血後、腹大動脈切断により放血致死させ、病理学検査に供した。妊娠の有無を確

認した結果、着床が認められなかったため不妊とみなし、妊娠期間中のデータは統計解析より除外した。また、授乳期間中に全哺育児が死亡した対照群の母動物（動物番号 1107）は、その時点で同様に検査を行った。

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。出産児の外表異常[注]の有無を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。

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

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

5.11.8 尿検査（摂水量測定を含む）

検査は投与期間終了週（投与 6 週、投与 36~37 日）及び回復期間終了週（回復 2 週、回復 8~9 日）に行った。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、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）

5.11.9　血液学検査

全例について、剖検前日（最終投与日あるいは回復 14 日）から一夜（16~21 時間）絶食させた。そのうちの各群雌雄各 5 匹注 1（動物番号が若い順、ただし、交配群雌は分娩順の 5 匹注 2）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（設定：3,100 rpm、1,690×g、12 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。不妊であった妊娠 25 日未分娩動物及び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。

動物番号 4001 の表 3.-1)に記載した項目の測定において、試料のサンプリング途中で吸引不良を起こし、正常な測定が行われなかった（エラー表示が示された）ことから、再測定を実施し、再測定値を採用した。

注 1：　非交配群雌の高用量群は、投与 6 週検査で 4 匹、回復 2 週検査で 3 匹であった。
注 2：　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、1103、1105、1111
低用量群	2104、2105、2106、2108、2111
中用量群	3104、3105、3106、3110、3111
高用量群	4102、4104、4105、4107、4108

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)		

5.11.10　血液化学検査

血液学検査用試料と同時に採取した血液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（設定：3,100 rpm、1,690×g、12 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（設定：3,100 rpm、1,690×g、12 分間）して得られた血漿について表 4.-2)に記載の項目及び方法により検査した。妊娠 25 日未分娩動物及び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（妊娠 25 日未分娩動物及び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用に約 0.5 mL×3 本をサンプルチューブに分注し、残余の血清と共に−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）		

5.11.11　血中ホルモン測定

血液化学検査用試料採取時に分注した血中ホルモン測定用の血清について、表 5.に記載の項目及び方法により検査した。

表 5.血中ホルモン測定の項目、測定法及び使用機器など

検査項目	測定方法	単位
T_3	CLEIA 法 a)	ng/dL
T_4	CLEIA 法 a)	μg/dL
TSH	CLEIA 法 a)	ng/mL
使用測定機器 a)　：全自動免疫化学発光測定システム IMMULYZE（Siemens Healthcare Diagnostics Inc., Illinois, USA）		

5.11.12　病理学検査

1)　剖検及び器官重量測定

最終投与翌日及び回復期間終了日に全ての生存動物について、採血した動物は採血後に、その他の動物はイソフルラン麻酔下で腹大動脈切断により放血致死させ、それぞれ体外表並びに頭部、胸部及び腹部の器官・組織の肉眼検査を行った。不妊であっ

た妊娠 25 日未分娩動物及び授乳期間中に全哺育児が死亡した母動物は、採血して放血致死させた後、死亡動物は発見後、それぞれ速やかに病理学検査に供した。なお、母動物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、死亡動物、不妊であった妊娠 25 日未分娩動物及び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。肺は固定時にリン酸緩衝 10 vol%ホルマリン液を注入した。ただし、眼球、視神経はリン酸緩衝液で調製した 3 vol%グルタルアルデヒド・2.5 vol%ホルマリン液で固定後、精巣及び精巣上体はブアン液で固定した後、リン酸緩衝 10 vol%ホルマリン液に置換し保存した。次いで、パラフィン包埋した後、切片とし（下線を施した器官・組織は固定・保存のみとした）、ヘマトキシリン・エオジン（H・E）染色標本を作製した。鏡検は、まず投与終了時剖検群における対照群及び高用量群の採血を行った動物、死亡動物、不妊であった妊娠 25 日未分娩動物及びその交配相手雄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、大腿骨（骨髄を含む）及び大腿部骨格筋は片側、精巣、卵巣、精巣上体及び精嚢（凝固腺含む）は両側並びに子宮は両角部を鏡検した。なお、舌下腺及び視神経は H･E 染色標本作製までとし、病理組織学検査は実施しなかった。その結果、高用量群の雌雄の肝臓及び甲状腺、雄の腎臓、雌の副腎で被験物質投与の影響が疑われたため、中及び低用量群の採血を行った動物並びに回復動物の当該器官についても、回復終了時剖検群の肉眼的異常部位（動物番号 1118、1122 及び 4119 の胃、動物番号 4120 の腎臓）とともに鏡検を行った。

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

（回復終了時剖検群は鏡検を実施）

更に、雄の高用量群で尿細管上皮細胞の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及び PAS 染色標本を作製し、鏡検した。

5.12　統計解析

5.12.1　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

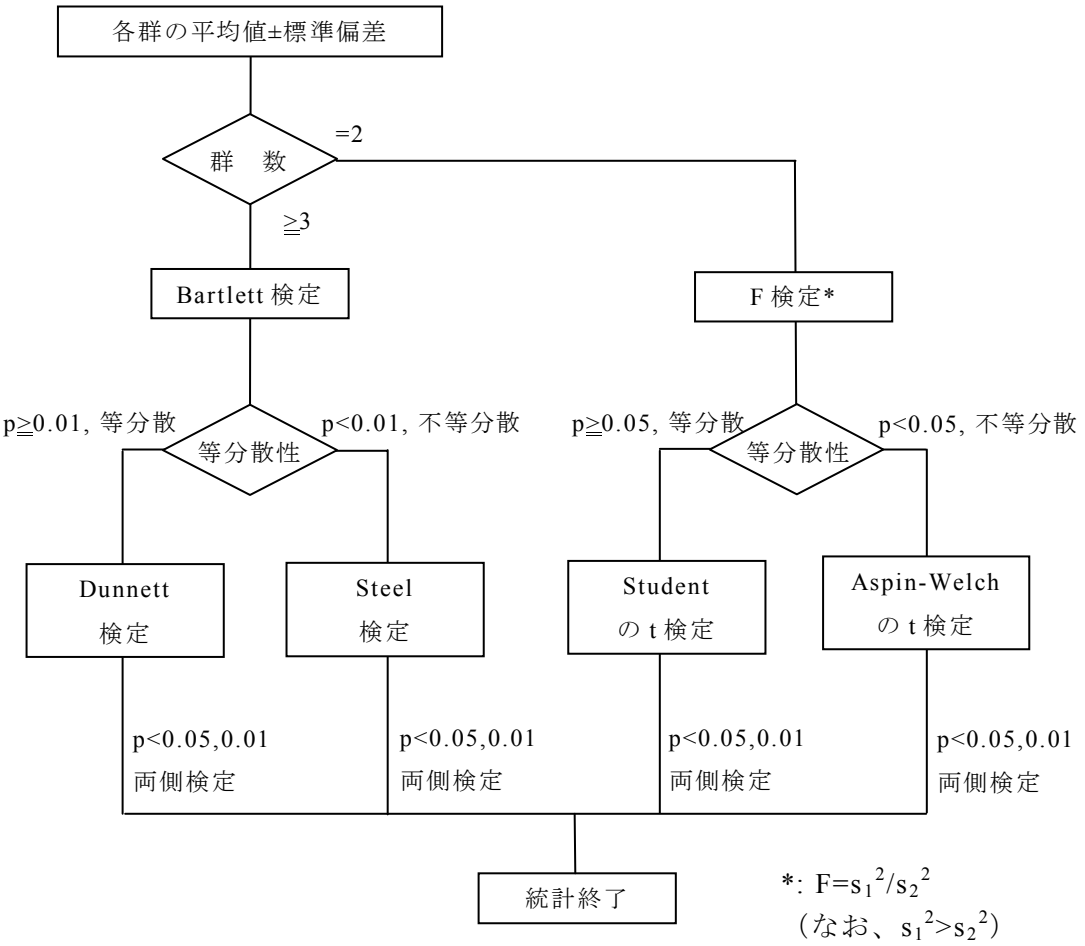
5.12.2　検定

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

体重、体重増加量（雄及び非交配群雌：投与 1~42 日及び回復 1~14 日、交配群雌：投与 1~15 日、妊娠 0~20 日及び授乳 0~4 日、出生児：生後 0~4 日）、摂餌量、摂水量、発情期像発現回数、性周期（発情周期）、交尾までに要した日数、妊娠期間、黄体数、着床痕数、生存児数、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、血中ホルモン及び器官重量（含、剖検時体重）は、群ごとに平均値及び標準偏差を求め、次に示す模式図の方法に従って検定した

[3][4][5]。

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



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

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[6]。

6. 試験結果

6.1 死亡動物（Appendix 1-16、1-20、1-28~1-30、3-8、3-12、3-18、4-8、4-12、4-18、9-97、9-100、9-105、9-106、9-110、9-112、9-114）

500 mg/kg 投与群の交配群雌で交配前投与 10 日、妊娠 12、13、及び 17 日に各 1 例、非交配群雌で投与 15 日に 2 例、投与 29 日に 1 例の計 7 例が死亡した。

個体毎の死亡前の状態、主な剖検所見及び病理組織学検査所見を下表に示した。

動物番号	発現日	瀕死/死亡前の状態、主な剖検所見及び病理組織学検査所見
4103 (交配群)	妊娠 13 日	妊娠 7 日から死亡まで体重増加の抑制（+7g の増加）がみられ、妊娠 13 日の投与前に死亡を発見した。肉眼的に異常はなかったが、組織学的に副腎の束状帯細胞の肥大（軽微）、肝臓の小葉中心性の肝細胞肥大（軽度）、脾臓の白脾髄の萎縮（軽度）が観察された。
4106 (交配群)	妊娠 17 日	妊娠 14 日から死亡まで体重増加の抑制（+1g の増加）がみられ、妊娠 17 日の投与前に死亡を発見した。肉眼的に異常はなかったが、組織学的に副腎の束状帯細胞の肥大（軽微）、肝臓の小葉中心性の肝細胞肥大（軽微）、顎下腺のび漫性の腺房細胞の萎縮（軽微）、脾臓の白脾髄の萎縮（軽度）が観察された。
4111 (交配群)	妊娠 12 日	死亡時までの一般状態及び体重増加に異常はなかったが、妊娠 12 日の投与後 4 時間に間代性痙攣及び流涎を呈し、死亡した。肉眼的に異常はなかったが、組織学的に副腎の束状帯細胞の肥大（軽微）、肝臓の小葉中心性の肝細胞肥大（軽微）、顎下腺のび漫性の腺房細胞の萎縮（軽微）が観察された。
4112 (交配群)	投与 10 日	死亡時までの一般状態及び体重増加に異常はなかったが、投与 10 日の詳細な一般状態の観察時に間代性痙攣を呈し、死亡した。肉眼的に異常はなかったが、組織学的に副腎の束状帯細胞の肥大（軽微）が観察された。
4116 (非交配群)	投与 15 日	死亡時までの体重増加に異常はなかったが、投与 11 及び 12 日の投与後 1~3 時間の間に流涎、投与 15 日の投与後約 5 時間（交配時）に死亡を発見した。肉眼的に結腸に暗赤色巣、組織学的に小脳（橋）の出血（第 4 脳室、軽微）、大脳の出血（第 3 脳室、側脳室、中脳水道、軽度）、結腸の出血（粘膜から粘膜下組織、壊死と炎症を伴う）、顎下腺のび漫性の腺房細胞の萎縮（軽微）が観察された。
4118 (非交配群)	投与 15 日	死亡時までの体重増加に異常はなかったが、投与 12~15 日の投与後 1~3 時間の間に流涎、投与 15 日の投与後約 5 時間に死亡を発見した。肉眼的に異常はなかったが、組織学的に大脳の出血（第 3 脳室、第 4 脳室、新鮮、軽度）、肝臓の小葉中心性の肝細胞肥大（軽微）、顎下腺のび漫性の腺房細胞の萎縮（軽微）が観察された。
4120 (非交配群)	投与 29 日	死亡時までの一般状態及び体重増加に異常はなかったが、投与 29 日の投与前に死亡を発見した。肉眼的に右腎臓に暗赤色巣、組織学的に腎臓の出血（間質、新鮮、片側、軽微）、肝臓の小葉中心性の肝細胞肥大（軽度）、顎下腺のび漫性の腺房細胞の萎縮（軽微）が観察された。

6.2 生存動物の一般状態（Table 1-1~1-11、Appendix 1-1~1-34）

1) 投与期間

500 mg/kg 投与群の雄 4 例で流涎、交配群雌及び非交配群雌の各 3 例で流涎及びあるいは間代性痙攣がみられた。

性	動物番号	症状	発現日
雄	4002	流涎	投与 11 及び 12 日の投与後 1~3 時間
	4005	流涎	投与 13 日の投与後 1~3 時間
	4007	流涎	投与 12 及び 14 日の投与後 1~3 時間
	4008	流涎	投与 11 及び 12 日の投与後 1~3 時間
雌	4102 (交配群)	流涎 間代性痙攣	妊娠 13 日の投与後 1~3 時間 妊娠 13 日の投与後 1~3 時間
	4104 (交配群)	流涎 間代性痙攣	投与 11~13 日及び妊娠 13 日の投与後 1~3 時間 妊娠 13 日の投与後 1~3 時間
	4105 (交配群)	流涎 間代性痙攣	投与 12 及び 13 日の投与後 1~3 時間 妊娠 18 日の投与後 1~3 時間
	4113 (非交配群)	流涎 間代性痙攣	投与 15 及び 29 日の投与後 1~3 時間 投与 15 日の投与後 1~3 時間
	4114 (非交配群)	流涎	投与 18 日の投与後 1~3 時間
	4119 (非交配群)	流涎 間代性痙攣	投与 13、14 及び 22 日の投与後 1~3 時間 投与 22 日の投与後 1~3 時間

その他、哺育行動の減少と腟口からの出血が対照群の 1 例（動物番号 1107）で授乳 1 日にみられた。

2) 回復期間

いずれの動物にも異常はなく、回復性が認められた。

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

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

500 mg/kg 投与群の非交配群雌の 2 例で間代性痙攣がみられた。

性	動物番号	症状	検査日
雌	4116(非交配群)	間代性痙攣	投与 2 週
	4119(非交配群)	間代性痙攣	投与 4 週

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

500 mg/kg 投与群の雄 1 例で流涎、交配群雌の 3 例及び非交配群雌の 2 例で流涎がみられた。

性	動物番号	症状	検査日
雄	4002	流涎	投与 3、4 週
雌	4104 (交配群)	流涎	妊娠 1 日
	4105 (交配群)	流涎	妊娠 14 日
	4109 (交配群)	流涎	投与 2 週
	4116 (非交配群)	流涎	投与 2 週
	4119 (非交配群)	流涎	投与 4 週

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

500 mg/kg 投与群の交配群雌及び非交配群雌の各 1 例で間代性痙攣がみられた。

性	動物番号	症状	検査日
雌	4109 (交配群)	間代性痙攣	授乳 4 日
	4117 (非交配群)	間代性痙攣	投与 3 週

立ち上がり回数では、対照群と比べ 500 mg/kg 投与群の交配群雌の妊娠 14 日に有意な高値が認められたが、いずれも一時的変化であり、変動範囲内の変化と判断した。また、同群の非交配群雌で回復 2 週に有意な高値が認められたが、投与期間中にみられない変化であり、変動範囲内の変化と判断した。

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。

6.3.4 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なかった。

着地開脚幅では、雄、非交配群雌及び交配群雌の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なかった。

着地開脚幅では、雄及び非交配群雌の対照群と 500 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間終了週測定

対照群と各被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了週測定

対照群と比べ 500 mg/kg 投与群の雄で有意な低値が認められたが、投与期間終了週にみられない変化であり、変動範囲内の変化と判断した。

6.3.6 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

雄では、対照群と比べ 500 mg/kg 投与群で 0－60 の合計測定に有意な高値が認められたが、軽微な変動であり、10 分ごとの測定値に有意差がなく、かつ回復期間終了週

の対照群と同等値であることから変動範囲内の変化と判断した。150 mg/kg 以下の投与群では対照群と同等値を示し、有意差は認められなかった。

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

2) 回復期間終了週測定

対照群と 500 mg/kg 投与群との間に有意差は認められなかった。

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

1) 投与期間

雄では、500 mg/kg 投与群で体重増加の抑制傾向がみられ、投与期間中の体重増加量に低値（対照群と比べ−16%）がみられたが、有意差はなかった。150 mg/kg 以下の投与群では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、対照群と比べて 500 mg/kg 投与群で妊娠 20 日と妊娠期間中の体重増加量に有意な低値が認められた。

非交配群雌では、500 mg/kg 投与群で対照群と同様な体重推移を示し、有意差は認められなかった。

2) 回復期間

雄では、500 mg/kg 投与群で対照群を上回る体重増加を示し、回復期間中の体重増加量に有意な高値が認められた。雌では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。

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

1) 投与期間

雄では、対照群と比べて 500 mg/kg 投与群で投与 2 日に有意な低値、その後は対照群と同等度な摂餌量を示し、有意差は認められなかった。150 mg/kg 以下の投与群では対照群と同等値を示し、有意差は認められなかった。

交配群雌では、対照群と比べて 500 mg/kg 投与群で投与 2 及び 8 日に有意な低値が認められたが、その後の妊娠及び授乳期間に有意差は認められなかった。なお、150 mg/kg 投与群で投与 8 日に有意な低値が認められたが、一時的なごく軽微な変化であり、体重に変動がないことから変動範囲内の変化と判断した。

非交配群雌では、対照群と比べて 500 mg/kg 投与群で投与 2 日に有意な低値が認められた。この変化は交配群雌と同様な変動を示したことから、被験物質投与の影響と判断した。その他に同群の投与 15 日に有意な高値が認められたが、軽微な一時的変化であることから変動範囲内の変化と判断した。

2) 回復期間

雄及び非交配群雌の 500 mg/kg 投与群では、回復期間中対照群を上回る摂餌量を示し、雄で投与 8 日、雌で投与 14 日に有意差が認められた。

6.6　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、被験物質投与による異常はなかった。

定量項目については、対照群と比べて雄の 500 mg/kg 投与群で摂水量及び尿量の高値傾向に伴い尿浸透圧の低値、ナトリウム及びカリウム排泄量の高値傾向並びに塩素排出量の有意な高値が認められた。

非交配群雌では、対照群と比べて 500 mg/kg 投与群で摂水量及び尿量の高値傾向に伴い尿浸透圧の有意な低値が認められた。

2)　回復期間終了週検査

定性項目については、被験物質投与による異常はなかった。

定量項目については、対照群と比べて雄の 500 mg/kg 投与群で摂水量の高値傾向及び尿量の有意な高値に伴う尿浸透圧の低値、塩素排出量の有意な高値が認められた。

非交配群雌では対照群と 500 mg/kg 投与群の間に有意差は認められなかった。

6.7　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、対照群と比べ 150 mg/kg 投与群で平均赤血球容積及び平均赤血球血色素量の有意な高値が認められたが、用量との関連はなかった。また、対照群と比べ 500 mg/kg 投与群でプロトンビン時間の有意な延長とフィブリノーゲン量の有意な高値が認められた。

交配群雌では、対照群と比べ 150 mg/kg 投与群で活性化部分トロンボプラスチン時間の有意な延長が認められたが、用量との関連はなかった。

非交配群雌では、対照群と比べ 500 mg/kg 投与群で赤血球数の有意な低値が認められた。その他、同群で単球比率の有意な高値が認められたが、軽微な変化であり、単球数に有意差がないことから偶発的変化と判断した。

2)　回復期間終了時検査

雄では、500 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。非交配群雌では、500 mg/kg 投与群でヘマトクリット値に有意な低値が認められたが、投与期間終了時検査の対照群と同等値であることから偶発的変化と判断した。

6.8　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、対照群と比べ 500 mg/kg 投与群で総胆汁酸及びグルコースの有意な低値が認められた。

その他に、雄の 500 mg/kg 投与群で総たん白質の有意な高値（試験施設の背景データ、Mean±2S.D.：5.9±0.4、n=95、2009/04~2013/03）が認められたが、背景データ内の変化で回復期間終了時検査の対照群と同等値であることから、被験物質投与との関連はないと判断した。

交配群雌では、対照群との間に被験物質投与による有意差は認められなかった。

その他、150 mg/kg 投与群でカリウムに有意な高値が認められたが、軽微な変化であり、用量との関連はないことから偶発的変化と判断した。

非交配群雌では、対照群と比べて 500 mg/kg 投与群で総胆汁酸の有意な低値が認められた。

その他、同群で AST 及び ALP 活性の有意な低値、無機リン(試験施設の背景データ(Mean±2S.D.：4.7±1.8、n=75、2009/04~2013/03)の有意な高値が認められたが、AST と ALP は低下方向の変化、無機リンは回復期間終了時検査の対照群と同等値であり、背景データ内であることから、偶発的変化と判断した。

2) 回復期間終了時検査

500 mg/kg 投与群の雌雄ともに対照群との間に被験物質投与による有意差は認められなかった。

その他、対照群と比べて雄で LDH の有意な高値、雌で A/G 比の有意な低値が認められたが、軽微な変化であり、投与期間終了時検査に変化がないことから偶発的変化と判断した。

6.9 血中ホルモン測定（Table 7-11~7-15、Appendix 7-29~7-42）

1) 投与期間終了時検査

雄、交配群雌及び非交配群雌では、T3、T4 及び TSH ともに対照群と被験物質投与群との間に有意差は認められなかった。

2) 回復期間終了時検査

雄及び非交配群雌では、T3、T4 及び TSH ともに対照群と被験物質投与群との間に有意差は認められなかった。

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

1) 投与期間終了時検査

雄では、肝臓及び腎臓に被験物質投与の影響が認められた。

肝臓 : 絶対及び相対重量の高値又は有意な高値が 50 mg/kg 以上の投与群に認められた。

腎臓 : 相対重量の有意な高値が 50 及び 150 mg/kg 投与群に、絶対及び相対重量の有意な高値が 500 mg/kg 投与群に認められた。

交配群雌では、肝臓、腎臓及び副腎に被験物質投与の影響が認められた。

肝臓 : 相対重量の有意な高値が 150 mg/kg 投与群に、絶対及び相対重量の有意な高値が 500 mg/kg 投与群に認められた。

腎臓 : 相対重量の有意な高値が 150 mg/kg 以上の投与群に認められた。

副腎　　：　相対重量の有意な高値が 150 mg/kg 投与群に、絶対及び相対重量の有意な高値が 500 mg/kg 投与群に認められた。

他に、胸腺の絶対及び相対重量の有意な低値が 500 mg/kg 投与群に認められた。

非交配群雌では、甲状腺及び肝臓に被験物質投与の影響が認められた。

甲状腺　　：　絶対及び相対重量の高値又は有意な高値が 500 mg/kg 投与群に認められた。

肝臓　　：　絶対及び相対重量の有意な高値が 500 mg/kg 投与群に認められた。

他に、胸腺の絶対及び相対重量の有意な低値が 500 mg/kg 投与群に認められた。

2)　回復期間終了時検査

雄の腎臓に被験物質投与の影響が認められた。

腎臓　　：　絶対及び相対重量の有意な高値が 500 mg/kg 投与群に認められた。

その他、500 mg/kg 投与群の雄で脾臓の相対重量に有意な高値が認められたが、軽微であり、投与期間終了時検査にみられないことから変動範囲内の変化と判断した。また、500 mg/kg 投与群の雌で胸腺の相対重量に有意な高値が認められたが、投与期間終了時検査と逆方向の変動であり、変動範囲内の変化と判断した。

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

死亡の剖検所見は「7.1 の項」に記載したため省略する。

1)　投与期間終了時検査

雄では、腎臓及び肝臓に被験物質投与の影響がみられた。

腎臓　　：　大型化が 150 及び 500 mg/kg 投与群でそれぞれ 3 及び 1 例みられた。

肝臓　　：　大型化が 150 mg/kg 投与群で 2 例みられた。

その他、腺胃部の暗赤色巣が 50 mg/kg 投与群で 2/12（動物番号 2006、2011、組織学検査は未実施）及び 500 mg/kg 投与群で 1/7 例（動物番号 4005、組織学的にびらん）みられたが、いずれも発現状況から偶発的変化と判断した。

非交配群及び交配群雌（授乳 5 日に剖検）の雌では、被験物質投与による異常はみられなかった。

その他、非交配群の雌で腎盂拡張が 500 mg/kg 投与群で 1/4 例（動物番号 4117、組織学的に腎盂拡張）みられた。また、交配群の雌で腎臓ののう胞が 500 mg/kg 投与群で 1/8 例（動物番号 4105、組織学的にのう胞）、前胃の陥凹巣と隆起巣が 150 mg/kg 投与群で 1/12 例（動物番号 3106、組織学検査は未実施）、腺胃部の白色巣が 500 mg/kg 投与群で 1/8 例（動物番号 4109、組織学検査は未実施）、腺胃部の暗赤色巣が 50 及び 500 mg/kg 投与群でそれぞれ 1/12（動物番号 2109、組織学検査は未実施）及び 2/8 例（動物番号 4108、組織学的にびらん、4109、組織学検査は未実施）みられたが、

いずれも発現状況から偶発的変化と判断した。

2) 回復期間終了時検査

雌雄ともに被験物質投与の影響はみられなかった。

その他、雌で前胃の白色巣が対照群に 1/5 例（動物番号 1122、組織学的にのう胞）、腺胃部の暗赤色巣が対照群で 1/5 例（動物番号 1118、組織学的にびらん）及び 500 mg/kg 投与群で 1/3 例（動物番号 4119、組織学的にびらん）みられた。

3) 妊娠 25 日未分娩（不妊）及び全哺育児死亡動物

妊娠 25 日未分娩（不妊）動物が対照群の 1 例（動物番号 1106）、全哺育児死亡動物が対照群の 1 例（動物番号 1107）にみられた。以下に剖検所見を示す。

動物番号 1106 : 腎臓の小型化、腟の閉塞と白色物貯留、子宮の白色物貯留

動物番号 1107 : 脾臓の白色巣、前胃の白色巣

いずれも対照群であり、被験物質投与との関連はない。

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

死亡の病理組織学検査所見は「7.1 の項」に記載したため省略する。

1) 投与期間終了時検査

腎臓、肝臓、甲状腺及び副腎に被験物質投与による影響がみられた。

【腎臓】

雄のみに変化がみられた。すなわち、再生尿細管（軽微~中等度）が 150 mg/kg 以上の投与群、尿細管の拡張（軽微、軽度）、顆粒円柱（軽微、軽度）及び間質の細胞浸潤（軽微、軽度）が 500 mg/kg 投与群に、尿細管上皮細胞の好酸性小体（軽微~中等度）50 mg/kg 以上の投与群にみられた。なお、尿細管上皮細胞の好酸性小体は、α2μ グロブリンの免疫組織化学的染色標本で陽性を示し、PAS 染色で陰性を示したことから α2μ グロブリンに由来した物質と考える。

性	雄				交配群雌				非交配群雌	
投与量（mg/kg）	0	50	150	500	0	50	150	500	0	500
動物数	6	5	5	5	5	0	0	5	5	5
再生尿細管	4	4	4	5	1	0	0	1	3	1
軽微	4	4	3	1	1	0	0	1	3	1
軽度	0	0	1	3	0	0	0	0	0	0
中等度	0	0	0	1	0	0	0	0	0	0
尿細管の拡張	0	0	0	2	0	0	0	0	0	0
軽微	0	0	0	1	0	0	0	0	0	0
軽度	0	0	0	1	0	0	0	0	0	0
顆粒円柱	0	0	0	3	0	0	0	0	0	0
軽微	0	0	0	2	0	0	0	0	0	0
軽度	0	0	0	1	0	0	0	0	0	0
間質の細胞浸潤	1	0	0	2	0	0	0	0	0	0
軽微	1	0	0	0	0	0	0	0	0	0
軽度	0	0	0	2	0	0	0	0	0	0
尿細管上皮細胞の好酸性小体	0	5	5	5	0	0	0	0	0	0
軽微	0	3	1	0	0	0	0	0	0	0
軽度	0	2	3	0	0	0	0	0	0	0
中等度	0	0	1	5	0	0	0	0	0	0

【肝臓】

小葉中心性の肝細胞肥大（軽微、軽度）が雄と交配群の雌の 150 mg/kg 以上の投与群及び非交配群の雌の 500 mg/kg 投与群にみられた。

性	雄				交配群雌				非交配群雌	
投与量（mg/kg）	0	50	150	500	0	50	150	500	0	500
動物数	6	5	5	5	5	5	5	5	5	4
小葉中心性の肝細胞肥大	0	0	4	5	0	0	4	5	0	4
軽微	0	0	4	1	0	0	4	1	0	1
軽度	0	0	0	4	0	0	0	4	0	3

【甲状腺】

ろ胞上皮細胞の肥大（軽微、軽度）が雄の 150 mg/kg 以上の投与群、交配群と非交配群の雌の 500 mg/kg 投与群にみられた。

性	雄				交配群雌				非交配群雌	
投与量（mg/kg）	0	50	150	500	0	50	150	500	0	500
動物数	6	5	5	5	5	5	5	5	5	4
ろ胞上皮細胞の肥大	0	0	2	3	0	0	0	1	0	1
軽微	0	0	2	2	0	0	0	1	0	1
軽度	0	0	0	1	0	0	0	0	0	0

【副腎】

皮質細胞の空胞化（軽微、軽度）が交配群及び非交配群の雌の 500 mg/kg 投与群にみられた。なお、束状帯細胞を主体とした皮質細胞における脂肪滴と考えられる小型空胞は、対照群に比してび漫性に増加し、生理的にみられる空胞に類似しており、空胞の出現とともに胞体は腫大して淡明化し、束状帯領域はやや伸長していた。

性	雄				交配群雌				非交配群雌	
投与量（mg/kg）	0	50	150	500	0	50	150	500	0	500
動物数	6	5	5	5	5	5	5	5	5	4
皮質細胞の空胞化	0	0	0	0	0	0	0	3	0	4
軽微	0	0	0	0	0	0	0	1	0	3
軽度	0	0	0	0	0	0	0	2	0	1

2) 回復期間終了時検査

【腎臓】

再生尿細管（軽微、軽度）及び顆粒円柱（軽微）は、投与期間終了時検査との間に明らかな発現状況の差はみられず、回復性はみられなかった。しかし、尿細管の拡張、間質の細胞浸潤及び尿細管上皮細胞の好酸性小体は消失又は程度及び頻度が減弱し、回復性が認められた。

性	雄		非交配群雌	
投与量（mg/kg）	0	500	0	500
動物数	5	5	5	5
再生尿細管	3	4	0	0
軽微	3	0	0	0
軽度	0	4	0	0
顆粒円柱	0	4	0	0
軽微	0	4	0	0
尿細管上皮細胞の好酸性小体	0	2	0	0
軽微	0	2	0	0

【肝臓】

小葉中心性の肝細胞肥大（軽微、軽度）が雄及び非交配群の雌の 500 mg/kg 投与群にみられたが、程度及び頻度が減弱し、回復性が認められた。

性	雄		非交配群雌	
投与量（mg/kg）	0	500	0	500
動物数	5	5	5	3
小葉中心性の肝細胞肥大	0	3	0	1
軽微	0	2	0	1
軽度	0	1	0	0

【甲状腺】

ろ胞上皮細胞の肥大（軽微）が雄の 500 mg/kg 投与群にみられたが、発現頻度及び程度は減弱又は消失し、回復性が認められた。

性	雄		非交配群雌	
投与量（mg/kg）	0	500	0	500
動物数	5	5	5	3
ろ胞上皮細胞の肥大	0	1	0	0
軽微	0	1	0	0

【副腎】

皮質細胞の空胞化（軽微）が非交配群の雌の 500 mg/kg 投与群にみられたが、発現頻度及び程度は減弱し、回復性が認められた。

性	雄		非交配群雌	
投与量（mg/kg）	0	500	0	500
動物数	5	5	5	3
皮質細胞の空胞化	0	0	0	2
軽微	0	0	0	2

3) 妊娠 25 日未分娩（不妊）及び全哺育児死亡動物

妊娠 25 日未分娩（不妊）は、対照群の 1 例（動物番号 1106）に以下の所見がみられ、不妊の原因は子宮の変化と推測された。

腎臓における間質の細胞浸潤（リンパ球、軽微）、線維症（軽度）及び色素含有マクロファージ（緑黄色、軽微）、脾臓の髄外造血亢進（軽微）、子宮における炎症細胞浸潤（軽微、両角部）

全哺育児死亡動物は、対照群の 1 例（動物番号 1107）に以下の所見がみられ、全哺育児死亡の原因は腹腔内の器官・組織における病変による過度のストレスと推測された。

結腸粘膜の萎縮（軽微）、腎臓の近位尿細管の空胞化（軽度）、肝臓の辺縁部肝細胞の空胞化（軽微）、顎下腺のび漫性の腺房細胞の萎縮（軽微）、脾臓の皮膜炎（軽度）と白脾髄の萎縮（軽微）、前胃の潰瘍（軽度）、前胃の扁平上皮細胞の過形成（軽度）、胸腺の萎縮（中等度）

6.13 性周期（Table 11、Appendix 10-1~10-4）

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平均性周期日数には対照群と各被験物質投与群との間に有意差は認められなかった。

6.14　交配成績（Table 12、Appendix 11-1~11-5）

全ての組み合わせにおいて、交配 5 日までに交尾が成立し（交尾見逃しの 50 及び 500 mg/kg 投与群の各 1 例は性周期から判断して交配 2 日）、交尾までに要した日数、交尾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。また、不妊雌は対照群の 1 例のみであり、授精率及び受胎率にも対照群と各被験物質投与群との間に有意差は認められなかった。

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

出産率、妊娠期間、黄体数、着床痕数、着床率、分娩率、死産児率及び出生児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。なお、外表異常はみられなかった。

妊娠動物は妊娠 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。哺育状態では各被験物質投与群に児集め、営巣及び授乳行動に異常はなかった。

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

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。

6.17　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。

6.18　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が、用量に関連して生後 4 日の雌雄体重及び生後 0~4 日の間の体重増加量が低下し、対照群と比べ 500 mg/kg 投与群で体重増加量が 17%以上低かった。

6.19　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なかった。

6.20　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なかった。

7. 考察

2-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）、50、150 及び 500 mg/kg を Sprague-Dawley 系 SPF ラット（交配群として雌雄各 12 匹/群、雌には非交配群として対照群及び 500 mg/kg 投与群に各 10 匹を追加）の雄には交配前 14 日間に加え交配期間を通して剖検前日まで（42 日間）、雌には交配前 14 日間に加え交配期間及び妊娠期間を通して授乳 4 日まで（41~46 日間）、非交配群雌には 42 日間強制経口投与し、反復投与毒性及び生殖発生毒性を検討した。更に、0 及び 500 mg/kg 群の一部の動物（交配群雄各 5 匹と非交配群雌 5 及び 3 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。

7.1 反復投与毒性

死亡動物は 500 mg/kg 投与群の交配群雌 4 例と非交配群雌 3 例みられた。これの動物は死亡前に軽度な体重増加の抑制、間代性痙攣及び流涎あるいは結腸又は右腎臓に暗赤色巣、小葉中心性の肝細胞肥大、出血（脳、結腸、腎臓）、副腎の束状帯細胞の肥大、顎下腺のび漫性の腺房細胞萎縮あるいは脾臓の白脾髄萎縮がみられた。これら変化のうち、小葉中心性の肝細胞肥大は薬物代謝との関連が疑われる変化、副腎の束状帯細胞肥大及び脾臓の白脾髄萎縮は一部の動物に体重増加抑制もみられたことから、ストレスを反映した変化、顎下腺のび漫性の腺房細胞の萎縮は流涎と関連した変化、出血はいずれも限局的で脳及び腎臓では新鮮であったことから、出血は死亡時又は死亡直前の変化と推察される。また、壊死や炎症を伴った結腸の出血は 1 例に限定した変化であり、急激な死に直結する所見がないことから、死因はストレスによる中枢興奮を疑わせる間代性痙攣及び自律神経への影響を疑わせる流涎、循環系への影響を疑わせる出血がみられたことから、自律神経の交感神経及び副交感神経のアンバランスによる急性の循環器系への影響の可能性が考えられた。

生存動物の 500 mg/kg 投与群の雌雄で流涎及びあるいは間代性痙攣がみられた。これら症状も自律神経の交感神経及び副交感神経のアンバランスの可能性が考えられた。これら症状は回復期間で消失し、回復性が認められた。

雄の 500 mg/kg 投与群で体重増加の抑制傾向、交配群雌の 500 mg/kg 投与群で妊娠期間中に体重増加の抑制がみられた。回復期間では 500 mg/kg 投与群の雄で対照群を上回る体重増加を示し、速やかに回復すると考えられた。

雄、交配群雌及び非交配群雌の 500 mg/kg 投与群で投与初期に摂餌量の低値が認められた。この変化は被験物質投与の一時的な影響であるが、毒性学的意義は少ない。回復期間では 500 mg/kg 投与群の雌雄で回復期間中対照群を上回る摂餌量を示し、速やかに回復すると考えられた。

雄の 500 mg/kg 投与群で摂水量及び尿量の高値傾向に伴い尿浸透圧の低値、ナトリウム及びカリウム排泄量の高値傾向並びに塩素排出量の高値が認められた。これと関

連して、腎臓で雄の 50 及び 150 mg/kg 投与群で相対重量の高値、500 mg/kg 投与群で絶対及び相対重量の高値が認められ、雄の 150 mg/kg 以上の投与群で大型化、雄の 50 mg/kg 以上の投与群で尿細管上皮細胞に α2μ グロブリンに由来による好酸性小体、150 mg/kg 以上の投与群で再生尿細管、500 mg/kg 投与群で尿細管の拡張、顆粒円柱及び間質の細胞浸潤がみられた。腎臓の変化は尿細管上皮細胞における α2μ グロブリンに由来による好酸性小体の程度の増強とともに再生尿細管、尿細管の拡張、顆粒円柱及び間質の細胞浸潤がみられた。α2μ グロブリンの蓄積は雄性ラットに種特異的に発現し、また被験物質の投与によって増強し、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[7]、[8]、[9]ことから、尿検査及び腎臓の諸病変は発現状況から α2μ グロブリンの蓄積が関与している可能性が考えられた。本変化は雄ラットに特異的な変化であり、雌ラットや他の動物種ではみられない[9]。なお、交配群雌の 150 mg/kg 以上の投与群でも腎臓の相対重量の高値が認められたが、絶対重量に有意差はなく、組織学的にも異常がないことから毒性学的意義は少ないが、被験物質投与の影響と考えられる。回復期間終了週又は終了時の検査においても、雄の 500 mg/kg 投与群で摂水量の高値傾向及び尿量の高値に伴う尿浸透圧の低値、塩素排出量の高値、腎臓の絶対及び相対重量の高値が認められ、再生尿細管及び顆粒円柱が観察された。再生尿細管及び顆粒円柱は投与期間終了時検査との間に明らかな発現状況の差はなかった。しかし、他の変化は、消失又は程度及び頻度が減弱し、回復性が示唆された。なお、非交配群雌で 500 mg/kg 投与群で摂水量及び尿量の増加傾向に伴う尿浸透圧の低値が認められたが、電解質排泄量は対照群と同等値であり、腎臓に組織学的異常がないことから、毒性学的意義は少ないと判断した。

雄で 500 mg/kg 投与群でプロトンビン時間の延長（試験施設の背景データ、Mean±2S.D.：14.4±4.6、n=95、2009/04~2013/03）とフィブリノーゲン量の高値（試験施設の背景データ、Mean±2S.D.：274±56、n=95、2009/04~2013/03）が認められたが、出血、フィブリノーゲンの低値、炎症性変化及び肝機能障害を示唆する変化がなく、回復期間終了時検査の対照群の値及び背景データと大差なことから、毒性学的意義は少ないと判断した。非交配群雌の 500 mg/kg 投与群で赤血球数の低値が認められたが、病理学検査に異常がみられないことから、その作用機序は明らかでない。

雄及び非交配群雌の 500 mg/kg 投与群で総胆汁酸の低値が認められたが、回腸における吸収障害が考えられたが、回腸に吸収障害を示唆する変化がみられていないことから、その詳細は明らかでない。また、雄の 500 mg/kg 投与群でグルコースの低値（試験施設の背景データ、Mean±2S.D.：136±30、n=95、2009/04~2013/03）が認められた。平均値を低下させた 2/5 例（動物番号 4003：108 mg/dL、動物番号 4005：101 mg/dL）に小葉中心性の肝細胞肥大がみられたが、膵臓、体重及び摂餌量に異常はなく、本変化の機序はあきらかでないものの、同群で流涎がみられ、自律神経の交感神経及び副交感神経のアンバランスの可能性が疑われていることから、交感神経系ホルモンやグルカゴンの分泌に影響を及ぼした可能性が考えられる。

病理学検査では、前述の腎臓の変化に加え、肝臓、甲状腺及び副腎に被験物質投与

の影響が認められた。

肝臓で雄の 50 mg/kg 以上の投与群で絶対及び相対重量の高値、交配群雌の 150 mg/kg 投与群で相対重量の高値、500 mg/kg 投与群で絶対及び相対重量の高値、非交配群雌の 500 mg/kg 投与群で絶対及び相対重量の高値が認められ、雄の 150 mg/kg 投与群で大型化、雄と交配群の雌の 150 mg/kg 以上の投与群及び非交配群の雌の 500 mg/kg 投与群で小葉中心性の肝細胞肥大がみられた。これと関連して、甲状腺で非交配群雌の 500 mg/kg 投与群で絶対及び相対重量の高値、組織学的に雄の 150 mg/kg 以上の投与群及び交配群と非交配群の雌の 500 mg/kg 投与群でろ胞上皮細胞の肥大がみられた。小葉中心性の肝細胞肥大と甲状腺のろ胞上皮細胞肥大の変化は、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。回復期間終了時検査では、重量及び肉眼的変化は消失し、組織学的変化も発現頻度及び程度は減弱又は消失し、回復性が認められた。

副腎で交配群雌の 150 mg/kg 投与群で相対重量の高値、500 mg/kg 投与群で絶対及び相対重量の高値、交配群及び非交配群の雌の 500 mg/kg 投与群で皮質細胞の空胞化がみられた。空胞化は束状帯細胞を主体とした皮質細胞における脂肪滴と考えられる小型空胞が、対照群に比してび漫性に増加し、生理的にみられる空胞に類似しており、空胞の出現とともに胞体は腫大して淡明化し、束状帯領域はやや伸長していた。このような変化は副腎皮質合成阻害作用を有する薬剤で発現することが知られている[10]が、本被験物質における発現機序は明らかでない。回復期間終了時検査においても、非交配群の雌の 500 mg/kg 投与群で皮質細胞の空胞化がみられたが、発現頻度及び程度は減弱し、回復性が認められた。

その他、胸腺で交配群雌及び非交配群雌の 500 mg/kg 投与群で絶対及び相対重量の低値が認められた。また、回復期間終了時検査でも非交配群雌の 500 mg/kg 投与群で相対重量の高値が認められ、被験物質投与の影響の可能性が示唆された。

7.2 生殖発生毒性

雌雄動物の 500 mg/kg 投与群でも被験物質投与の影響は認められず、雌雄動物の交尾能、授精能及び受胎能、母動物の妊娠維持、分娩及び哺育行動などの生殖機能への影響はないと判断した。しかし、500 mg/kg 投与群で出生児の生後 0~4 日の体重増加量に低値傾向がみられた。

これらの結果から、50 mg/kg 以上の投与群で肝臓（雄）及び腎臓（雄）、150 mg/kg 以上の投与群で肝臓（雌）、腎臓（雌）、甲状腺（雄）、副腎（雌）がみられたことから、反復投与毒性に対する無影響量及び無毒性量は雄で 50 mg/kg 未満、雌で 50 mg/kg と判断した。親動物には被験物質投与による影響は認められなかったが、500 mg/kg 投与群で児の生後 0~4 日の体重増加量に低値傾向がみられことから、雌雄親動物の生殖能力に対する無影響量及び無毒性量は雌雄で 500 mg/kg、児動物における無影響量及び無毒性量はいずれも 150 mg/kg と判断した。

8. 文献

[1] [redacted]：2-tert-ブチルシクロヘキサン-1-イル＝アセタートの GC を用いた被験液中濃度測定法バリデーション及び安定性試験（媒体：コーン油）並びに IR を用いた特性及び安定性試験（株式会社ボゾリサーチセンター　御殿場研究所、試験番号：A-2516、2012 年）

[2] [redacted]：2-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-R036、2012 年）

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

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

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

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

[7] 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).

[8] 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）.

[9] 伊東信行編著：III.標的器官の毒性病理（2）, 泌尿器系 C. 腎臓, In：最新 毒性病理組織学, 名古屋, 中山書店, 東京，200 （1994）.

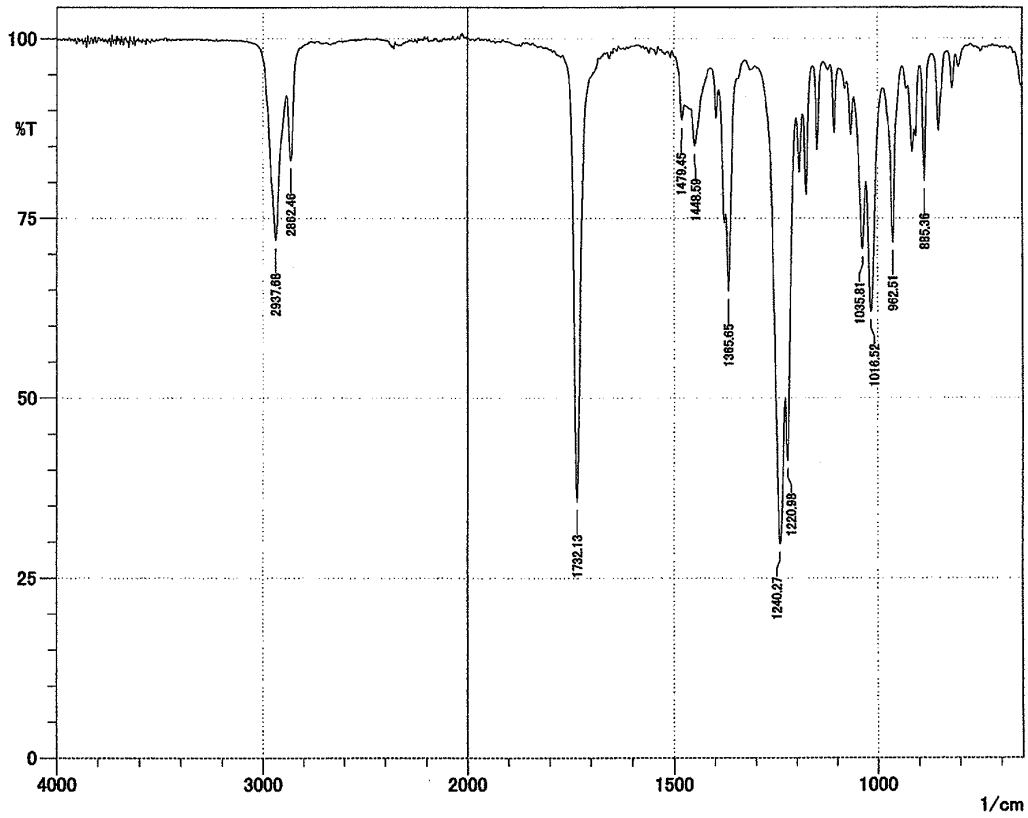
[10] 伊東信行発行：各論 14 章, 下垂体/副腎/松果体, In：毒性病理組織学, 日本毒性病理学会, 名古屋, 421 （2000）.

R-1105
添付資料　1

試験番号：A-2516

試験成績書
[2-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	:	被験物質の使用前
測定日	:	2012 年 8 月 17 日
被験物質	:	2-tert-ブチルシクロヘキサン-1-イル＝アセタート （ロット番号：02404AA-209）
試験項目	:	赤外吸収スペクトルの確認（ATR 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]　2012 年 8 月 23 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

試験成績書
[2-tert-ブチルシクロヘキサン-1-イル＝アセタートの安定性]

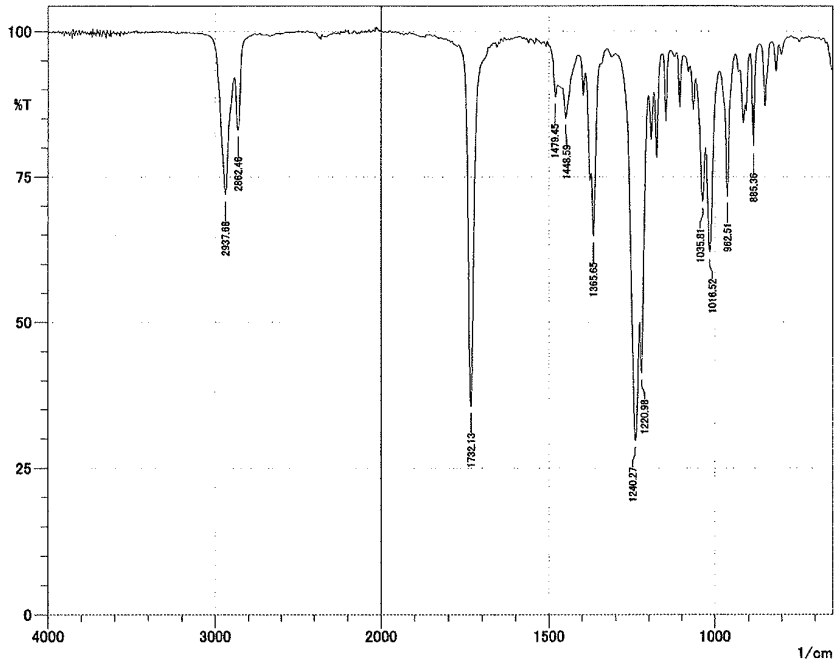
ステージ	:	投与期間終了後
測定日	:	2013 年 2 月 5 日
被験物質	:	2-tert-ブチルシクロヘキサン-1-イル＝アセタート （ロット番号：02404AA-209）
試験項目	:	赤外吸収スペクトルの確認（ATR 法）
評価基準	:	安定性のスペクトルを特性のスペクトル（A-2516）と比較するとき、同様な赤外吸収スペクトルである。
結果	:	安定性のスペクトルを特性のスペクトルと比較したとき、同様な赤外吸収スペクトルが得られた。 なお、赤外吸収スペクトルは次のページに示す。
基準	:	「新規化学物質等に係る試験を実施する試験施設に関する基準」（平成 23 年 3 月 31 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）
判定	:	適

[redacted]　　2013 年　2 月　26 日

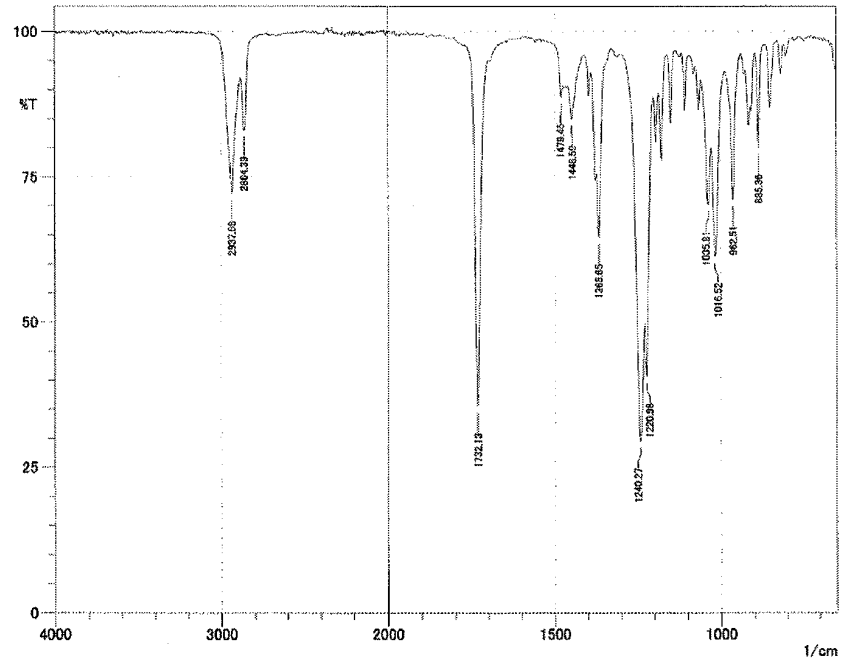
化学分析責任者
株式会社ボゾリサーチセンター　御殿場研究所

結果　　：　赤外吸収スペクトル

（特性のスペクトル：A-2516）



（安定性のスペクトル）



R-1105
添付資料　3

試験番号：A-2516

試験成績書
（2-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　：　2-tert-ブチルシクロヘキサン-1-イル＝アセタート
（ロット番号：02404AA-209）
形態（媒体）　：　溶液（コーン油）
保存条件　：　褐色ガラスビンにて、冷所（冷蔵庫内、許容値：1~10°C）又は室温保存
保存期間　：　冷所 8 日間＋室温 24 時間保存
評価基準
安定性　：　残存率が 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 8 日間+ 室温 24 時間保存後
1.00		0.937	0.983
		0.920	0.915
		0.947	0.897
	平均値	0.935	0.932
	残存率（%）	–	99.7
200		203	197
		203	197
		202	200
	平均値	203	198
	残存率（%）	–	97.5

判定　：　適

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

[redacted]　2012 年　9 月　4 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-1105
測定項目　：　濃度
ステージ　：　初回投与
測定開始日　：　2012 年 10 月 17 日

測定試料
　被験物質　：　2-tert-ブチルシクロヘキサン-1-イル＝アセタート
　　（Lot No. 02404AA-209）
　表示濃度　：　10、30 及び 100 mg/mL
　形態（媒体）　：　溶液（コーン油）
　調製日　：　2012 年 10 月 17 日
　測定対象物質　：　2-tert-ブチルシクロヘキサン-1-イル＝アセタート

評価基準
　濃度許容範囲　：　表示値に対する割合；100.0±10%

結果　：

濃　度 (mg/mL)	測　定　濃　度 (mg/mL)	表示値に対する割合 (%)
10	10.5	105.0
30	31.4	104.7
100	106	106.0

判定　：　適

分析結果

試験番号　：　R-1105
測定項目　：　濃度
ステージ　：　投与 6 週
測定開始日　：　2012 年 11 月 28 日

測定試料
　被験物質　：　2-tert-ブチルシクロヘキサン-1-イル＝アセタート
　　（Lot No. 02404AA-209）
　表示濃度　：　10、30 及び 100 mg/mL
　形態（媒体）　：　溶液（コーン油）
　調製日　：　2012 年 11 月 28 日
　測定対象物質　：　2-tert-ブチルシクロヘキサン-1-イル＝アセタート

評価基準
　濃度許容範囲　：　表示値に対する割合；100.0±10%

結果　：

濃　度 (mg/mL)	測　定　濃　度 (mg/mL)	表示値に対する割合 (%)
10	10.2	102.0
30	30.3	101.0
100	101	101.0

判定　：　適

R-1105
添付資料 6

2-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-R036

被験物質		媒体 a)	2-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	0/5
死亡発現時期		−	−	−	投与 1、2、5、8 及び 11 日に各 1 例(♀)
一般状態	生存	−	−	強直性痙攣、流涎、糞量の減少(♀)	糞量の減少、流涎(♂)
	死亡				強直性痙攣、流涎、跳躍、疾走、旋回、糞量の減少、自発運動の減少(♀)
体重	生存		−	体重増加の抑制（♂投与 1~14 日、♀投与 1~4 日）	体重減少、体重増加の抑制(♂投与 1~14 日)
	死亡				体重減少、体重増加の抑制(♀)
摂餌量	生存		摂餌量の低値（♀投与 4 日）	摂餌量の低値（♂♀投与 4 日）	摂餌量の低値（♂投与 4 日）
	死亡				摂餌量の低値（♀投与 4 日）
血液学検査			−	ヘモグロビン量：↓↓(♀)	−
血液化学検査			−	−	総たん白質：↑↑(♂)
器官重量	絶対		−	腎臓：↑↑(♂) 肝臓：↑↑(♀) 副腎：↑(♀)	腎臓：↑↑(♂) 肝臓：↑(♂)
	相対		肝臓：↑(♂)	肝臓：↑(♂)、↑↑(♀) 腎臓：↑↑(♂) 甲状腺：↑(♀) 副腎：↑(♀)	腎臓：↑↑(♂) 肝臓：↑↑(♂)
剖検	生存	−	−	−	−
	死亡				胸腺の小型化(♀) 脾臓の小型化(♀) 腺胃の暗赤色巣(♀)

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)

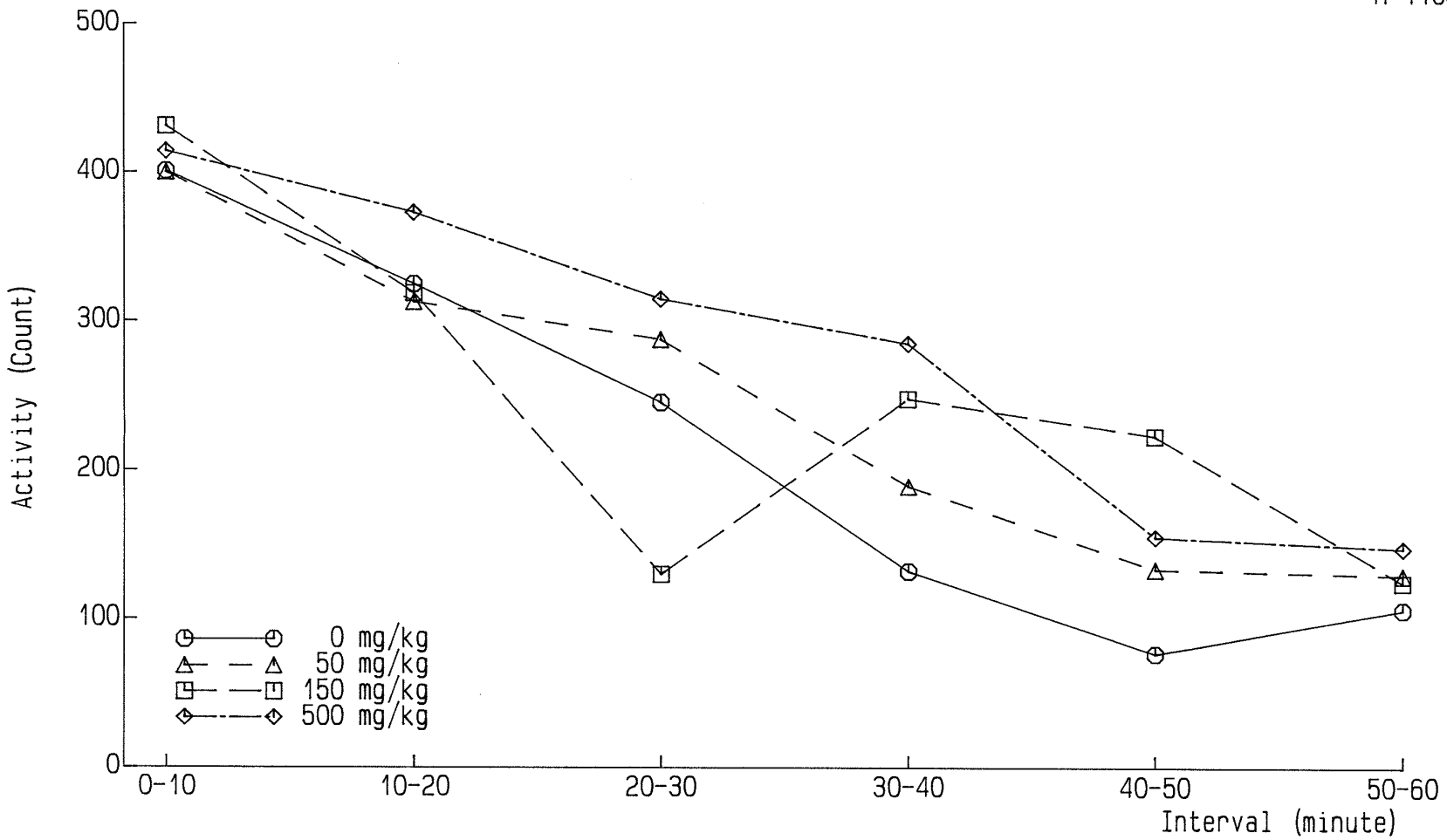


Fig.1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Motor activity of male rats (Week 6 of administration)

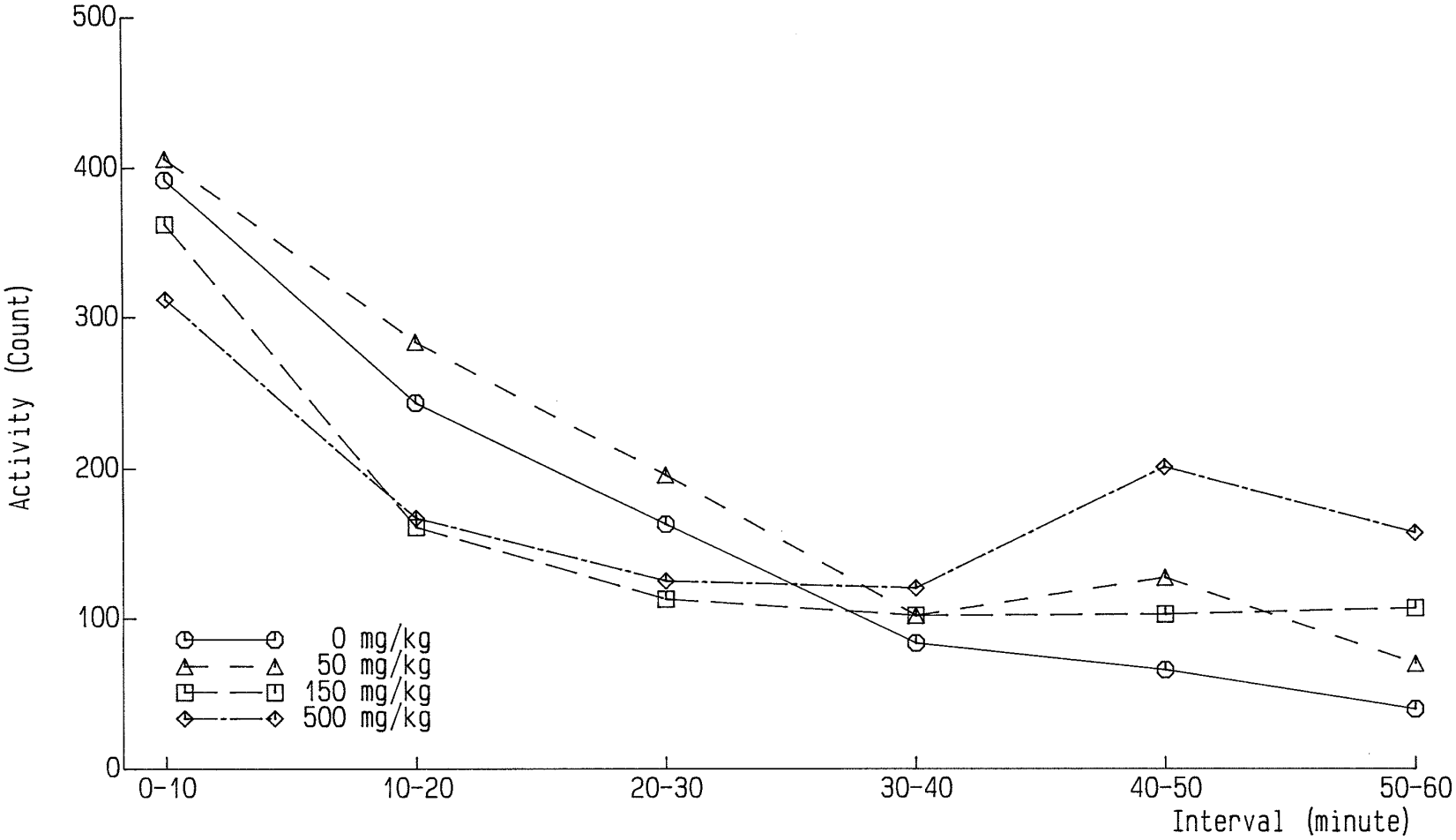


Fig.2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

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

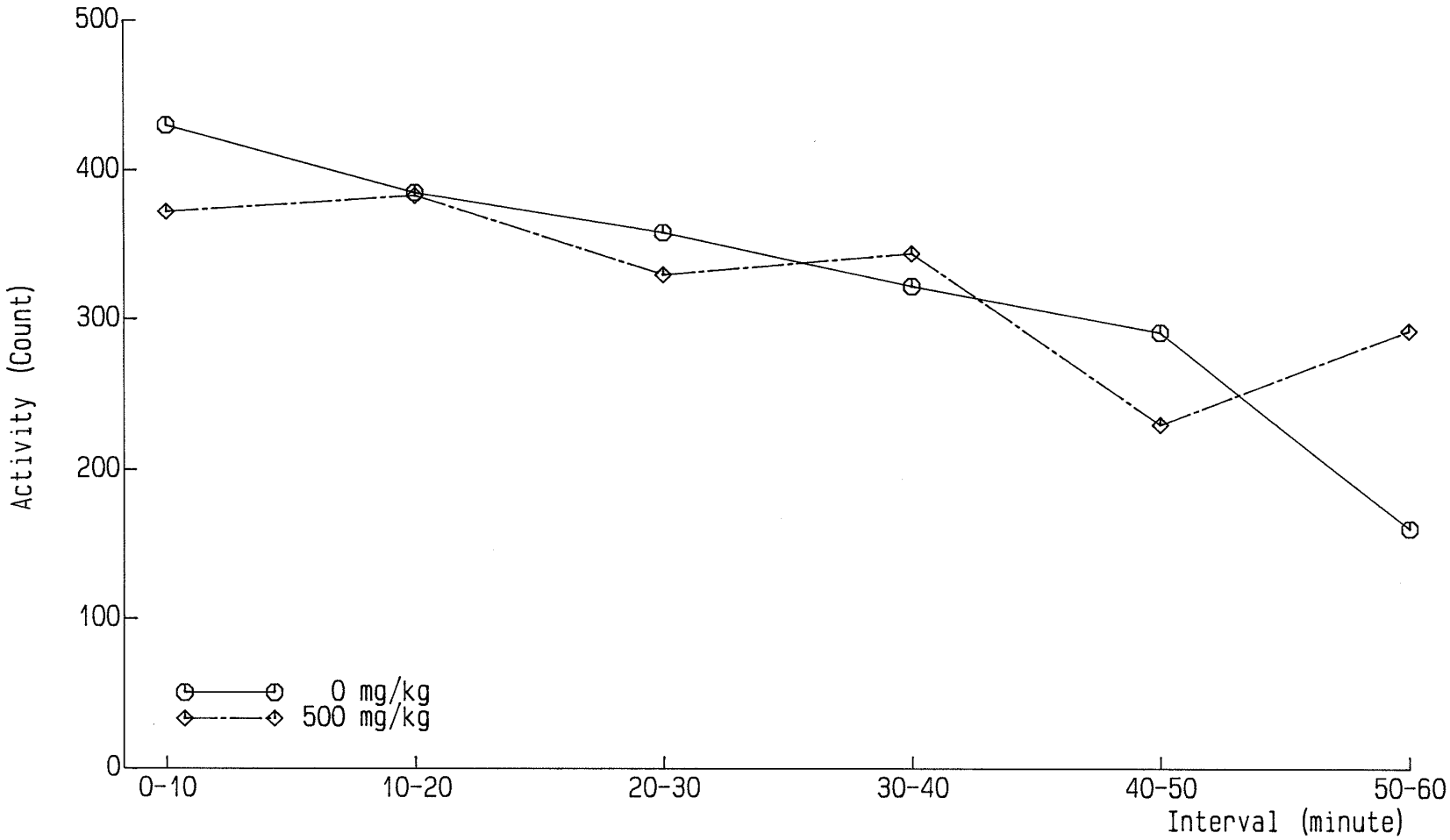


Fig.3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

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

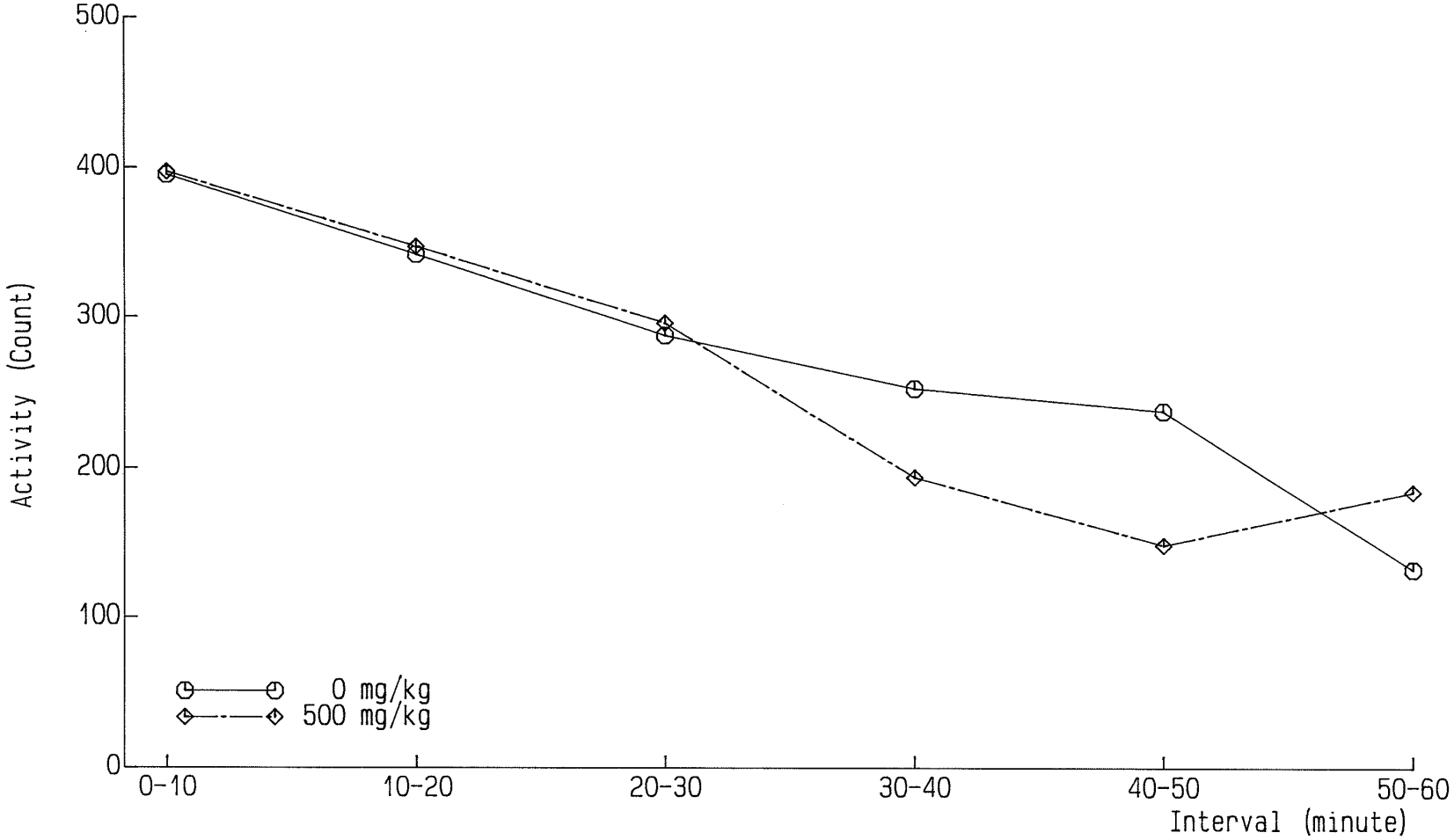


Fig.4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Motor activity of male rats (Week 2 of recovery)

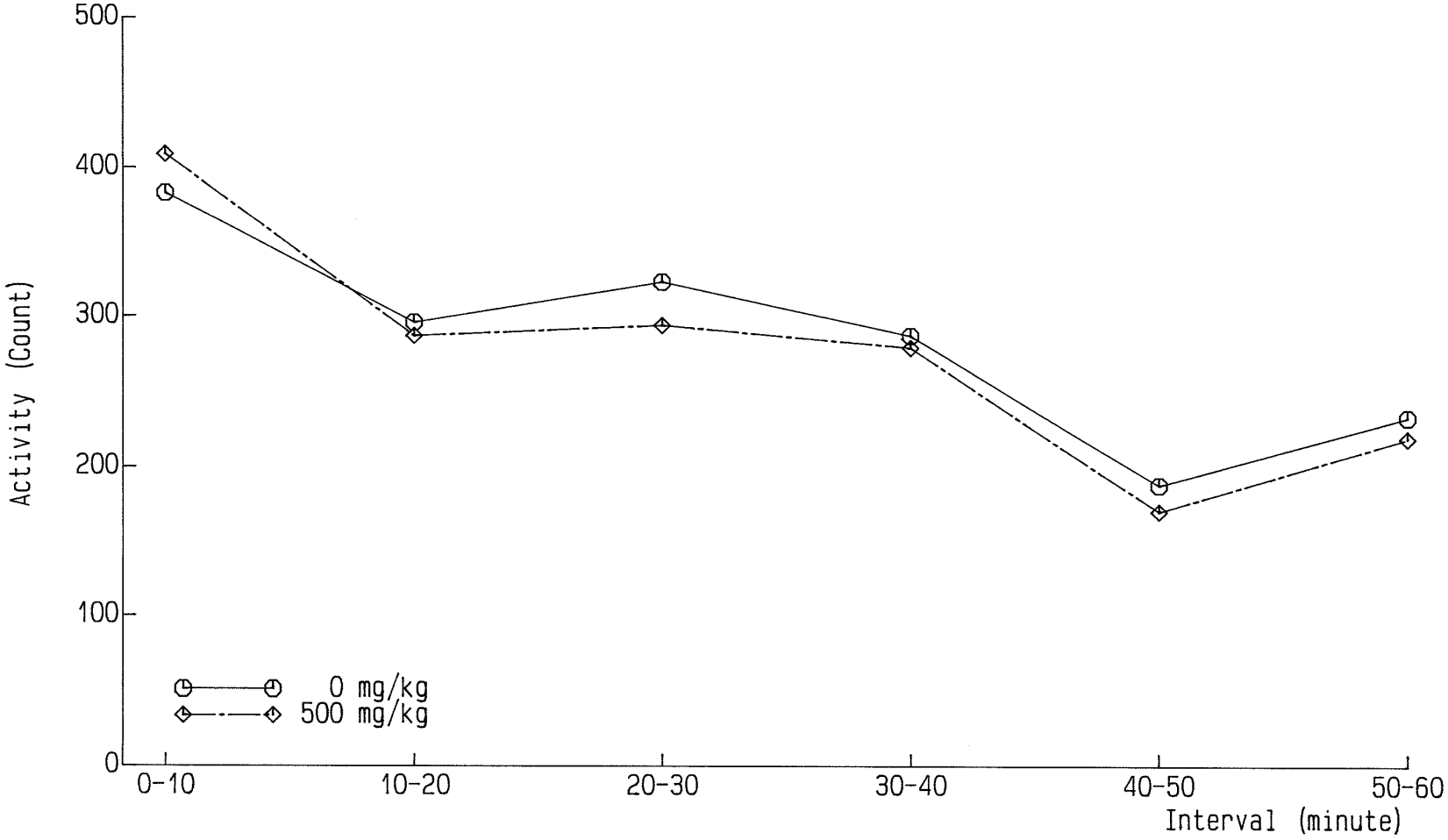


Fig.5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Motor activity of female rats (Week 2 of recovery)

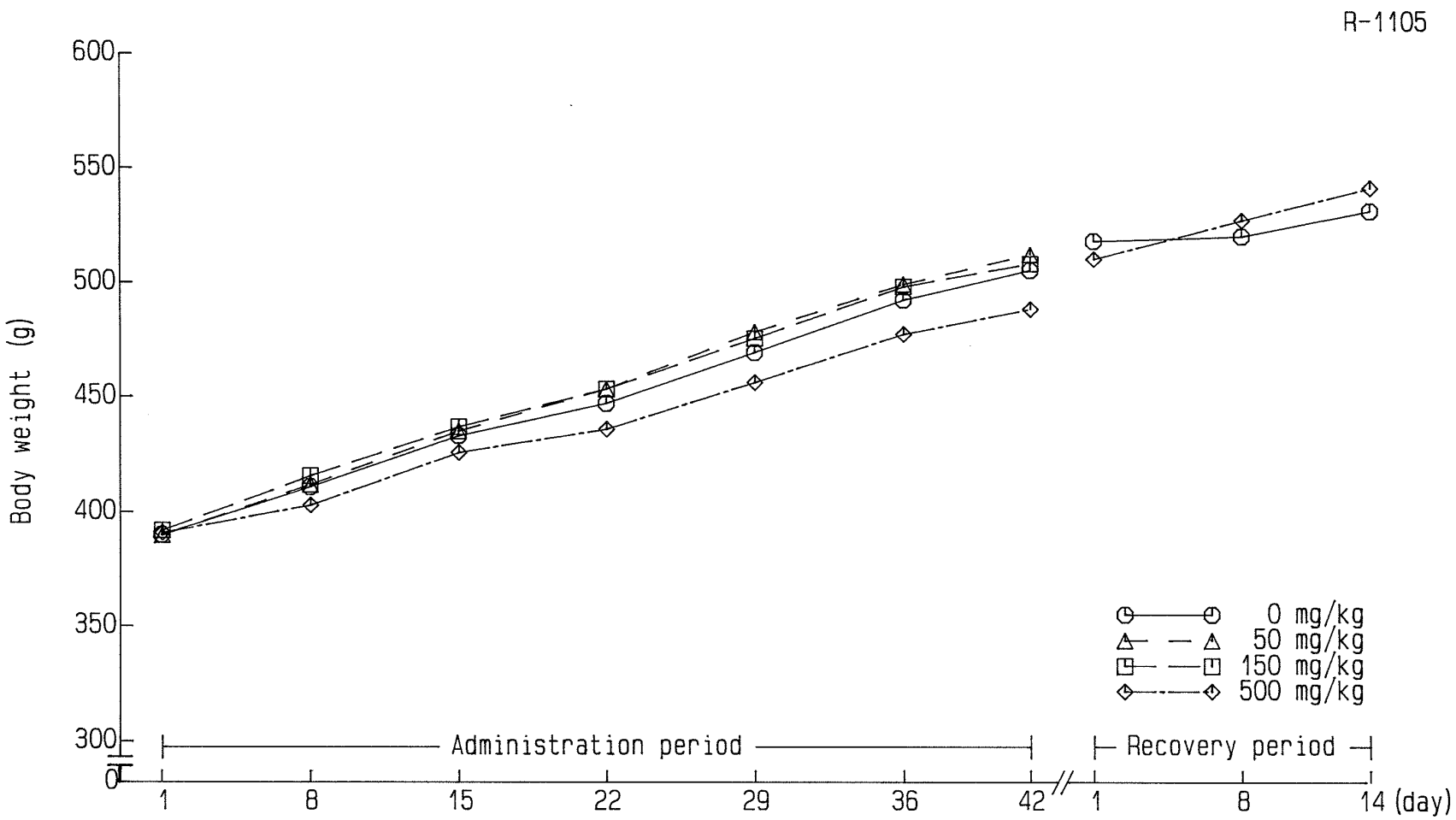


Fig.6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Body weight of male rats

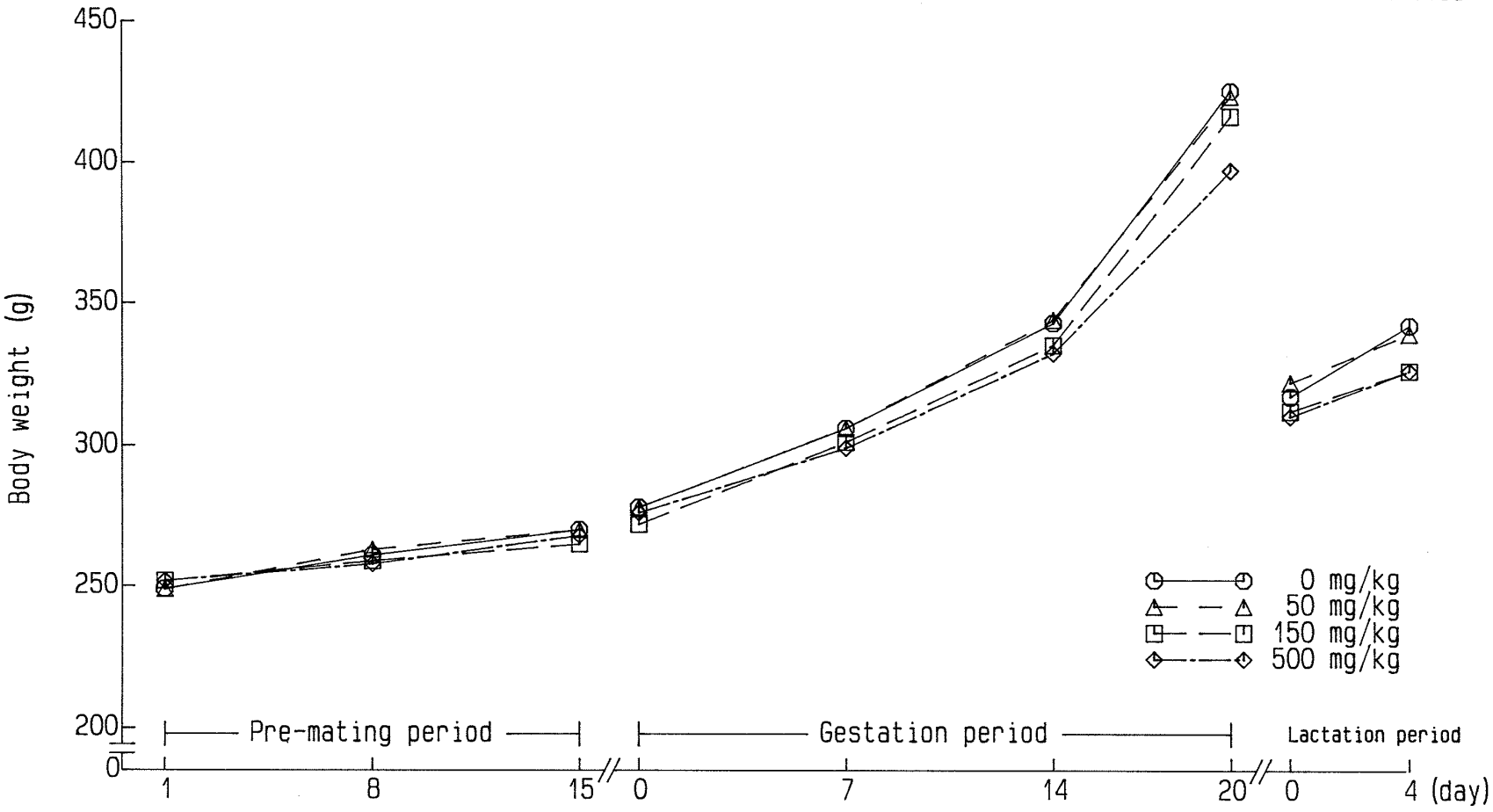


Fig.7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Body weight of female rats (Main group)

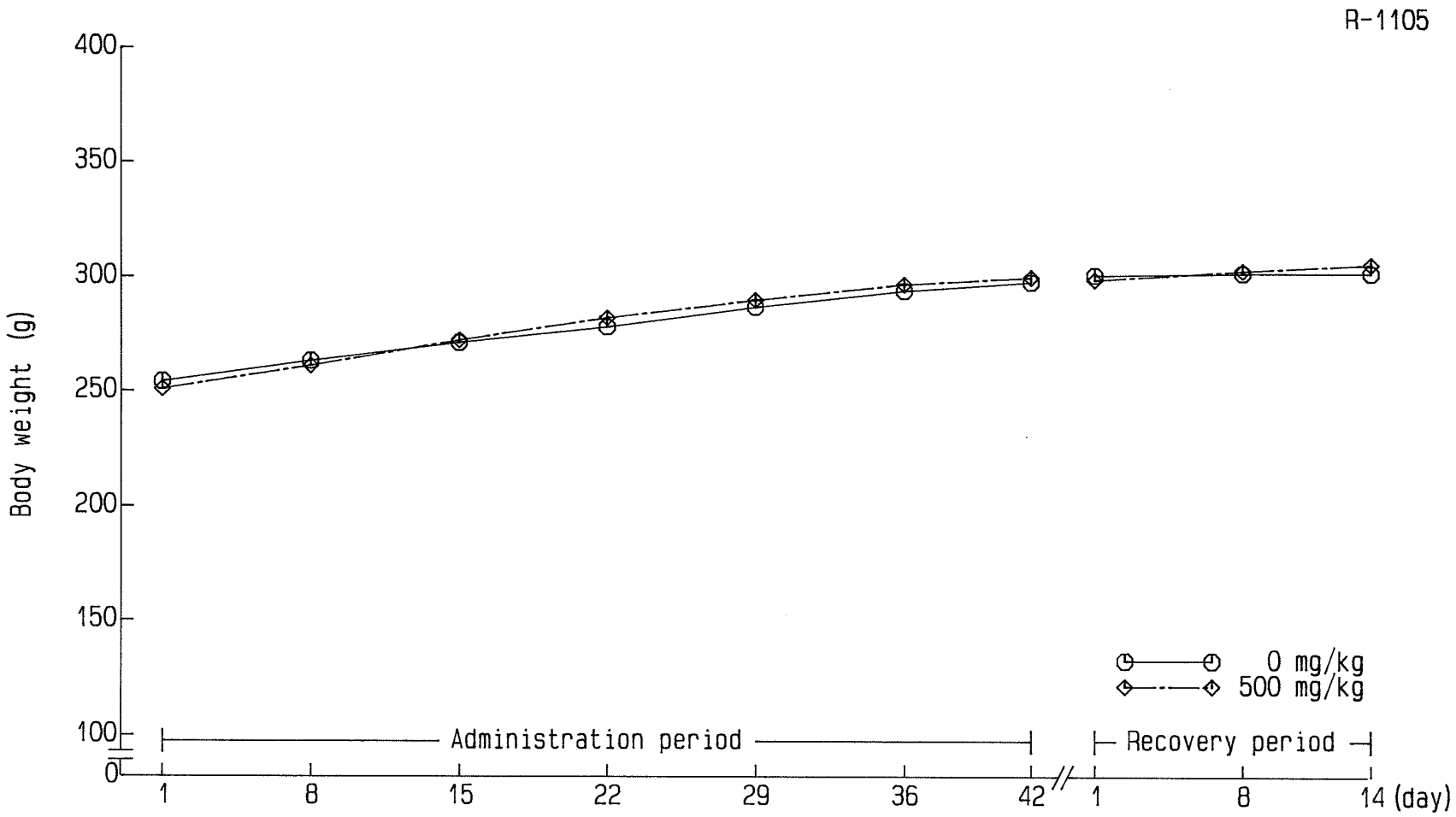


Fig.8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Body weight of female rats (Satellite group)

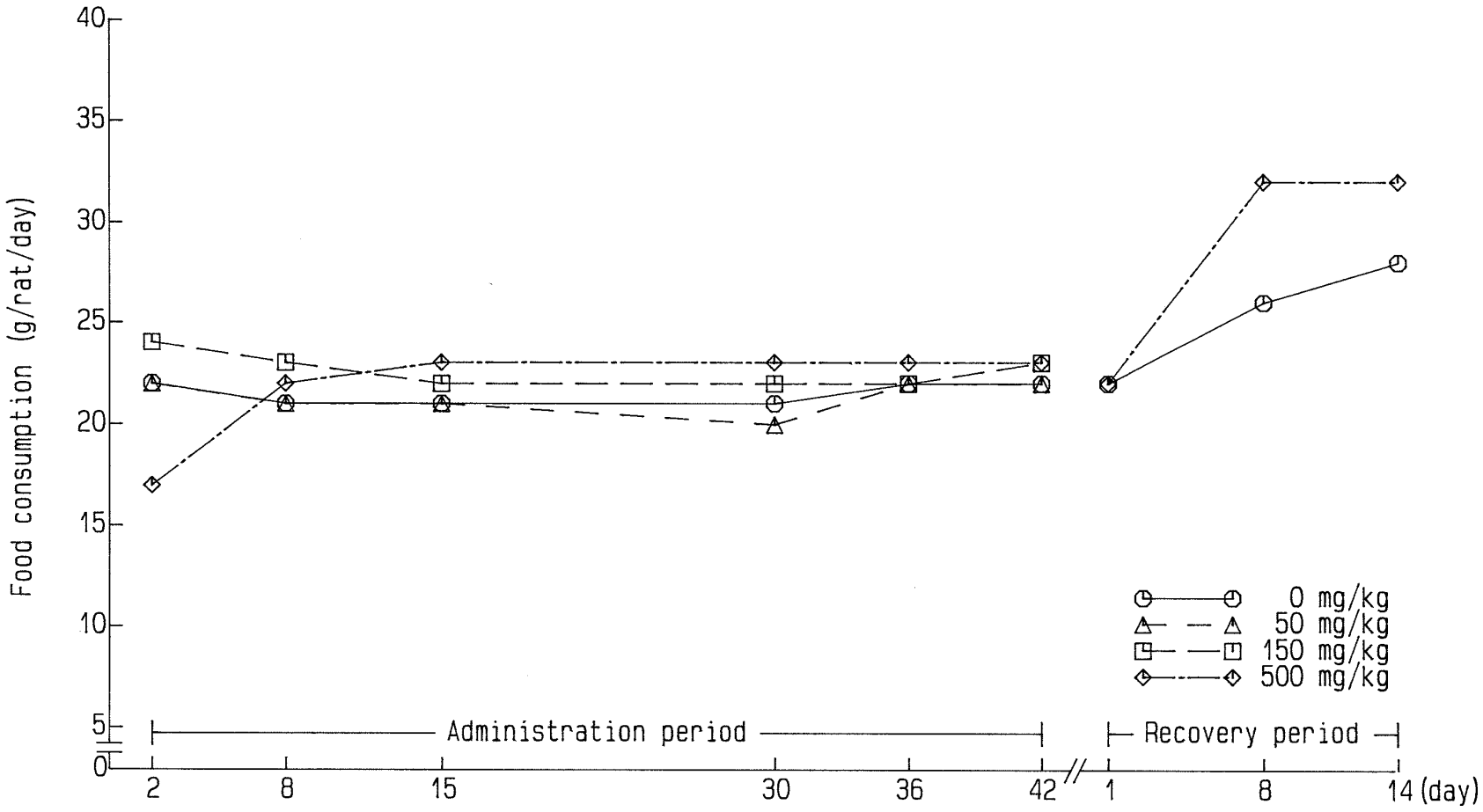


Fig.9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Food consumption of male rats

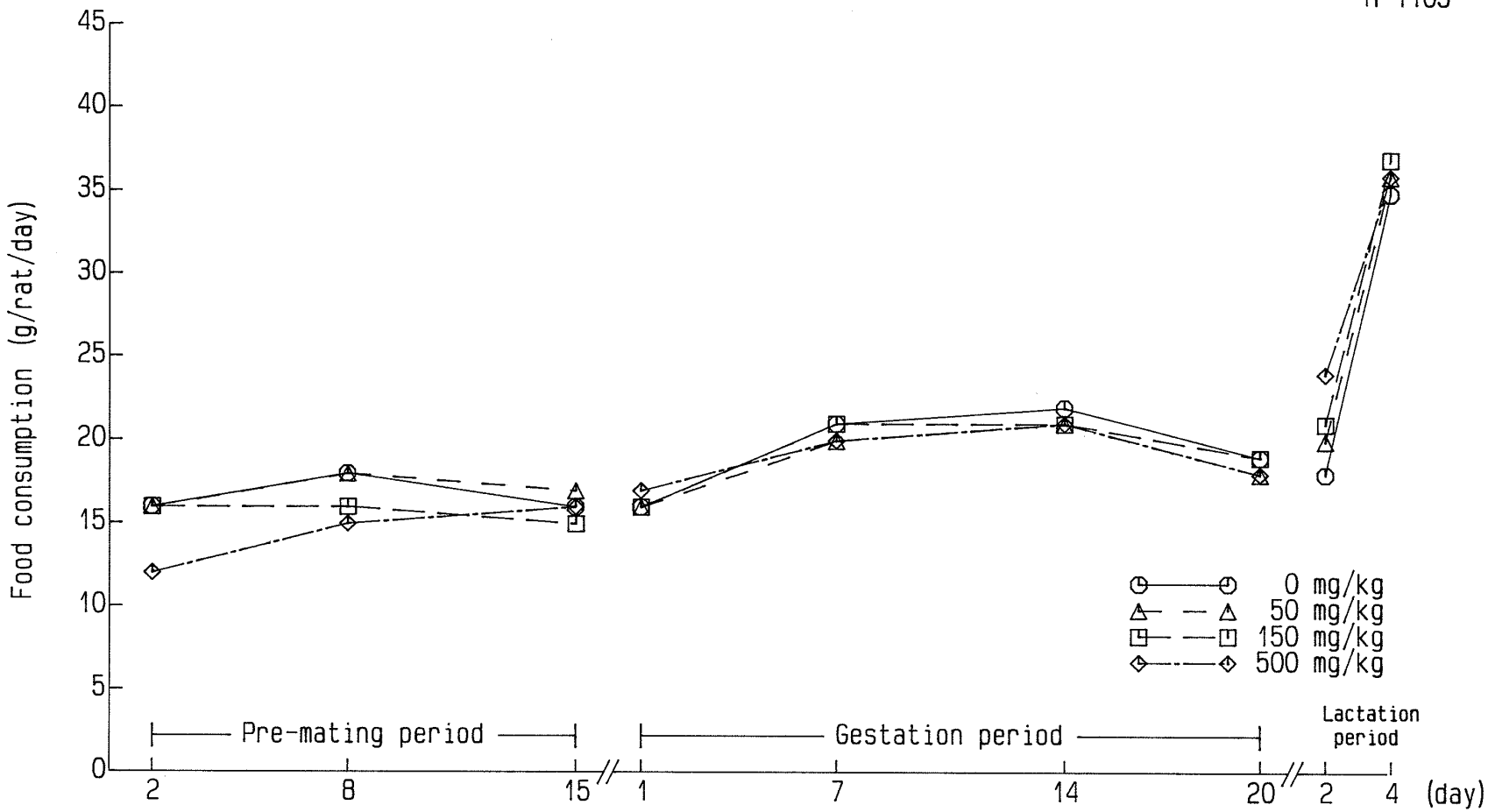


Fig.10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Food consumption of female rats (Main group)

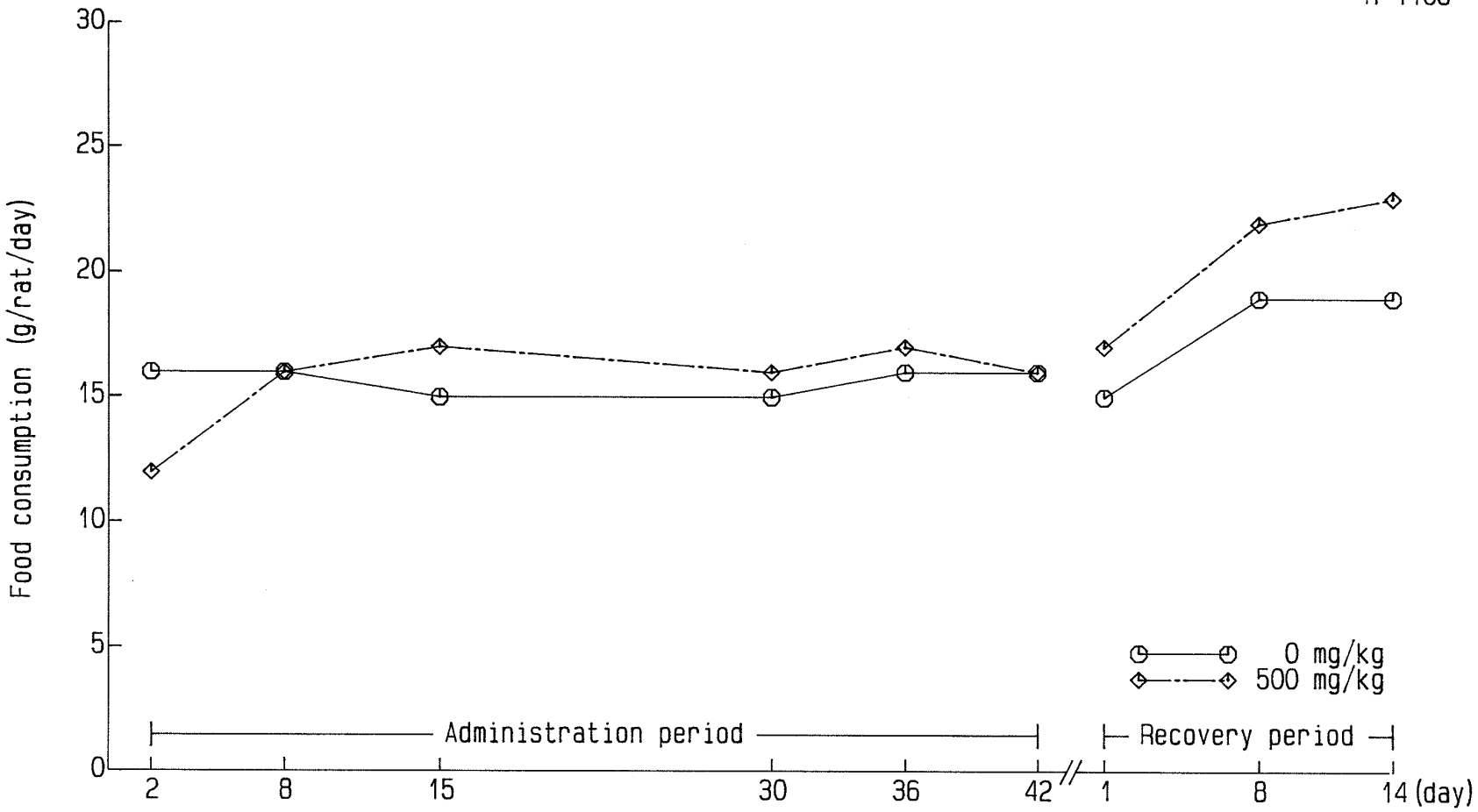


Fig.11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Food consumption of female rats (Satellite group)

Table 1-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
50	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
150	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
500	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	2	3	1	1
	Salivation	0	0	0	0	0	0	0	0	0	0	2	3	1	1

Table 1-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
50	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
150	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
500	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

Table 1-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
50	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
150	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
500	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

a): Day of necropsy

Table 1-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
50	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
150	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
500	No. of animals	12	12	12	12	12	12	12	12	12	12	11	11	11	11	11
	No. of animals with abnormal findings	0	0	0	0	0	0	0	0	0	1	1	3	3	0	0
	Clonic convulsion	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	Salivation	0	0	0	0	0	0	0	0	0	0	1	3	3	0	0
	Dead	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

Table 1-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	4	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	
50	No. of dams	11b)	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	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		
150	No. of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	2	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	
500	No. of dams	10b)	10	10	10	10	10	10	10	10	10	10	10	10	9	8	8	8	8	7	7	7	6	0	
	No. of dams with abnormal findings	0	0	0	0	0	0	0	0	0	0	0	0	1	3	0	0	0	1	1	0	0	0		
	Clonic convulsion	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	1	0	0	0		
	Salivation	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0		
	Dead	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0		

a): Gestation day
b): Data from one dam in which the signs of copulation were overlooked were excluded from the study results.

Table 1-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	11	11	11	10c)	10	10
	No. of dams with abnormal findings	0	1	0	0	0	0
	Decrease in nursing behavior	0	1	0	0	0	0
	Vaginal hemorrhage	0	1	0	0	0	0
50	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
150	No. of dams	12	12	12	12	12	12
	No. of dams with abnormal findings	0	0	0	0	0	0
500	No. of dams	8	8	8	8	8	8
	No. of dams with abnormal findings	0	0	0	0	0	0

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

Table 1-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
500	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	1	2	2	2
	Salivation	0	0	0	0	0	0	0	0	0	0	1	2	2	2

Table 1-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
500	No. of animals	10	8	8	8	8	8	8	8	8	8	8	8	8	8
	No. of animals with abnormal findings	3	0	0	1	0	0	0	1	0	0	0	0	0	0
	Clonic convulsion	1	0	0	0	0	0	0	1	0	0	0	0	0	0
	Salivation	2	0	0	1	0	0	0	1	0	0	0	0	0	0
	Dead	2	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 1-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
500	No. of animals	8	7	7	7	7	7	7	7	7	7	7	7	7	7	4
	No. of animals with abnormal findings	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Salivation	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Dead	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a): Day of necropsy

Table 1-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
500	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 2-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
500	No. of animals	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	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 2-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	50	150	500
	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 2-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	50	150	500
	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 2-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	50	150	500
	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 2-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	50	150	500
	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 2-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	50	150	500
	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 2-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	50	150	500
	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 2-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	50	150	500
	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 2-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	50	150	500
	No. of animals	12	12	12	11
Posture					
Normal		12	12	12	11
Convulsion					
None		12	12	12	11
Abnormal behavior					
None		12	12	12	11

Table 2-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	10
Posture					
Normal		11	11	12	10
Convulsion					
None		11	11	12	10
Abnormal behavior					
None		11	11	12	10

Table 2-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	10
Posture					
Normal		11	11	12	10
Convulsion					
None		11	11	12	10
Abnormal behavior					
None		11	11	12	10

Table 2-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	8
Posture					
Normal		11	11	12	8
Convulsion					
None		11	11	12	8
Abnormal behavior					
None		11	11	12	8

Table 2-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	7
Posture					
Normal		11	11	12	7
Convulsion					
None		11	11	12	7
Abnormal behavior					
None		11	11	12	7

Table 2-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	10	12	12	8
Posture					
Normal		10	12	12	8
Convulsion					
None		10	12	12	8
Abnormal behavior					
None		10	12	12	8

Table 2-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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 2-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	500
	No. of animals	10	10
Posture			
Normal		10	10
Convulsion			
None		10	9
Moderate		0	1a)
Abnormal behavior			
None		10	10

a): Clonic convulsion

Table 2-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	8
Posture			
Normal		10	8
Convulsion			
None		10	8
Abnormal behavior			
None		10	8

Table 2-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	8
Posture			
Normal		10	8
Convulsion			
None		10	7
Moderate		0	1a)
Abnormal behavior			
None		10	8

a): Clonic convulsion

Table 2-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	7
Posture			
Normal		10	7
Convulsion			
None		10	7
Abnormal behavior			
None		10	7

Table 2-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	7
Posture			
Normal		10	7
Convulsion			
None		10	7
Abnormal behavior			
None		10	7

Table 2-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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 2-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	500
	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 2-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	500
	No. of animals	5	3
Posture			
Normal		5	3
Convulsion			
None		5	3
Abnormal behavior			
None		5	3

Table 2-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	5	3
Posture			
Normal		5	3
Convulsion			
None		5	3
Abnormal behavior			
None		5	3

Table 2-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	10
Some resistance/avoidance		0	0	0	2
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	9	12
Soft		0	0	3	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 2-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	50	150	500
	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 2-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	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	11
Slight		0	0	0	1
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	10	12
Soft		0	0	2	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 2-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	50	150	500
	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	11
Slight		0	0	0	1
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	11	12
Soft		0	0	1	0
Reactivity to handling					
Easy		12	12	12	12

Table 2-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	11	12
Some resistance/avoidance		0	0	1	0
Fur condition					
Normal		12	12	12	12
Skin					
Normal		12	12	12	12
Secretions-Eye, Nose					
Absent		12	12	12	12
Exophthalmos					
Absent		12	12	12	12
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	12	9	12
Soft		0	0	3	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 2-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	50	150	500
	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	9	12
Soft		1	0	3	0
Reactivity to handling					
Easy		11	12	12	12
Slightly awkward		1	0	0	0

Table 2-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	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	11	11
Soft		0	1	1	1
Reactivity to handling					
Easy		12	12	12	12

Table 2-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	12	12	12	11
Ease of removal from cage					
Easy		12	12	12	11
Fur condition					
Normal		12	12	12	11
Skin					
Normal		12	12	12	11
Secretions-Eye, Nose					
Absent		12	12	12	11
Exophthalmos					
Absent		12	12	12	11
Palpebral closure					
Normal		12	12	12	11
Mucosal membranes					
Normal		12	12	12	11
Lacrimation					
Normal		12	12	12	11
Piloerection					
Absent		12	12	12	11
Pupil size					
Normal		12	12	12	11
Salivation					
None		12	12	12	10
Slight		0	0	0	1
Abnormal respiration					
Absent		12	12	12	11
Vocalization					
None		12	12	12	11
Reactivity to handling					
Easy		12	12	12	11

Table 2-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	10
Ease of removal from cage					
Easy		11	11	12	10
Fur condition					
Normal		11	11	12	10
Skin					
Normal		11	11	12	10
Secretions-Eye, Nose					
Absent		11	11	12	10
Exophthalmos					
Absent		11	11	12	10
Palpebral closure					
Normal		11	11	12	10
Mucosal membranes					
Normal		11	11	12	10
Lacrimation					
Normal		11	11	12	10
Piloerection					
Absent		11	11	12	10
Pupil size					
Normal		11	11	12	10
Salivation					
None		11	11	12	9
Slight		0	0	0	1
Abnormal respiration					
Absent		11	11	12	10
Vocalization					
None		11	11	10	9
Soft		0	0	2	1
Reactivity to handling					
Easy		11	11	12	10

Table 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	10
Ease of removal from cage					
Easy		11	11	12	10
Fur condition					
Normal		11	11	12	10
Skin					
Normal		11	11	12	10
Secretions-Eye, Nose					
Absent		11	11	12	10
Exophthalmos					
Absent		11	11	12	10
Palpebral closure					
Normal		11	11	12	10
Mucosal membranes					
Normal		11	11	12	10
Lacrimation					
Normal		11	11	12	10
Piloerection					
Absent		11	11	12	10
Pupil size					
Normal		11	11	12	10
Salivation					
None		11	11	12	10
Abnormal respiration					
Absent		11	11	12	10
Vocalization					
None		11	11	12	10
Reactivity to handling					
Easy		11	11	12	10

Table 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	8
Ease of removal from cage					
Easy		11	11	12	8
Fur condition					
Normal		11	11	12	8
Skin					
Normal		11	11	12	8
Secretions-Eye, Nose					
Absent		11	11	12	8
Exophthalmos					
Absent		11	11	12	8
Palpebral closure					
Normal		11	11	12	8
Mucosal membranes					
Normal		11	11	12	8
Lacrimation					
Normal		11	11	12	8
Piloerection					
Absent		11	11	12	8
Pupil size					
Normal		11	11	12	8
Salivation					
None		11	11	12	7
Slight		0	0	0	1
Abnormal respiration					
Absent		11	11	12	8
Vocalization					
None		10	9	12	8
Soft		1	2	0	0
Reactivity to handling					
Easy		11	11	12	8

Table 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	7
Ease of removal from cage					
Easy		11	11	12	6
Some resistance/avoidance		0	0	0	1
Fur condition					
Normal		11	11	12	7
Skin					
Normal		11	11	12	7
Secretions-Eye, Nose					
Absent		11	11	12	7
Exophthalmos					
Absent		11	11	12	7
Palpebral closure					
Normal		11	11	12	7
Mucosal membranes					
Normal		11	11	12	7
Lacrimation					
Normal		11	11	12	7
Piloerection					
Absent		11	11	12	7
Pupil size					
Normal		11	11	12	7
Salivation					
None		11	11	12	7
Abnormal respiration					
Absent		11	11	12	7
Vocalization					
None		11	11	12	6
Soft		0	0	0	1
Reactivity to handling					
Easy		11	11	12	7

Table 2-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	10	12	12	8
Ease of removal from cage					
Easy		10	12	12	8
Fur condition					
Normal		10	12	12	8
Skin					
Normal		10	12	12	8
Secretions-Eye, Nose					
Absent		10	12	12	8
Exophthalmos					
Absent		10	12	12	8
Palpebral closure					
Normal		10	12	12	8
Mucosal membranes					
Normal		10	12	12	8
Lacrimation					
Normal		10	12	12	8
Piloerection					
Absent		10	12	12	8
Pupil size					
Normal		10	12	12	8
Salivation					
None		10	12	12	8
Abnormal respiration					
Absent		10	12	12	8
Vocalization					
None		10	12	12	8
Reactivity to handling					
Easy		10	12	12	8

Table 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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	9
Soft		0	1
Reactivity to handling			
Easy		10	10

Table 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	10
Ease of removal from cage			
Easy		9	10
Some resistance/avoidance		1	0
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	9
Moderate		0	1
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 2-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	500
	No. of animals	10	8
Ease of removal from cage			
Easy		10	8
Fur condition			
Normal		10	8
Skin			
Normal		10	8
Secretions-Eye, Nose			
Absent		10	8
Exophthalmos			
Absent		10	8
Palpebral closure			
Normal		10	8
Mucosal membranes			
Normal		10	8
Lacrimation			
Normal		10	8
Piloerection			
Absent		10	8
Pupil size			
Normal		10	8
Salivation			
None		10	8
Abnormal respiration			
Absent		10	8
Vocalization			
None		10	5
Soft		0	3
Reactivity to handling			
Easy		10	7
Slightly awkward		0	1

Table 2-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	8
Ease of removal from cage			
Easy		10	8
Fur condition			
Normal		10	8
Skin			
Normal		10	8
Secretions-Eye, Nose			
Absent		10	8
Exophthalmos			
Absent		10	8
Palpebral closure			
Normal		10	8
Mucosal membranes			
Normal		10	8
Lacrimation			
Normal		10	8
Piloerection			
Absent		10	8
Pupil size			
Normal		10	8
Salivation			
None		10	7
Moderate		0	1
Abnormal respiration			
Absent		10	8
Vocalization			
None		10	8
Reactivity to handling			
Easy		10	7
Difficult		0	1

Table 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	7
Ease of removal from cage			
Easy		10	7
Fur condition			
Normal		10	7
Skin			
Normal		10	7
Secretions-Eye, Nose			
Absent		10	7
Exophthalmos			
Absent		10	7
Palpebral closure			
Normal		10	7
Mucosal membranes			
Normal		10	7
Lacrimation			
Normal		10	7
Piloerection			
Absent		10	7
Pupil size			
Normal		10	7
Salivation			
None		10	7
Abnormal respiration			
Absent		10	7
Vocalization			
None		10	7
Reactivity to handling			
Easy		10	7

Table 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	7
Ease of removal from cage			
Easy		10	7
Fur condition			
Normal		10	7
Skin			
Normal		10	7
Secretions-Eye, Nose			
Absent		10	7
Exophthalmos			
Absent		10	7
Palpebral closure			
Normal		10	7
Mucosal membranes			
Normal		10	7
Lacrimation			
Normal		10	7
Piloerection			
Absent		10	7
Pupil size			
Normal		10	7
Salivation			
None		10	7
Abnormal respiration			
Absent		10	7
Vocalization			
None		8	7
Soft		2	0
Reactivity to handling			
Easy		10	7

Table 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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 2-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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 2-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	500
	No. of animals	5	3
Ease of removal from cage			
Easy		5	3
Fur condition			
Normal		5	3
Skin			
Normal		5	3
Secretions-Eye, Nose			
Absent		5	3
Exophthalmos			
Absent		5	3
Palpebral closure			
Normal		5	3
Mucosal membranes			
Normal		5	3
Lacrimation			
Normal		5	3
Piloerection			
Absent		5	3
Pupil size			
Normal		5	3
Salivation			
None		5	3
Abnormal respiration			
Absent		5	3
Vocalization			
None		5	3
Reactivity to handling			
Easy		5	3

Table 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	5	3
Ease of removal from cage			
Easy		5	3
Fur condition			
Normal		5	3
Skin			
Normal		5	3
Secretions-Eye, Nose			
Absent		5	3
Exophthalmos			
Absent		5	3
Palpebral closure			
Normal		5	3
Mucosal membranes			
Normal		5	3
Lacrimation			
Normal		5	3
Piloerection			
Absent		5	3
Pupil size			
Normal		5	3
Salivation			
None		5	3
Abnormal respiration			
Absent		5	3
Vocalization			
None		5	3
Reactivity to handling			
Easy		5	3

Table 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	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± 3	4± 2	4± 2	4± 2
Defecation count (Mean±S.D.)		1± 1	0± 0	0± 0	0± 0
Urination					
None		9	11	11	11
Small amount		3	1	1	1

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 2-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	50	150	500
	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.)		4± 2	3± 2	4± 2	4± 2
Defecation count (Mean±S.D.)		0± 1	0± 0	0± 0	0± 0
Urination					
None		11	12	11	11
Small amount		1	0	1	1

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 2-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	50	150	500
	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	0	1	0
Normal		12	12	11	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	4± 2	4± 2	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 1
Urination					
None		11	10	11	12
Small amount		1	2	1	0

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 2-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	50	150	500
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	5± 2	5± 1	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		9	10	9	9
Small amount		3	2	3	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 2-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	50	150	500
	No. of animals	12	12	12	12
Arousal					
Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior					
None		12	12	12	12
Stereotypy					
None		12	12	12	12
Gait					
Normal		12	12	12	12
Posture					
Normal		12	12	12	12
Grooming					
None		12	12	12	12
Rearing (Mean±S.D.)		4± 2	4± 2	4± 3	4± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		9	10	11	10
Small amount		3	2	1	2

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 2-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	50	150	500
	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	6± 2	6± 1	5± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	11	9
Small amount		1	1	1	3

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 2-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	50	150	500
	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± 3	8± 2	6± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	12
Small amount		0	0	1	0

No significant difference in any treated groups from control group.

Table 2-54 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	12	12	12	11
Arousal					
Normal		12	12	12	11
Convulsion					
None		12	12	12	11
Abnormal behavior					
None		12	12	12	11
Stereotypy					
None		12	12	12	11
Gait					
Normal		12	12	12	11
Posture					
Normal		12	12	12	11
Grooming					
None		12	12	12	11
Rearing (Mean±S.D.)		7± 2	8± 3	6± 2	7± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		12	12	11	10
Small amount		0	0	1	1

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 2-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	50	150	500
	No. of animals	11	11	12	10
Arousal					
Normal		11	11	12	10
Convulsion					
None		11	11	12	10
Abnormal behavior					
None		11	11	12	10
Stereotypy					
None		11	11	12	10
Gait					
Normal		11	11	12	10
Posture					
Normal		11	11	12	10
Grooming					
None		11	11	12	10
Rearing (Mean±S.D.)		7± 3	7± 2	7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	11	8
Small amount		0	0	1	2

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 2-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	50	150	500
	No. of animals	11	11	12	10
Arousal					
Normal		11	11	12	10
Convulsion					
None		11	11	12	10
Abnormal behavior					
None		11	11	12	10
Stereotypy					
None		11	11	12	10
Gait					
Normal		11	11	12	10
Posture					
Normal		11	11	12	10
Grooming					
None		11	11	12	10
Rearing (Mean±S.D.)		7± 2	6± 2	7± 2	8± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	12	8
Small amount		0	0	0	2

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 2-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	50	150	500
	No. of animals	11	11	12	8
Arousal					
Normal		11	11	12	8
Convulsion					
None		11	11	12	8
Abnormal behavior					
None		11	11	12	8
Stereotypy					
None		11	11	12	8
Gait					
Normal		11	11	12	8
Posture					
Normal		11	11	12	8
Grooming					
None		11	11	12	8
Rearing (Mean±S.D.)		5± 2	6± 2	6± 2	8± 3**D
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	10	11	7
Small amount		0	1	1	1

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

Table 2-58 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	No. of animals	11	11	12	7
Arousal					
Normal		11	11	12	7
Convulsion					
None		11	11	12	7
Abnormal behavior					
None		11	11	12	7
Stereotypy					
None		11	11	12	7
Gait					
Normal		11	11	12	7
Posture					
Normal		11	11	12	7
Grooming					
None		11	11	12	7
Rearing (Mean±S.D.)		6± 2	6± 3	5± 1	6± 1
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		11	11	12	7

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 2-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	50	150	500
	No. of animals	10	12	12	8
Arousal					
Normal		10	12	12	8
Convulsion					
None		10	12	12	7
Minor		0	0	0	1a)
Abnormal behavior					
None		10	12	12	8
Stereotypy					
None		10	12	12	8
Gait					
Normal		10	12	12	8
Posture					
Normal		10	12	12	8
Grooming					
None		10	12	12	8
Rearing (Mean±S.D.)		7± 2	7± 2	7± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		10	12	12	8

No significant difference in any treated groups from control group.
a): Clonic convulsion

Table 2-60 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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.)		6± 2	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	9
Small amount		0	1

No significant difference between treated group and control group.

Table 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	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.)		5± 3	7± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	10

No significant difference between treated group and control group.

Table 2-62 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	8
Arousal			
Normal		10	8
Convulsion			
None		10	7
Minor		0	1a)
Abnormal behavior			
None		10	8
Stereotypy			
None		10	8
Gait			
Normal		10	8
Posture			
Normal		10	8
Grooming			
None		10	8
Rearing (Mean±S.D.)		7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	7
Small amount		0	1

No significant difference between treated group and control group.
a): Clonic convulsion

Table 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	10	8
Arousal			
Normal		10	8
Convulsion			
None		10	8
Abnormal behavior			
None		10	8
Stereotypy			
None		10	8
Gait			
Normal		10	8
Posture			
Normal		10	8
Grooming			
None		10	8
Rearing (Mean±S.D.)		7± 2	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	6
Small amount		0	2

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 2-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	500
	No. of animals	10	7
Arousal			
Normal		10	7
Convulsion			
None		10	7
Abnormal behavior			
None		10	7
Stereotypy			
None		10	7
Gait			
Normal		10	7
Posture			
Normal		10	7
Grooming			
None		10	7
Rearing (Mean±S.D.)		8± 2	10± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		9	5
Small amount		1	2

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 2-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	500
	No. of animals	10	7
Arousal			
Normal		10	7
Convulsion			
None		10	7
Abnormal behavior			
None		10	7
Stereotypy			
None		10	7
Gait			
Normal		10	7
Posture			
Normal		10	7
Grooming			
None		10	7
Rearing (Mean±S.D.)		8± 1	9± 3
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		10	7

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 2-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	500
	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.)		3± 1	4± 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 2-67 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	5	5
Arousal			
Normal		5	5
Convulsion			
None		5	5
Abnormal behavior			
None		5	5
Stereotypy			
None		5	5
Gait			
Normal		5	5
Posture			
Normal		5	5
Grooming			
None		5	5
Rearing (Mean±S.D.)		4± 3	6± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		4	5
Small amount		1	0

No significant difference between treated group and control group.

Table 2-68 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
	No. of animals	5	3
Arousal			
Normal		5	3
Convulsion			
None		5	3
Abnormal behavior			
None		5	3
Stereotypy			
None		5	3
Gait			
Normal		5	3
Posture			
Normal		5	3
Grooming			
None		5	3
Rearing (Mean±S.D.)		7± 2	9± 2
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		5	3

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 2-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	500
	No. of animals	5	3
Arousal			
Normal		5	3
Convulsion			
None		5	3
Abnormal behavior			
None		5	3
Stereotypy			
None		5	3
Gait			
Normal		5	3
Posture			
Normal		5	3
Grooming			
None		5	3
Rearing (Mean±S.D.)		7± 1	12± 3**T
Defecation count (Mean±S.D.)		0± 0	0± 0
Urination			
None		4	3
Small amount		1	0

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

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

Parameter	Dose (mg/kg)	0	50	150	500
	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± 6	68±12	63±11	56±15

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 2-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	50	150	500
	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.)		52±10	51±24	53±13	53± 6

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 2-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	500
	No. of animals	5	3
Auditory response			
Normal		5	3
Approach response			
Normal		5	3
Touch response			
Normal		5	3
Tail pinch response			
Normal		5	3
Pupillary reflex			
Pass, both		5	3
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		55±14	44±18

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of male rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	5
Auditory response			
Normal		5	5
Approach response			
Normal		5	5
Touch response			
Normal		5	5
Tail pinch response			
Normal		5	5
Pupillary reflex			
Pass, both		5	5
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		62±19	65±29

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Manipulative test of female rats (Week 2 of recovery)

Parameter	Dose (mg/kg)	0	500
	No. of animals	5	3
Auditory response			
Normal		5	3
Approach response			
Normal		5	3
Touch response			
Normal		5	3
Tail pinch response			
Normal		5	3
Pupillary reflex			
Pass, both		5	3
Aerial righting reflex			
(Total score: Mean±S.D.)		0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		60±15	53±25

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 2-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	1388	533
	S.D.	255	40
50	No.	5	5
	Mean	1199	549
	S.D.	129	61
150	No.	5	5
	Mean	1379	574
	S.D.	296	155
500	No.	5	5
	Mean	1331	547
	S.D.	228	65

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 2-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	1329	644
	S.D.	171	148
50	No.	5	5
	Mean	1127	575
	S.D.	67	112
150	No.	5	5
	Mean	1172	523
	S.D.	151	98
500	No.	5	5
	Mean	1195	539
	S.D.	151	35

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 2-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	1213	512
	S.D.	184	40
500	No.	3	3
	Mean	1049	538
	S.D.	366	56

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 2-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	1294	685
	S.D.	254	71
500	No.	5	5
	Mean	1195	569*
	S.D.	201	66T

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

Table 2-79 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1227	610
	S.D.	103	125
500	No.	3	3
	Mean	1075	613
	S.D.	114	128

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 2-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	401	325	246	132	77	106	1287
	S.D.	50	76	40	123	95	28	220
50	No.	5	5	5	5	5	5	5
	Mean	400	313	288	189	133	129	1451
	S.D.	26	83	55	90	97	81	213
150	No.	5	5	5	5	5	5	5
	Mean	431	319	130	248	223	124	1476
	S.D.	28	55	63	96	121	78	200
500	No.	5	5	5	5	5	5	5
	Mean	414	373	315	285	155	147	1689*
	S.D.	57	68	137	86	102	49	323D

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 2-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	392	244	163	84	66	40	988
	S.D.	42	156	130	96	83	35	465
50	No.	5	5	5	5	5	5	5
	Mean	406	284	196	102	127	70	1186
	S.D.	72	67	130	109	122	112	438
150	No.	5	5	5	5	5	5	5
	Mean	362	161	113	102	103	107	947
	S.D.	31	156	144	70	86	127	492
500	No.	5	5	5	5	5	5	5
	Mean	312	167	125	120	201	157	1081
	S.D.	125	107	116	106	117	126	601

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 2-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	430	385	358	322	291	160	1945
	S.D.	36	74	76	52	104	149	399
500	No.	3	3	3	3	3	3	3
	Mean	372	383	330	344	230	292	1950
	S.D.	58	29	44	36	134	115	311

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 2-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	395	342	288	253	238	132	1648
	S.D.	18	21	58	117	139	143	373
500	No.	5	5	5	5	5	5	5
	Mean	397	347	296	194	148	184	1566
	S.D.	53	68	102	137	99	121	328

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 2-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	383	296	323	287	188	233	1708
	S.D.	48	41	62	25	54	145	132
500	No.	3	3	3	3	3	3	3
	Mean	409	287	294	279	170	219	1659
	S.D.	28	20	56	38	125	171	377

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 2-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	390	411	433	447	469	492	505	116
	S.D.	24	27	30	33	37	39	39	23
	No.	12	12	12	12	12	12	12	12
50	Mean	390	412	435	453	478	499	512	122
	S.D.	28	32	33	30	32	33	35	23
	No.	12	12	12	12	12	12	12	12
150	Mean	392	416	437	453	475	498	508	116
	S.D.	22	29	30	33	33	36	37	22
	No.	12	12	12	12	12	12	12	12
500	Mean	391	403	426	436	456	477	488	97
	S.D.	28	30	33	34	39	44	46	23

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 2-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	249	261	270	20
	S.D.	13	13	16	8
	No.	12	12	12	12
50	Mean	249	263	270	21
	S.D.	14	15	15	9
	No.	12	12	12	12
150	Mean	252	259	265	13
	S.D.	14	12	13	9
	No.	12	12	11a)	11
500	Mean	252	258	268	17
	S.D.	10	13	13	11

Unit: g
No.: No. of animals
a): One animal died on day 10 of administration.
No significant difference in any treated groups from control group.

Table 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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.	11	11	11	11	11
0	Mean	278	306	343	425	147
	S.D.	14	17	17	22	14
	No.	11b)	11	11	11	11
50	Mean	278	306	344	423	145
	S.D.	16	16	20	21	14
	No.	12	12	12	12	12
150	Mean	272	301	335	416	144
	S.D.	13	11	15	17	15
	No.	10b)	10	8c)	7d)	7
500	Mean	276	299	332	397*	117**
	S.D.	16	17	23	28D	19D

Unit: g
No.: No. of dams
a): Gestation day
b): Data from one dam in which the signs of copulation were overlooked were excluded from statistical analysis.
c): Two dams died on gestation days 12 and 13.
d): One dam died on gestation day 17.
*: $p<0.05$; **: $p<0.01$ (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 2-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.	11	10b)	10
0	Mean	317	342	18
	S.D.	26	19	15
	No.	12	12	12
50	Mean	322	339	17
	S.D.	28	20	16
	No.	12	12	12
150	Mean	312	326	14
	S.D.	18	29	18
	No.	8	8	8
500	Mean	310	326	17
	S.D.	29	27	11

Unit: g
No.: No. of dams
a): Lactation day
b): One dam was sacrificed on day 2 of lactation 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 2-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
0	No.	10	10	10	10	10	10	10	10
	Mean	254	263	271	278	287	294	298	44
	S.D.	16	16	18	18	20	18	22	16
500	No.	10	10	10	8a)	7b)	7	7	7
	Mean	251	261	272	282	290	297	300	49
	S.D.	13	15	19	19	29	26	25	20

Unit: g
No.: No. of animals
a): Two animals died on day 15 of administration.
b): One animal died on day 29 of administration.
No significant difference between treated group and control group.

Table 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
0	No.	5	5	5	5
	Mean	518	520	531	13
	S.D.	46	45	45	5
500	No.	5	5	5	5
	Mean	510	527	541	31**
	S.D.	58	55	62	9T

Unit: g
No.: No. of animals
**: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
0	No.	5	5	5	5
	Mean	301	302	302	1
	S.D.	25	31	27	3
500	No.	3	3	3	3
	Mean	299	303	306	7
	S.D.	11	20	17	7

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 2-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	22	21	21	21	22	22
	S.D.	3	3	3	2	3	3
	No.	12	12	12	12	12	12
50	Mean	22	21	21	20	22	22
	S.D.	3	3	2	2	2	2
	No.	12	12	12	12	12	12
150	Mean	24	23	22	22	22	23
	S.D.	3	3	2	2	3	2
	No.	12	12	12	12	12	12
500	Mean	17**	22	23	23	23	23
	S.D.	4D	4	3	3	4	3

Unit: g/rat/day
No.: No. of animals
**: p<0.01 (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 2-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	16	18	16
	S.D.	3	2	2
	No.	12	12	12
50	Mean	16	18	17
	S.D.	3	2	2
	No.	12	12	12
150	Mean	16	16*	15
	S.D.	3	3D	2
	No.	12	12	11a)
500	Mean	12**	15**	16
	S.D.	3D	2D	2

Unit: g/rat/day
No.: No. of animals
a): One animal died on day 10 of administration.
*: $p<0.05$; **: $p<0.01$ (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 2-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)
0	No.	11	11	11	11
	Mean	16	21	22	19
	S.D.	2	3	2	1
50	No.	11b)	11	11	11
	Mean	16	20	21	18
	S.D.	2	2	3	3
150	No.	12	12	12	12
	Mean	16	21	21	19
	S.D.	2	1	3	2
500	No.	10b)	10	8c)	7d)
	Mean	17	20	21	18
	S.D.	2	3	4	3

Unit: g/rat/day
No.: No. of dams
a): Gestation day
b): Data from one dam in which the signs of copulation were overlooked were excluded from statistical analysis.
c): Two dams died on gestation days 12 and 13.
d): One dam died on gestation day 17.
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 2-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)
	No.	10b)	10
0	Mean	18	35
	S.D.	9	7
	No.	12	12
50	Mean	20	36
	S.D.	5	4
	No.	12	12
150	Mean	21	37
	S.D.	8	9
	No.	8	8
500	Mean	24	36
	S.D.	4	4

Unit: g/rat/day
No.: No. of dams
a): Lactation day
b): One dam was sacrificed on day 2 of lactation 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 2-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
0	No.	10	10	10	10	10	10
	Mean	16	16	15	15	16	16
	S.D.	3	2	2	3	2	3
500	No.	10	10	10	7a)	7	7
	Mean	12*	16	17*	16	17	16
	S.D.	3T	1	1T	4	3	3

Unit: g/rat/day
No.: No. of animals
a): Three animals died on days 15 and 29 of administration.
*: $p<0.05$ (Significant difference from control group)
T: Student's t-test

Table 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of male rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
	No.	5	5	5
0	Mean	22	26	28
	S.D.	3	2	3
	No.	5	5	5
500	Mean	22	32**	32
	S.D.	3	3T	4

Unit: g/rat/day
No.: No. of animals
**: p<0.01 (Significant difference from control group)
T: Student's t-test

Table 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Food consumption of female rats (Recovery period)

Dose mg/kg		Day of recovery 1	8	14
	No.	5	5	5
0	Mean	15	19	19
	S.D.	2	4	1
	No.	3	3	3
500	Mean	17	22	23**
	S.D.	3	6	2T

Unit: g/rat/day
No.: No. of animals
**: p<0.01 (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 2-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	2	1	0	0	2	0	0	1	4	0	0	0	5	0	0	5	0	0	0	0
50	5	0	0	0	0	0	1	2	0	2	1	0	1	3	0	0	1	4	0	0	5	0	0	0	0
150	5	0	0	0	0	3	1	0	1	0	0	1	0	4	0	0	1	2	2	0	5	0	0	0	0
500	5	0	0	0	1	4	0	0	0	0	0	1	4	0	0	1	2	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 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	3	1	1	0	4	1	0	0	0	5	0
50	5	2	3	0	0	0	4	1	0	0	5	0	0	0	0	5	0
150	5	3	1	0	0	1	3	2	0	0	5	0	0	0	0	5	0
500	5	4	0	0	0	1	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 2-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 2-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	13.1	1686	0.96	3.17	1.29
		S.D.	8	5.8	590	0.22	0.72	0.32
50	5	Mean	38	11.5	1885	1.09	3.43	1.40
		S.D.	8	3.5	292	0.39	0.98	0.40
150	5	Mean	41	15.7	1525	1.09	3.51	1.55
		S.D.	7	6.6	425	0.11	0.46	0.11
500	5	Mean	52	20.8	1444	1.49	3.94	1.98*
		S.D.	6	6.0	259	0.53	1.04	0.51D

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

Table 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of female rats (Satellite group, 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	2	2	0	0	1	0	0	0	0	4	1	0	0	4	1	0	0	5	0	0	0	0
500	3	0	0	2	1	0	0	0	0	0	1	1	1	0	0	1	2	0	0	0	3	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 2-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	5	0	0	0	0	2	3	0	0	5	0	0	0	0	5	0
500	3	3	0	0	0	0	3	0	0	0	3	0	0	0	0	3	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 2-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 2-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	27	7.3	2008	0.75	2.12	0.93
		S.D.	6	3.8	440	0.33	0.59	0.32
500	3	Mean	39	11.9	1185*	0.78	1.85	0.97
		S.D.	10	4.2	377T	0.09	0.18	0.25

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

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

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	0	3	2	0	0	1	2	2	0	1	0	4	0	0	5	0	0	0	0
500	5	0	0	0	0	0	1	1	2	1	0	2	3	0	0	0	3	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 2-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	1	4	0	0	0	4	1	0	0	5	0	0	0	0	5	0
500	5	4	0	0	0	1	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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Urinalysis of male rats (Week 2 of recovery)

| | | URINE SEDIMENT | | |

Table 5-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	16.0	1836	1.31	4.69	1.80
		S.D.	8	3.6	289	0.14	0.93	0.29
500	5	Mean	55	22.6*	1602	1.62	5.82	2.40*
		S.D.	8	4.3T	211	0.34	0.66	0.28T

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

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

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	1	2	1	1	0	0	0	1	1	2	1	0	3	2	0	0	0	5	0	0	0	0
500	3	0	0	0	0	1	0	0	1	1	0	2	1	0	0	0	3	0	0	0	3	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 2-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	5	0	0	0	5	0	0	0	0	5	0
500	3	3	0	0	0	0	3	0	0	0	3	0	0	0	0	3	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 2-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 2-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	34	7.0	2596	0.84	2.61	1.09
		S.D.	5	3.3	884	0.24	0.56	0.25
500	3	Mean	31	9.2	2185	1.07	2.98	1.25
		S.D.	3	2.0	488	0.13	0.03	0.12

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 2-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	863	15.0	43.2	50.0	17.4	34.7	2.2	99.7	14.6	20.5	242
		S.D.	23	0.4	1.3	0.9	0.4	0.3	0.2	12.2	1.1	3.1	9
50	5	Mean	849	15.0	43.0	50.6	17.6	34.8	2.0	105.9	15.0	17.3	274
		S.D.	21	0.4	1.1	0.6	0.1	0.6	0.1	7.7	1.5	2.8	46
150	5	Mean	820	14.8	42.9	52.3**	18.1*	34.5	2.4	108.2	17.0	19.7	267
		S.D.	34	0.3	1.0	1.1D	0.5D	0.3	0.2	14.8	3.5	2.0	32
500	5	Mean	844	14.4	42.1	49.8	17.0	34.2	1.9	107.3	18.4*	21.8	324**
		S.D.	33	0.6	2.3	1.2	0.4	0.6	0.6	11.9	1.8D	2.8	27D

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

Table 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	80.6	72.3	23.4	1.2	0.3	2.0	0.8	58.9	18.3	0.9	0.3	1.6	0.7
		S.D.	18.8	6.9	6.5	0.6	0.1	0.7	0.4	17.8	4.0	0.5	0.1	0.4	0.3
50	5	Mean	61.5	70.5	24.1	1.7	0.3	2.6	0.9	43.6	14.6	1.0	0.2	1.6	0.5
		S.D.	9.1	5.9	5.9	0.5	0.1	1.1	0.3	8.9	2.6	0.3	0.0	0.7	0.2
150	5	Mean	92.2	73.9	21.9	1.2	0.3	1.9	0.8	69.3	19.2	1.0	0.3	1.6	0.7
		S.D.	29.5	6.0	4.9	0.7	0.1	0.7	0.5	26.4	3.2	0.4	0.2	0.3	0.3
500	5	Mean	82.0	76.7	19.4	1.1	0.3	1.8	0.6	63.1	15.7	0.9	0.3	1.5	0.5
		S.D.	14.3	6.1	5.2	0.3	0.1	0.4	0.3	13.8	4.2	0.2	0.1	0.3	0.3

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

Table 6-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	713	13.2	39.1	54.8	18.5	33.8	7.6	152.0	11.2	12.9	296
		S.D.	28	0.6	2.0	1.4	0.5	0.2	1.0	20.9	0.7	1.4	71
50	5	Mean	717	13.4	39.7	55.3	18.7	33.8	7.9	156.9	11.7	14.7	300
		S.D.	17	0.6	2.2	3.1	0.9	0.4	0.8	8.4	0.5	1.9	64
150	5	Mean	730	13.6	40.1	55.0	18.7	33.9	6.5	149.4	11.9	15.8*	241
		S.D.	20	0.5	1.3	1.2	0.5	0.4	0.7	15.3	0.8	0.6D	33
500	5	Mean	675	13.0	38.0	56.4	19.2	34.1	7.2	163.9	11.2	14.2	244
		S.D.	42	0.5	0.8	3.2	0.6	1.0	2.7	21.9	0.5	2.1	23

*: $p<0.05$ (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 2-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	112.6	57.1	38.5	0.5	0.3	2.6	1.1	62.9	44.7	0.5	0.3	2.9	1.3
		S.D.	36.8	10.7	11.4	0.3	0.1	1.2	0.7	18.7	26.3	0.2	0.2	1.6	1.0
50	5	Mean	107.7	55.8	40.2	0.6	0.3	2.4	0.7	60.4	43.1	0.6	0.3	2.5	0.8
		S.D.	13.3	4.3	4.1	0.3	0.1	0.8	0.3	10.6	5.4	0.4	0.1	0.8	0.3
150	5	Mean	93.2	56.4	38.6	0.7	0.2	3.4	0.7	52.4	36.2	0.7	0.2	3.1	0.7
		S.D.	19.0	8.8	8.9	0.3	0.1	0.7	0.2	12.8	10.8	0.4	0.1	0.5	0.2
500	5	Mean	122.5	58.4	36.3	0.3	0.3	3.4	1.3	70.4	45.6	0.4	0.4	4.2	1.6
		S.D.	27.4	5.9	6.7	0.1	0.1	1.5	0.5	9.3	17.4	0.1	0.2	2.0	0.7

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 2-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	821	15.0	43.3	52.8	18.3	34.7	2.4	104.4	11.4	15.9	196
		S.D.	28	0.8	2.2	1.3	0.4	0.4	0.4	6.0	0.5	2.3	10
500	4	Mean	770*	14.5	41.4	53.8	18.9	35.0	2.3	113.9	10.9	15.5	209
		S.D.	26T	0.6	2.0	3.0	1.0	0.5	0.5	17.1	0.5	1.0	17

*: $p<0.05$ (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 2-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	58.1	79.3	17.1	1.3	0.3	1.5	0.6	46.7	9.4	0.7	0.2	0.8	0.3
		S.D.	18.4	5.4	5.0	0.5	0.1	0.5	0.4	17.2	2.3	0.2	0.1	0.1	0.2
500	4	Mean	76.2	79.7	16.1	1.4	0.3	2.0	0.7	60.5	12.5	1.0	0.2	1.5**	0.5
		S.D.	18.3	2.2	2.4	0.4	0.1	0.4	0.3	13.6	4.2	0.2	0.1	0.3T	0.4

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

Table 6-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	940	15.8	46.0	49.0	16.9	34.4	1.7	90.7	17.0	21.3	295
		S.D.	24	0.2	0.7	1.5	0.5	0.2	0.2	5.8	1.0	1.3	26
500	5	Mean	904	15.4	44.9	49.6	17.0	34.4	1.9	98.5	17.2	22.5	285
		S.D.	27	0.5	1.6	0.7	0.3	0.4	0.2	7.3	2.1	1.7	20

No significant difference between treated group and control group.

Table 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	68.3	75.0	19.9	1.4	0.4	2.2	1.1	51.9	13.0	1.0	0.3	1.5	0.8
		S.D.	21.3	7.8	8.0	0.8	0.1	0.6	0.7	18.9	4.3	1.0	0.1	0.4	0.6
500	5	Mean	83.0	75.6	19.4	1.9	0.4	1.9	0.9	63.4	15.4	1.5	0.3	1.6	0.7
		S.D.	23.4	8.4	7.7	0.6	0.2	0.7	0.3	20.5	5.1	0.6	0.3	0.9	0.1

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 2-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	879	16.0	45.7	52.0	18.2	34.9	1.7	102.9	12.1	17.2	180
		S.D.	29	0.2	0.6	1.5	0.7	0.5	0.3	16.1	0.5	1.7	13
500	3	Mean	857	15.6	44.0*	51.4	18.2	35.5	1.7	111.8	11.5	15.3	202
		S.D.	45	0.2	0.7T	2.6	0.9	0.3	0.6	6.8	0.5	1.7	21

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

Table 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	56.5	75.0	20.5	1.7	0.3	1.8	0.7	42.2	11.7	1.0	0.2	1.0	0.4
		S.D.	13.8	7.7	7.2	0.8	0.1	0.7	0.2	10.6	4.8	0.5	0.1	0.5	0.1
500	3	Mean	65.3	73.0	22.2	1.8	0.3	1.9	0.8	48.4	13.8	1.1	0.2	1.2	0.5
		S.D.	21.0	10.8	9.7	0.8	0.1	0.9	0.3	21.1	6.4	0.3	0.1	0.6	0.3

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 2-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	56	27	43	1	351	15.0	45	39	79	0.1	156
		S.D.	7	4	6	1	74	8.6	7	7	8	0.0	11
50	5	Mean	56	24	44	1	358	7.6	47	31	75	0.1	138
		S.D.	2	4	5	1	85	6.1	8	12	12	0.0	18
150	5	Mean	60	27	50	1	421	6.0	48	41	80	0.1	140
		S.D.	10	5	9	0	99	3.6	7	16	10	0.1	14
500	5	Mean	56	28	50	1	432	4.1*	46	32	75	0.1	118**
		S.D.	5	3	12	0	70	1.5D	12	18	16	0.1	13D

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

Table 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	0.32	143	4.7	107	9.6	6.1	5.5	3.2	1.34
		S.D.	2	0.03	1	0.1	2	0.3	0.5	0.1	0.1	0.10
50	5	Mean	13	0.31	143	4.7	106	9.9	6.1	5.6	3.1	1.28
		S.D.	1	0.05	1	0.3	2	0.4	0.4	0.2	0.1	0.13
150	5	Mean	13	0.29	142	4.8	105	9.7	6.4	5.5	3.0	1.20
		S.D.	2	0.05	2	0.2	2	0.5	0.4	0.2	0.1	0.07
500	5	Mean	13	0.32	144	4.6	105	9.9	6.7	5.9**	3.2	1.19
		S.D.	1	0.05	1	0.3	1	0.6	0.8	0.1D	0.1	0.07

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

Table 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	79	53	53	1	328	17.3	55	68	109	0.1	117
		S.D.	10	10	17	0	106	9.0	8	48	14	0.0	7
50	5	Mean	82	53	55	1	268	14.0	52	44	102	0.1	118
		S.D.	18	10	15	1	131	3.9	13	18	21	0.0	10
150	5	Mean	79	50	69	1	239	23.0	51	30	96	0.1	118
		S.D.	11	9	40	1	22	10.0	5	18	6	0.0	6
500	5	Mean	73	47	45	1	197	21.1	67	43	119	0.1	116
		S.D.	9	8	12	0	56	17.3	6	15	8	0.1	4

No significant difference in any treated groups from control group.

Table 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	15	0.35	141	4.0	108	10.1	6.3	6.0	3.4	1.28
		S.D.	2	0.02	2	0.1	2	0.3	1.0	0.3	0.2	0.14
50	5	Mean	15	0.35	141	4.1	107	10.4	6.9	6.0	3.5	1.38
		S.D.	1	0.02	1	0.3	2	0.3	0.5	0.3	0.2	0.09
150	5	Mean	13	0.33	140	4.6**	106	10.2	6.8	6.1	3.4	1.25
		S.D.	1	0.04	1	0.2D	1	0.2	0.4	0.2	0.1	0.06
500	5	Mean	13	0.31	142	4.3	105	10.5	6.9	6.2	3.5	1.25
		S.D.	4	0.02	2	0.2	2	0.3	0.4	0.3	0.2	0.08

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

Table 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	67	28	56	1	346	12.4	60	17	115	0.1	135
		S.D.	7	8	8	1	132	1.8	16	8	26	0.0	16
500	4	Mean	50**	23	55	1	172*	6.4**	66	31	119	0.1	125
		S.D.	5T	4	16	0	13AT	3.2T	11	13	16	0.1	23

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

Table 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	14	0.37	141	4.2	107	9.6	3.8	6.1	3.6	1.43
		S.D.	1	0.01	1	0.2	2	0.2	0.6	0.4	0.2	0.10
500	4	Mean	16	0.36	141	4.4	105	10.1	4.9*	6.4	3.7	1.38
		S.D.	1	0.04	1	0.3	1	0.4	0.6T	0.1	0.1	0.11

*: $p<0.05$ (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 2-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	64	34	43	0	354	13.1	46	39	81	0.1	116
		S.D.	6	4	4	0	9	14.5	8	20	18	0.0	8
500	5	Mean	69	31	51*	1	352	6.1	49	37	82	0.0	124
		S.D.	12	5	6T	1	126	3.9	10	21	16	0.1	4

*: $p<0.05$ (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 2-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	16	0.35	144	4.6	107	9.7	5.9	6.1	3.2	1.09
		S.D.	1	0.02	1	0.1	2	0.1	0.5	0.2	0.1	0.06
500	5	Mean	16	0.33	143	4.5	107	9.5	6.0	6.0	3.1	1.11
		S.D.	2	0.03	1	0.2	1	0.4	0.6	0.5	0.1	0.14

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 2-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	78	36	53	1	182	9.8	68	15	125	0.1	127
		S.D.	14	13	19	0	50	3.5	12	3	14	0.0	4
500	3	Mean	86	44	66	1	173	7.3	76	17	130	0.1	128
		S.D.	30	28	21	0	17	2.7	5	2	10	0.0	4

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 2-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	18	0.40	143	4.6	109	9.8	5.3	6.3	3.6	1.32
		S.D.	2	0.04	1	0.3	1	0.3	0.4	0.2	0.2	0.09
500	3	Mean	18	0.42	142	4.6	107	9.9	5.4	6.5	3.5	1.17*
		S.D.	2	0.01	1	0.1	2	0.1	0.1	0.2	0.1	0.04T

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

Table 7-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Hormones of male rats (End of administration)

Dose mg/kg	No.		T^3 ng/dL	T^4 µg/dL	TSH ng/mL
0	5	Mean	71.1	4.9	13.08
		S.D.	13.8	1.7	7.79
50	5	Mean	70.8	5.5	25.51
		S.D.	10.7	0.6	22.22
150	5	Mean	75.1	5.2	22.46
		S.D.	18.4	1.0	10.12
500	5	Mean	73.2	4.5	24.22
		S.D.	6.2	0.6	11.75

No significant difference in any treated groups from control group.

Table 7-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Hormones of female rats (Lactation day 5)

Dose mg/kg	No.		T^3 ng/dL	T^4 µg/dL	TSH ng/mL
0	5	Mean	70.8	3.6	25.15
		S.D.	16.3	0.7	11.13
50	5	Mean	75.7	4.3	22.34
		S.D.	15.7	1.2	7.02
150	5	Mean	67.0	3.3	10.87
		S.D.	11.6	0.9	5.14
500	5	Mean	61.8	3.6	23.03
		S.D.	11.1	0.4	11.17

No significant difference in any treated groups from control group.

Table 7-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Hormones of female rats (Satellite group, End of administration)

Dose mg/kg	No.		T^3 ng/dL	T^4 µg/dL	TSH ng/mL
0	5	Mean	66.6	3.9	4.17
		S.D.	7.5	0.7	3.16
500	4	Mean	59.5	3.8	4.62
		S.D.	11.5	0.7	1.55

No significant difference between treated group and control group.

Table 7-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Hormones of male rats (End of recovery)

Dose mg/kg	No.		T^3 ng/dL	T^4 µg/dL	TSH ng/mL
0	5	Mean	71.4	5.1	14.41
		S.D.	8.7	0.2	5.38
500	5	Mean	65.0	4.9	23.20
		S.D.	9.6	0.6	25.29

No significant difference between treated group and control group.

Table 7-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Hormones of female rats (End of recovery)

Dose mg/kg	No.		T^3 ng/dL	T^4 µg/dL	TSH ng/mL
0	5	Mean	91.9	2.9	9.65
		S.D.	14.1	0.4	6.26
500	3	Mean	95.8	3.4	16.27
		S.D.	21.2	0.8	5.80

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 2-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	473	2.10	13.2	23.3	256	1.41	11.98
		S.D.	37	0.08	2.4	2.1	74	0.07	1.16
	50	No.	12	12	12	12	12	12	12
		Mean	489	2.14	14.1	22.7	285	1.46	13.67*
		S.D.	33	0.08	1.5	4.1	58	0.12	1.56D
	150	No.	12	12	12	12	12	12	12
		Mean	482	2.11	13.5	23.6	271	1.48	13.81*
		S.D.	33	0.08	1.6	4.2	42	0.14	1.47D
	500	No.	7	7	7	7	7	7	7
		Mean	442	2.11	13.5	23.7	213	1.35	13.67
		S.D.	28	0.07	1.0	4.7	47	0.14	0.88
Relative	0	No.		7	7	7	7	7	7
		Mean		0.45	2.8	4.9	54	0.30	2.53
		S.D.		0.03	0.3	0.6	15	0.02	0.10
	50	No.		12	12	12	12	12	12
		Mean		0.44	2.9	4.6	58	0.30	2.79*
		S.D.		0.03	0.2	0.8	12	0.02	0.18D
	150	No.		12	12	12	12	12	12
		Mean		0.44	2.8	4.9	57	0.31	2.87**
		S.D.		0.03	0.2	0.8	10	0.02	0.24D
	500	No.		7	7	7	7	7	7
		Mean		0.48	3.1	5.4	48	0.31	3.10**
		S.D.		0.03	0.3	1.2	9	0.02	0.10D

*: $p<0.05$; **: $p<0.01$ (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 2-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	3.14	61	3.33	1354	1.82	1.30
		S.D.	0.12	0.18	10	0.31	106	0.16	0.25
		No.	12	12	12	12	12	12	12
	50	Mean	0.72	3.48	65	3.43	1366	1.78	1.26
		S.D.	0.07	0.42	8	0.35	127	0.29	0.18
		No.	12	12	12	12	12	12	12
	150	Mean	0.68	3.61	65	3.30	1310	1.84	1.26
		S.D.	0.08	0.38	14	0.25	144	0.32	0.23
		No.	7	7	7	7	7	7	7
	500	Mean	0.65	3.81*	67	3.13	1274	1.69	1.25
		S.D.	0.08	0.65D	10	0.25	131	0.15	0.16
		No.	7	7	7	7	7	7	7
Relative	0	Mean	0.16	0.66	13	0.71	288	0.38	0.27
		S.D.	0.02	0.03	2	0.06	31	0.02	0.03
		No.	12	12	12	12	12	12	12
	50	Mean	0.15	0.71*	14	0.70	280	0.37	0.26
		S.D.	0.01	0.06ST	1	0.06	25	0.06	0.03
		No.	12	12	12	12	12	12	12
	150	Mean	0.14	0.75*	14	0.69	273	0.38	0.27
		S.D.	0.02	0.07ST	3	0.06	38	0.07	0.06
		No.	7	7	7	7	7	7	7
	500	Mean	0.15	0.86**	15	0.71	290	0.39	0.29
		S.D.	0.02	0.13ST	2	0.08	42	0.04	0.05

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

Table 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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.	10	10	10	10	10	10	10
		Mean	312	1.98	17.2	16.3	199	1.01	9.77
		S.D.	18	0.02	2.3	3.1	60	0.09	0.53
	50	No.	12	12	12	12	12	12	12
		Mean	306	1.97	18.3	17.2	166	0.99	10.19
		S.D.	18	0.05	1.3	2.1	57	0.07	0.63
	150	No.	12	12	12	12	12	12	12
		Mean	293	1.98	18.7	18.2	175	0.97	10.12
		S.D.	25	0.08	3.4	3.8	65	0.06	0.94
	500	No.	8	8	8	8	8	8	8
		Mean	290	1.99	16.6	17.4	114*	0.95	11.08**
		S.D.	24	0.05	1.9	2.8	44D	0.09	1.15D
Relative	0	No.		10	10	10	10	10	10
		Mean		0.64	5.5	5.2	63	0.32	3.14
		S.D.		0.04	0.8	1.0	16	0.02	0.20
	50	No.		12	12	12	12	12	12
		Mean		0.65	6.0	5.6	54	0.32	3.33
		S.D.		0.03	0.3	0.8	17	0.02	0.18
	150	No.		12	12	12	12	12	12
		Mean		0.68	6.4	6.2	59	0.33	3.45**
		S.D.		0.06	1.0	1.1	19	0.02	0.19D
	500	No.		8	8	8	8	8	8
		Mean		0.69	5.7	6.0	39*	0.33	3.81**
		S.D.		0.05	0.6	0.8	13D	0.01	0.14D

*: $p<0.05$; **: $p<0.01$ (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 2-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.	10	10	10	10	10
		Mean	0.65	2.04	71	100.9	742
		S.D.	0.13	0.12	5	6.4	169
	50	No.	12	12	12	12	12
		Mean	0.66	2.10	80	102.1	720
		S.D.	0.10	0.08	12	19.4	100
	150	No.	12	12	12	12	12
		Mean	0.64	2.10	80	103.4	728
		S.D.	0.13	0.18	9	12.6	85
	500	No.	8	8	8	8	8
		Mean	0.61	2.14	97**	102.9	660
		S.D.	0.11	0.16	13D	16.2	96
Relative	0	No.	10	10	10	10	10
		Mean	0.21	0.66	23	32.5	239
		S.D.	0.05	0.05	2	3.3	55
	50	No.	12	12	12	12	12
		Mean	0.22	0.69	26	33.2	235
		S.D.	0.03	0.04	5	5.1	30
	150	No.	12	12	12	12	12
		Mean	0.22	0.72*	27*	35.4	249
		S.D.	0.08	0.08D	4D	4.6	29
	500	No.	8	8	8	8	8
		Mean	0.21	0.74*	34**	35.3	227
		S.D.	0.04	0.02D	4D	3.3	28

*: $p<0.05$; **: $p<0.01$ (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 2-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	280	1.97	16.2	14.4	362	0.94	7.10
		S.D.	15	0.06	2.7	2.7	65	0.05	0.59
	500	No.	4	4	4	4	4	4	4
		Mean	278	2.04	17.2	18.3	246*	0.98	8.74*
		S.D.	32	0.04	1.0	3.6	47T	0.13	1.18T
Relative	0	No.		5	5	5	5	5	5
		Mean		0.71	5.8	5.1	130	0.34	2.54
		S.D.		0.04	0.8	0.9	23	0.02	0.17
	500	No.		4	4	4	4	4	4
		Mean		0.74	6.2	6.6*	89*	0.36	3.14**
		S.D.		0.07	0.3	0.7T	13T	0.03	0.11T

*: $p<0.05$; **: $p<0.01$ (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 2-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	0.54	1.89	74	84.0	603
		S.D.	0.08	0.15	13	12.7	117
	500	No.	4	4	4	4	4
		Mean	0.53	1.98	90	98.5	578
		S.D.	0.04	0.14	13	11.2	125
Relative	0	No.	5	5	5	5	5
		Mean	0.20	0.68	27	30.2	215
		S.D.	0.04	0.05	5	5.7	36
	500	No.	4	4	4	4	4
		Mean	0.19	0.72	33	35.9	210
		S.D.	0.03	0.05	5	6.4	49

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 2-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	500	2.13	12.8	20.4	217	1.44	12.12
		S.D.	47	0.06	0.7	4.4	54	0.15	1.43
	500	No.	5	5	5	5	5	5	5
		Mean	506	2.22	13.9	26.1	286	1.49	13.49
		S.D.	55	0.15	0.9	4.3	117	0.06	2.22
Relative	0	No.		5	5	5	5	5	5
		Mean		0.43	2.6	4.1	44	0.29	2.42
		S.D.		0.04	0.3	0.6	13	0.03	0.20
	500	No.		5	5	5	5	5	5
		Mean		0.44	2.8	5.2	57	0.29	2.65
		S.D.		0.04	0.3	1.1	22	0.02	0.17

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 2-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	0.70	3.29	58	3.14	1293	1.86	1.40
		S.D.	0.03	0.42	5	0.16	67	0.39	0.34
	500	No.	5	5	5	5	5	5	5
		Mean	0.77	3.83*	64	3.10	1311	2.07	1.40
		S.D.	0.12	0.31T	8	0.28	106	0.35	0.15
Relative	0	No.	5	5	5	5	5	5	5
		Mean	0.14	0.66	12	0.63	259	0.37	0.28
		S.D.	0.01	0.05	2	0.03	20	0.08	0.08
	500	No.	5	5	5	5	5	5	5
		Mean	0.15*	0.76*	13	0.62	262	0.41	0.28
		S.D.	0.01T	0.05T	1	0.09	39	0.07	0.04

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

Table 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	286	1.93	17.2	17.7	224	0.94	7.05
		S.D.	27	0.15	1.9	3.8	48	0.10	0.80
		No.	3	3	3	3	3	3	3
	500	Mean	286	2.01	17.1	16.1	329	0.89	7.15
		S.D.	18	0.04	2.7	3.0	93	0.10	1.07
		No.		5	5	5	5	5	5
Relative	0	Mean		0.68	6.0	6.2	77	0.33	2.46
		S.D.		0.07	0.3	1.5	12	0.02	0.12
		No.		3	3	3	3	3	3
	500	Mean		0.71	6.0	5.7	114*	0.31	2.50
		S.D.		0.04	0.6	1.2	25T	0.03	0.25

*: $p<0.05$ (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 2-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	0.52	1.93	73	85.2	564
		S.D.	0.05	0.17	11	15.5	98
	500	No.	3	3	3	3	3
		Mean	0.53	1.88	86	82.6	626
		S.D.	0.07	0.15	14	12.9	156
Relative	0	No.	5	5	5	5	5
		Mean	0.18	0.68	25	29.7	201
		S.D.	0.02	0.07	3	3.8	52
	500	No.	3	3	3	3	3
		Mean	0.19	0.66	30	29.1	220
		S.D.	0.03	0.04	5	5.5	57

No significant difference between treated group and control group.

R-1105

Table 9-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
Findings	Number:	7	12	12	7
Kidney					
Large		0	0	3	1
Liver					
Large		0	0	2	0
Stomach					
Focus,dark red,glandular stomach		0	2	0	1

M : Male

R-1105

Table 9-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
Findings	Number:	5	4
Kidney			
Dilatation,pelvic		0	1

F : Female

R-1105

Table 9-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
Findings	Number:	10	12	12	8
Kidney					
Cyst		0	0	0	1
Stomach					
Focus,depressed,forestomach		0	0	1	0
Focus,white,glandular stomach		0	0	0	1
Focus,dark red,glandular stomach		0	1	0	2
Focus,raised,glandular stomach		0	0	1	0

F : Female

R-1105

Table 9-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
Findings	Number:	5	5
All tissues			
Not remarkable		5	5

M : Male

Table 9-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
Findings	Number:	5	3
Stomach			
Focus,white,forestomach		1	0
Focus,dark red,glandular stomach		1	1

F : Female

Table 9-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (Undelivered)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Kidney		
Small		1
Uterus		
Retention,white material		1
Vagina		
Atresia		1
Retention,white material		1

F : Female

Table 9-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (All littermates died)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Spleen		
Focus,white		1
Stomach		
Focus,white,forestomach		1

F : Female

R-1105

Table 9-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Gross pathological findings (Found dead)

Organs	Sex:	F	F
	Dose(mg/kg):	500a)	500b)
Findings	Number:	4	3
Intestine,colon			
Focus,dark red		0	1
Kidney			
Focus,dark red		0	1

F : Female
a): Main group
b): Satellite group

Table 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	Number:	7	12	12	7
Adrenal					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Bone+Bone marrow,femoral					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Cerebellum(pons)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Cerebrum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Epididymis					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Eye					
Number examined		6	0	0	5
Not remarkable		6	0	0	4
Dysplasia,retinal		0	0	0	1
minimal		0	0	0	1
Heart					
Number examined		6	0	0	5
Not remarkable		5	0	0	4
Cell infiltration		1	0	0	1
minimal		1	0	0	1
Intestine,duodenum					
Number examined		6	0	0	5
Not remarkable		5	0	0	5
Regeneration,mucosal		1	0	0	0
minimal		1	0	0	0
Intestine,jejunum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,ileum(Peyer's patch)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,cecum					
Number examined		6	0	0	5
Not remarkable		5	0	0	5
Cell infiltration,mucosal		1	0	0	0
minimal		1	0	0	0
Intestine,colon					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Intestine,rectum					
Number examined		6	0	0	5
Not remarkable		6	0	0	5

M : Male

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

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	50	150	500
Findings	Number:	7	12	12	7
Kidney					
Number examined		6	5	5	5
Not remarkable		2	0	0	0
Cyst		1	0	0	0
minimal		1	0	0	0
Dilatation,tubular		0	0	0	2
minimal		0	0	0	1
mild		0	0	0	1
Regeneration,tubular		4	4	4	5
minimal		4	4	3	1
mild		0	0	1	3
moderate		0	0	0	1
Eosinophilic body,tubular cell		0	5	5	5
minimal		0	3	1	0
mild		0	2	3	0
moderate		0	0	1	5
Urinary cast,granular		0	0	0	3
minimal		0	0	0	2
mild		0	0	0	1
Cell infiltration,interstitial		1	0	0	2
minimal		1	0	0	0
mild		0	0	0	2
Liver					
Number examined		6	5	5	5
Not remarkable		2	1	1	0
Vacuolation,hepatocyte,periportal		1	1	1	0
minimal		1	1	1	0
Microgranuloma		4	4	3	3
minimal		4	4	3	3
Hypertrophy,hepatocytic,centrilobular		0	0	4	5
minimal		0	0	4	1
mild		0	0	0	4
Lung(bronchus)					
Number examined		6	0	0	5
Not remarkable		1	0	0	1
Aggregation,alveolar macrophage		5	0	0	4
minimal		5	0	0	4
Lymph node,mesenteric					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Lymph node,submandibular					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Pancreas					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Parathyroid					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Pituitary					
Number examined		6	0	0	5
Not remarkable		6	0	0	5

M : Male

Table 10-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
	Number:	7	12	12	7
Prostate					
Number examined		6	0	0	5
Cell infiltration		6	0	0	5
minimal		5	0	0	4
mild		1	0	0	1
Salivary gland,submandibular					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Sciatic nerve					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Seminal vesicle(coagulating gland)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Skeletal muscle,femoral					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Spinal cord(thoracic)					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Spleen					
Number examined		6	0	0	5
Not remarkable		2	0	0	3
Hematopoiesis,extramedullary		4	0	0	2
minimal		4	0	0	2
Stomach					
Number examined		6	0	0	5
Not remarkable		6	0	0	4
Erosion,glandular stomach		0	0	0	1
minimal		0	0	0	1
Testis					
Number examined		6	0	0	5
Not remarkable		5	0	0	4
Atrophy,seminiferous tubular		1	0	0	1
minimal		1	0	0	1
Thymus					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Thyroid					
Number examined		6	5	5	5
Not remarkable		6	5	3	2
Hypertrophy,follicular cell		0	0	2	3
minimal		0	0	2	2
mild		0	0	0	1
Trachea					
Number examined		6	0	0	5
Not remarkable		6	0	0	5
Urinary bladder					
Number examined		6	0	0	5
Not remarkable		6	0	0	5

M : Male

R-1105

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

Organs	Sex:	M	M	M	M
	Dose(mg/kg):	0	50	150	500
Findings	Number:	7	12	12	7
Kidney(alpha2u globulin)					
Number examined		0	0	0	2
Alpha2u globulin immunohistochemistry positive		0	0	0	2
Kidney(PAS stain)					
Number examined		0	0	0	2
PAS reaction negative		0	0	0	2

M : Male

Table 10-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
Findings	Number:	5	4
Adrenal			
Number examined		5	4
Not remarkable		5	0
Vacuolation,cortical cell		0	4
minimal		0	3
mild		0	1
Bone+Bone marrow,femoral			
Number examined		5	4
Not remarkable		5	4
Cerebellum(pons)			
Number examined		5	4
Not remarkable		5	4
Cerebrum			
Number examined		5	4
Not remarkable		5	4
Eye			
Number examined		5	4
Not remarkable		5	4
Heart			
Number examined		5	4
Not remarkable		5	3
Cell infiltration		0	1
minimal		0	1
Intestine,duodenum			
Number examined		5	4
Not remarkable		5	4
Intestine,jejunum			
Number examined		5	4
Not remarkable		5	4
Intestine,ileum(Peyer's patch)			
Number examined		5	4
Not remarkable		5	4
Intestine,cecum			
Number examined		5	4
Not remarkable		5	4
Intestine,colon			
Number examined		5	4
Not remarkable		5	4
Intestine,rectum			
Number examined		5	4
Not remarkable		5	4
Kidney			
Number examined		5	4
Not remarkable		2	3
Cyst		1	0
minimal		1	0
Dilatation,pelvic		0	1
mild		0	1
Regeneration,tubular		3	1
minimal		3	1

F : Female

Table 10-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
Findings	Number:	5	4
Liver			
Number examined		5	4
Microgranuloma		5	3
minimal		5	3
Hypertrophy,hepatocytic,centrilobular		0	4
minimal		0	1
mild		0	3
Lung(bronchus)			
Number examined		5	4
Not remarkable		5	4
Lymph node,mesenteric			
Number examined		5	4
Not remarkable		5	4
Lymph node,submandibular			
Number examined		5	4
Not remarkable		5	4
Ovary			
Number examined		5	4
Not remarkable		5	4
Pancreas			
Number examined		5	4
Not remarkable		5	3
Atrophy,acinar,focal		0	1
minimal		0	1
Parathyroid			
Number examined		5	4
Not remarkable		5	4
Pituitary			
Number examined		5	4
Not remarkable		5	4
Salivary gland,submandibular			
Number examined		5	4
Not remarkable		5	4
Sciatic nerve			
Number examined		5	4
Not remarkable		5	4
Skeletal muscle,femoral			
Number examined		5	4
Not remarkable		5	4
Spinal cord(thoracic)			
Number examined		5	4
Not remarkable		5	4
Spleen			
Number examined		5	4
Not remarkable		5	4
Stomach			
Number examined		5	4
Not remarkable		5	4

F : Female

Table 10-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	500
Findings	Number:	5	4
Thymus			
Number examined		5	4
Not remarkable		5	4
Thyroid			
Number examined		5	4
Not remarkable		5	3
Hypertrophy,follicular cell		0	1
minimal		0	1
Trachea			
Number examined		5	4
Not remarkable		5	4
Urinary bladder			
Number examined		5	4
Not remarkable		5	4
Uterus			
Number examined		5	4
Not remarkable		5	4
Vagina			
Number examined		5	4
Not remarkable		5	4

F : Female

Table 10-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
Findings	Number:	10	12	12	8
Adrenal					
Number examined		5	5	5	5
Not remarkable		5	4	5	2
Vacuolation,cortical cell		0	0	0	3
minimal		0	0	0	1
mild		0	0	0	2
Hypertrophy,zona fasciculata		0	1	0	0
minimal		0	1	0	0
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		4	0	0	5
Dysplasia,retinal		1	0	0	0
mild		1	0	0	0
Heart					
Number examined		5	0	0	5
Not remarkable		5	0	0	5
Intestine,duodenum					
Number examined		5	0	0	5
Not remarkable		3	0	0	5
Regeneration,mucosal		1	0	0	0
minimal		1	0	0	0
Erosion		1	0	0	0
minimal		1	0	0	0
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		4	0	0	5
Erosion		1	0	0	0
mild		1	0	0	0
Intestine,cecum					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Cell infiltration,mucosal		0	0	0	1
minimal		0	0	0	1
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

F : Female

Table 10-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
Findings / Number:	10	12	12	8
Kidney				
Number examined	5	0	0	5
Not remarkable	4	0	0	4
Cyst	0	0	0	1
mild	0	0	0	1
Regeneration,tubular	1	0	0	1
minimal	1	0	0	1
Liver				
Number examined	5	5	5	5
Not remarkable	3	4	0	0
Microgranuloma	2	1	2	1
minimal	2	0	2	1
mild	0	1	0	0
Hypertrophy,hepatocytic,centrilobular	0	0	4	5
minimal	0	0	4	1
mild	0	0	0	4
Lung(bronchus)				
Number examined	5	0	0	5
Not remarkable	1	0	0	1
Aggregation,alveolar macrophage	4	0	0	4
minimal	4	0	0	4
Lymph node,mesenteric				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Lymph node,submandibular				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Ovary				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Pancreas				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Parathyroid				
Number examined	5	0	0	5
Not remarkable	5	0	0	5
Pituitary				
Number examined	5	0	0	5
Not remarkable	4	0	0	4
Aberrant craniopharyngeal tissue	1	0	0	1
minimal	1	0	0	1
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

F : Female

Table 10-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	50	150	500
Findings	Number:	10	12	12	8
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		1	0	0	2
mild		4	0	0	3
Stomach					
Number examined		5	0	0	5
Not remarkable		4	0	0	4
Erosion,glandular stomach		1	0	0	1
minimal		1	0	0	1
Thymus					
Number examined		5	0	0	5
Not remarkable		5	0	0	4
Atrophy		0	0	0	1
minimal		0	0	0	1
Thyroid					
Number examined		5	5	5	5
Not remarkable		5	5	5	4
Hypertrophy,follicular cell		0	0	0	1
minimal		0	0	0	1
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 10-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	M	M
	Dose(mg/kg):	0	500
Findings	Number:	5	5
Kidney			
Number examined		5	5
Not remarkable		2	1
Regeneration,tubular		3	4
minimal		3	0
mild		0	4
Eosinophilic body,tubular cell		0	2
minimal		0	2
Urinary cast,granular		0	4
minimal		0	4
Cell infiltration,interstitial		1	0
minimal		1	0
Liver			
Number examined		5	5
Microgranuloma		5	5
minimal		4	5
mild		1	0
Hypertrophy,hepatocytic,centrilobular		0	3
minimal		0	2
mild		0	1
Thyroid			
Number examined		5	5
Not remarkable		5	4
Hypertrophy,follicular cell		0	1
minimal		0	1

M : Male

Table 10-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (End of recovery period)

Organs	Sex:	F	F
	Dose(mg/kg):	0	500
Findings	Number:	5	3
Adrenal			
Number examined		5	3
Not remarkable		5	1
Vacuolation,cortical cell		0	2
minimal		0	2
Liver			
Number examined		5	3
Not remarkable		1	0
Microgranuloma		4	2
minimal		4	2
Hypertrophy,hepatocytic,centrilobular		0	1
minimal		0	1
Stomach			
Number examined		2	1
Cyst,inclusion		1	0
minimal		1	0
Erosion,glandular stomach		1	1
minimal		0	1
mild		1	0
Thyroid			
Number examined		5	3
Not remarkable		5	3

F : Female

Table 10-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Adrenal		
Number examined		1
Not remarkable		1
Bone+Bone marrow,femoral		
Number examined		1
Not remarkable		1
Cerebellum(pons)		
Number examined		1
Not remarkable		1
Cerebrum		
Number examined		1
Not remarkable		1
Eye		
Number examined		1
Not remarkable		1
Heart		
Number examined		1
Not remarkable		1
Intestine,duodenum		
Number examined		1
Not remarkable		1
Intestine,jejunum		
Number examined		1
Not remarkable		1
Intestine,ileum(Peyer's patch)		
Number examined		1
Not remarkable		1
Intestine,cecum		
Number examined		1
Not remarkable		1
Intestine,colon		
Number examined		1
Not remarkable		1
Intestine,rectum		
Number examined		1
Not remarkable		1
Kidney		
Number examined		1
Cell infiltration,interstitial		1
minimal		1
Fibrosis		1
mild		1
Pigment-laden macrophage		1
minimal		1
Liver		
Number examined		1
Not remarkable		1

F : Female

Table 10-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Lung(bronchus)		
Number examined		1
Not remarkable		1
Lymph node,mesenteric		
Number examined		1
Not remarkable		1
Lymph node,submandibular		
Number examined		1
Not remarkable		1
Ovary		
Number examined		1
Not remarkable		1
Pancreas		
Number examined		1
Not remarkable		1
Parathyroid		
Number examined		1
Not remarkable		1
Pituitary		
Number examined		1
Not remarkable		1
Salivary gland,submandibular		
Number examined		1
Not remarkable		1
Sciatic nerve		
Number examined		1
Not remarkable		1
Skeletal muscle,femoral		
Number examined		1
Not remarkable		1
Spinal cord(thoracic)		
Number examined		1
Not remarkable		1
Spleen		
Number examined		1
Hematopoiesis,extramedullary		1
minimal		1
Stomach		
Number examined		1
Not remarkable		1
Thymus		
Number examined		1
Not remarkable		1
Thyroid		
Number examined		1
Not remarkable		1

F : Female

Table 10-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (Undelivered)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Trachea		
Number examined		1
Not remarkable		1
Urinary bladder		
Number examined		1
Not remarkable		1
Uterus		
Number examined		1
Cell infiltration,inflammatory		1
minimal		1
Vagina		
Number examined		1
Not remarkable		1

F : Female

Table 10-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (All littermates died)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Adrenal		
Number examined		1
Not remarkable		1
Bone+Bone marrow,femoral		
Number examined		1
Not remarkable		1
Cerebellum(pons)		
Number examined		1
Not remarkable		1
Cerebrum		
Number examined		1
Not remarkable		1
Eye		
Number examined		1
Not remarkable		1
Heart		
Number examined		1
Not remarkable		1
Intestine,duodenum		
Number examined		1
Not remarkable		1
Intestine,jejunum		
Number examined		1
Not remarkable		1
Intestine,ileum(Peyer's patch)		
Number examined		1
Not remarkable		1
Intestine,cecum		
Number examined		1
Not remarkable		1
Intestine,colon		
Number examined		1
Atrophy,mucosal		1
minimal		1
Intestine,rectum		
Number examined		1
Not remarkable		1
Kidney		
Number examined		1
Vacuolation,tubular		1
mild		1
Liver		
Number examined		1
Vacuolation,hepatocyte,periportal		1
minimal		1
Lung(bronchus)		
Number examined		1
Not remarkable		1

F : Female

Table 10-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (All littermates died)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Lymph node,mesenteric		
Number examined		1
Not remarkable		1
Lymph node,submandibular		
Number examined		1
Not remarkable		1
Ovary		
Number examined		1
Not remarkable		1
Pancreas		
Number examined		1
Not remarkable		1
Parathyroid		
Number examined		1
Not remarkable		1
Pituitary		
Number examined		1
Not remarkable		1
Salivary gland,submandibular		
Number examined		1
Atrophy,acinar,diffuse		1
minimal		1
Sciatic nerve		
Number examined		1
Not remarkable		1
Skeletal muscle,femoral		
Number examined		1
Not remarkable		1
Spinal cord(thoracic)		
Number examined		1
Not remarkable		1
Spleen		
Number examined		1
Capsulitis		1
mild		1
Atrophy,white pulp		1
minimal		1
Stomach		
Number examined		1
Ulcer,forestomach		1
mild		1
Hyperplasia,squamous,forestomach		1
mild		1
Thymus		
Number examined		1
Atrophy		1
moderate		1

F : Female

Table 10-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (All littermates died)

Organs	Sex:	F
	Dose(mg/kg):	0
Findings	Number:	1
Thyroid		
Number examined		1
Not remarkable		1
Trachea		
Number examined		1
Not remarkable		1
Urinary bladder		
Number examined		1
Not remarkable		1
Uterus		
Number examined		1
Not remarkable		1
Vagina		
Number examined		1
Not remarkable		1

F : Female

Table 10-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (Found dead)

Organs	Sex:	F	F
	Dose(mg/kg):	500a)	500b)
Findings	Number:	4	3
Adrenal			
Number examined		4	3
Not remarkable		0	3
Hypertrophy,zona fasciculata		4	0
minimal		4	0
Bone+Bone marrow,femoral			
Number examined		4	3
Not remarkable		4	3
Cerebellum(pons)			
Number examined		4	3
Not remarkable		4	2
Hemorrhage		0	1
minimal		0	1
Cerebrum			
Number examined		4	3
Not remarkable		4	1
Hemorrhage		0	2
mild		0	2
Eye			
Number examined		4	3
Not remarkable		3	3
Dysplasia,retinal		1	0
minimal		1	0
Heart			
Number examined		4	3
Not remarkable		4	3
Intestine,duodenum			
Number examined		4	3
Not remarkable		4	3
Intestine,jejunum			
Number examined		3	3
Not remarkable		3	3
Sample autolysed		1	0
Intestine,ileum(Peyer's patch)			
Number examined		4	2
Not remarkable		4	2
Sample autolysed		0	1
Intestine,cecum			
Number examined		4	3
Not remarkable		3	3
Cell infiltration,mucosal		1	0
minimal		1	0
Intestine,colon			
Number examined		2	2
Not remarkable		2	1
Sample autolysed		2	1
Hemorrhage		0	1
mild		0	1
Intestine,rectum			
Number examined		4	3
Not remarkable		4	3

F : Female
a): Main group
b): Satellite group

Table 10-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (Found dead)

Organs	Sex:	F	F
	Dose(mg/kg):	500a)	500b)
Findings	Number:	4	3
Kidney			
Number examined		4	3
Not remarkable		4	2
Hemorrhage,interstitial		0	1
minimal		0	1
Liver			
Number examined		4	3
Not remarkable		1	1
Microgranuloma		0	1
minimal		0	1
Hypertrophy,hepatocytic,centrilobular		3	2
minimal		2	1
mild		1	1
Lung(bronchus)			
Number examined		4	3
Not remarkable		3	2
Aggregation,alveolar macrophage		1	1
minimal		1	1
Lymph node,mesenteric			
Number examined		4	3
Not remarkable		4	3
Lymph node,submandibular			
Number examined		4	3
Not remarkable		4	3
Ovary			
Number examined		4	3
Not remarkable		4	3
Pancreas			
Number examined		4	3
Not remarkable		4	3
Parathyroid			
Number examined		4	3
Not remarkable		4	3
Pituitary			
Number examined		4	3
Not remarkable		4	3
Salivary gland,submandibular			
Number examined		4	3
Not remarkable		2	0
Atrophy,acinar,diffuse		2	3
minimal		2	3
Sciatic nerve			
Number examined		4	3
Not remarkable		4	3
Skeletal muscle,femoral			
Number examined		4	3
Not remarkable		4	3
Spinal cord(thoracic)			
Number examined		4	3
Not remarkable		4	3

F : Female
a): Main group
b): Satellite group

Table 10-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Histopathological findings (Found dead)

Organs	Sex:	F	F
	Dose(mg/kg):	500a)	500b)
Findings	Number:	4	3
Spleen			
Number examined		4	3
Not remarkable		1	2
Hematopoiesis,extramedullary		2	1
minimal		1	1
mild		1	0
Atrophy,white pulp		2	0
mild		2	0
Stomach			
Number examined		4	3
Not remarkable		4	3
Thymus			
Number examined		4	3
Not remarkable		4	3
Thyroid			
Number examined		4	3
Not remarkable		4	3
Trachea			
Number examined		4	3
Not remarkable		4	3
Urinary bladder			
Number examined		4	3
Not remarkable		4	3
Uterus			
Number examined		4	3
Not remarkable		4	3
Vagina			
Number examined		4	3
Not remarkable		4	3

F : Female
a): Main group
b): Satellite group

Table 11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1	11	3.9±0.3	4.0±0.1	0/12(0.0)
50	12	0	0	0	4	8	3.7±0.5	4.4±0.5	0/12(0.0)
150	12	0	0	0	6	6	3.5±0.5	4.2±0.4	0/12(0.0)
500	11	0	0	0	5	6	3.5±0.5	4.2±0.2	0/11(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 2-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	2.4±1.1	12/12(100.0)	11/12(91.7)	12	2.4±1.1	12/12(100.0)	11/12(91.7)
50	12	2.7±1.0d)	12/12(100.0)	12/12(100.0)	12	2.7±1.0d)	12/12(100.0)	12/12(100.0)
150	12	2.3±1.2	12/12(100.0)	12/12(100.0)	12	2.3±1.2	12/12(100.0)	12/12(100.0)
500	12	3.0±1.3d)	12/12(100.0)	11/12(91.7)	11	2.9±1.4d)	11/11(100.0)	11/11(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
d): One animal was overlooked on the day of copulation.
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 2-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	11	11	100.0		171	166			11	148	0
0	Mean				22.0	15.5	15.1	97.0	95.6	(6.4)	13.5	(0.0)
	S.D.				0.4	1.4	1.6	5.3	4.9	(16.8)	2.8	(0.0)
	Total	12	12	100.0		196	189			5	176	0
50	Mean				21.8	16.3	15.8	96.7	95.8	(2.6)	14.7	(0.0)
	S.D.				0.4	1.2	1.0	5.6	4.8	(6.1)	1.2	(0.0)
	Total	12	12	100.0		194	186			3	179	0
150	Mean				21.8	16.2	15.5	96.3	97.8	(1.8)	14.9	(0.0)
	S.D.				0.5	1.7	1.3	7.3	3.3	(3.2)	1.7	(0.0)
	Total	8g)	8	100.0		123	121			2	115	0
500	Mean				21.8	15.4	15.1	98.3	96.5	(1.6)	14.4	(0.0)
	S.D.				0.5	1.3	1.6	4.7	5.0	(4.4)	1.8	(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
g): Three out of eleven dams were excluded because they died on gestation days 12, 13 and 17.
No significant difference in any treated groups from control group.

Table 14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	11	148	159		11	148	140	
0	Mean		13.5	14.5	93.6		13.5	12.7	90.4
	S.D.		2.8	1.9	16.8		2.8	4.6	30.0
	Total	12	176	181		12	176	173	
50	Mean		14.7	15.1	97.5		14.7	14.4	98.5
	S.D.		1.2	1.2	6.1		1.2	0.9	3.8
	Total	12	179	182		12	179	177	
150	Mean		14.9	15.2	98.3		14.9	14.8	99.0
	S.D.		1.7	1.5	3.2		1.7	1.6	2.5
	Total	8	115	117		8	115	111	
500	Mean		14.4	14.6	98.4		14.4	13.9	96.6
	S.D.		1.8	1.9	4.4		1.8	1.9	5.3

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 2-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	73	75	6	4				69	71	
0	11	Mean	6.6	6.8	0.6	0.4	0.51	0.50	10d)	6.9	7.1	0.50
		S.D.	2.1	2.5	1.9	1.0	0.14	0.13		1.9	2.4	0.14
		Total	87	89	2	3				85	88	
50	12	Mean	7.3	7.4	0.2	0.3	0.49	0.49	12	7.1	7.3	0.49
		S.D.	2.2	2.0	0.6	0.6	0.14	0.14		2.1	2.1	0.14
		Total	96	83	1	1				94	83	
150	12	Mean	8.0	6.9	0.1	0.1	0.54	0.54	12	7.8	6.9	0.53
		S.D.	2.1	2.4	0.3	0.3	0.14	0.14		2.0	2.4	0.14
		Total	57	58	0	2				55	56	
500	8	Mean	7.1	7.3	0.0	0.3	0.48	0.48	8	6.9	7.0	0.49
		S.D.	3.5	2.6	0.0	0.7	0.23	0.23		3.3	2.9	0.24

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.
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 2-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
0	No.	11	10b)	10	11	10b)	10
	Mean	6.5	10.0	3.5	6.2	9.6	3.4
	S.D.	0.4	0.9	0.8	0.4	1.0	0.7
50	No.	12	12	12	12	12	12
	Mean	6.3	9.5	3.2	6.1	9.3	3.3
	S.D.	0.3	0.7	0.4	0.3	0.6	0.4
150	No.	12	12	12	12	12	12
	Mean	6.3	9.5	3.2	6.0	9.1	3.1
	S.D.	0.4	1.4	1.3	0.3	1.3	1.2
500	No.	8	8	8	8	8	8
	Mean	6.2	9.2	2.9	5.8	8.5	2.7
	S.D.	0.5	1.0	0.7	0.4	1.1	0.8

Unit: g
No.: No. of dams
a): Postnatal day
b): One dam was sacrificed on day 2 of lactation because of all pups died.
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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Externally for gross abnormalities in dead pups

Dose (mg/kg)	0	50	150	500
Male				
No. of pups examined	3	2	0	2
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	0	1	0	2
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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Externally for gross abnormalities in pups on postnatal day 4

Dose (mg/kg)	0	50	150	500
Male				
No. of pups examined	69	85	94	55
No. of pups with abnormal findings	0	0	0	0
Female				
No. of pups examined	71	88	83	56
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 2-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 2-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 2-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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 50

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 50

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 50

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 150

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 150

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 150

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 500

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

-: No abnormal findings
B: Salivation

Appendix 1-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 500

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

-: No abnormal findings

Appendix 1-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Administration period)
Dose (mg/kg): 500

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

a): Day of necropsy
-: No abnormal findings

Appendix 1-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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

-: No abnormal findings
A: Clonic convulsion
B: Salivation
+: Dead

Appendix 1-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	Non-pregnant																							
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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 50

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	
2104b)																								
2105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2107	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
2109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
2111	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/d		
2112	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	

a): Gestation day
b): Excluded from data because the signs of copulation were overlooked on the day of copulation.
-: No abnormal findings
d: Delivery
/d: Found delivery after the observation of general conditions.

Appendix 1-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 150

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the gestation period (Main group)
Dose (mg/kg): 500

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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4102	-	-	-	-	-	-	-	-	-	-	-	-	-	AB	-	-	-	-	-	-	-	-	d	
4103	-	-	-	-	-	-	-	-	-	-	-	-	-	+										
4104	-	-	-	-	-	-	-	-	-	-	-	-	-	AB	-	-	-	-	-	-	-	-/d		
4105	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	d	
4106	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+						
4107b)																								
4108	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4109	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d		
4110	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	d	
4111	-	-	-	-	-	-	-	-	-	-	-	-	AB+											
4112c)																								

a): Gestation day
b): Excluded from data because the signs of copulation were overlooked on the day of copulation.
c): Died on day 10 of administration
-: No abnormal findings
A: Clonic convulsion
B: Salivation
+: Dead
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 2-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	Non-pregnant					
1107c)	-	DF	-			
1108	-	-	-	-	-	-
1109	-	-	-	-	-	-
1110	-	-	-	-	-	-
1111	-	-	-	-	-	-
1112	-	-	-	-	-	-

a): Lactation day
b): Day of necropsy
c): Sacrificed on day 2 of lactation because all pups died
-: No abnormal findings
D: Decrease in nursing behavior
F: Vaginal hemorrhage

Appendix 1-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 50

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 150

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

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

Appendix 1-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in dams during the lactation period (Main group)
Dose (mg/kg): 500

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

a): Lactation day
b): Day of necropsy
c): Died on gestation day 13
d): Died on gestation day 17
e): Died on gestation day 12
f): Died on day 10 of administration
-: No abnormal findings

Appendix 1-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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 2-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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 500

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

-: No abnormal findings
B: Salivation

Appendix 1-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 500

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

-: No abnormal findings
A: Clonic convulsion
B: Salivation
+: Dead

Appendix 1-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Satellite group, Administration period)
Dose (mg/kg): 500

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

a): Day of necropsy
-: No abnormal findings
B: Salivation
+: Dead

Appendix 1-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in male rats (Recovery period)
Dose (mg/kg): 500

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 2-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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual clinical signs in female rats (Recovery period)
Dose (mg/kg): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12 D
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: Dead

Appendix 2-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	12
Posture a)	N	N	N	N	N		N	N	N	N	N	N
Convulsion b)	0	0	0	0	0		0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0		0	0	0	0	0	0

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

Appendix 2-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 d)	5	6	7	8	9	10	11	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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7 d)	8	9	10	11	12 D
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
d) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	12
Posture a)	N	N	N	N	N		N	N	N	N	N	N
Convulsion b)	0	0	0	0	0		0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0		0	0	0	0	0	0

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

Appendix 2-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 d)	5	6	7	8	9	10	11	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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7 d)	8	9	10	11	12 D
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
d) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
						NP						
Posture a)	N	N	N	N	N		N	N	N	N	N	N
Convulsion b)	0	0	0	0	0		0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0		0	0	0	0	0	0

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

Appendix 2-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 d)	5	6	7	8	9	10	11	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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D				d)				D	D
Posture a)	N	N		N	N	N		N	N	N		
Convulsion b)	0	0		0	0	0		0	0	0		
Abnormal behavior c)	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) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
						NP						
Posture a)	N	N	N	N	N		N	N	N	N	N	N
Convulsion b)	0	0	0	0	0		0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0		0	0	0	0	0	0

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

Appendix 2-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 d)	5	6	7	8	9	10	11	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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D			D	d)				D	D
Posture a)	N	N		N	N			N	N	N		
Convulsion b)	0	0		0	0			0	0	0		
Abnormal behavior c)	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) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-49 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
						NP	d)					
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
d) Sacrificed on day 2 of lactation because all pups died
NP: Non-pregnant

Appendix 2-50 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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 2-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): 150

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 2-52 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D			D					D	D
Posture a)	N	N		N	N		N	N	N	N		
Convulsion b)	0	0		0	0		0	0	0	0		
Abnormal behavior c)	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: Dead

Appendix 2-53 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

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 2-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 2-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): 500

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	2d)	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
d) Clonic convulsion

Appendix 2-57 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D				
Posture a)	N	N	N		N		N	N	N	N
Convulsion b)	0	0	0		0		0	0	0	0
Abnormal behavior c)	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: Dead

Appendix 2-59 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D				
Posture a)	N	N	N		N		N	N	N	N
Convulsion b)	0	0	0		0		2d)	0	0	0
Abnormal behavior c)	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) Clonic convulsion
D: Dead

Appendix 2-61 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D		D		
Posture a)	N	N	N		N		N		N	N
Convulsion b)	0	0	0		0		0		0	0
Abnormal behavior c)	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: Dead

Appendix 2-63 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D		D		
Posture a)	N	N	N		N		N		N	N
Convulsion b)	0	0	0		0		0		0	0
Abnormal behavior c)	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: Dead

Appendix 2-65 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

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 2-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 2-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): 500

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 2-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 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Posture a)		N		N	N
Convulsion b)		0		0	0
Abnormal behavior c)		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: Dead

Appendix 2-71 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Posture a)		N		N	N
Convulsion b)		0		0	0
Abnormal behavior c)		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: Dead

Appendix 2-73 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-74 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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 2-75 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	1	0	1	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 2-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): 500

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	1	0	0	0	0	1	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 2-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 2-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): 50

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 2-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): 150

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 2-80 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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 2-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 2-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): 50

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 2-83 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	1	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 2-84 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	1	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 2-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 2-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): 50

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 2-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): 150

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	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 2-88 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	1	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 2-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 2-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): 50

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0	0	0	0	0	0	0	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	0	0	0	0	0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult

Appendix 2-91 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	1	0
Fur condition b)	0	0	0	0	0	0	0	0	0	0	0	0
Skin c)	0	0	0	0	0	0	0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0	0	0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0	0	0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0	0	0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0	0	0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection i)	0	0	0	0	0	0	0	0	0	0	0	0
Pupil size j)	0	0	0	0	0	0	0	0	0	0	0	0
Salivation k)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0	0	0	0	0	0	0	0
Vocalization m)	0	0	1	0	1	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 2-92 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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 2-93 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1	0
Reactivity to handling n)	0	0	0	0	0	0	0	0	0	0	1	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 2-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): 50

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 2-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): 150

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	1	0	1	0	0	0	1	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 2-96 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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 2-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 2-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): 50

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	1	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 2-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): 150

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	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 2-100 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	1	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 2-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 2-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): 50

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 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12 D
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	1	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
D: Dead

Appendix 2-105 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0		0	0	0	0	0	0
Fur condition b)	0	0	0	0	0		0	0	0	0	0	0
Skin c)	0	0	0	0	0		0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0		0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0		0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0		0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0		0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0		0	0	0	0	0	0
Piloerection i)	0	0	0	0	0		0	0	0	0	0	0
Pupil size j)	0	0	0	0	0		0	0	0	0	0	0
Salivation k)	0	0	0	0	0		0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0		0	0	0	0	0	0
Vocalization m)	0	0	0	0	0		0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0		0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-106 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 o)	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
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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-107 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	1	0	0	0	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 2-108 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7 o)	8	9	10	11	12 D
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	1	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		1	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
o) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-109 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0		0	0	0	0	0	0
Fur condition b)	0	0	0	0	0		0	0	0	0	0	0
Skin c)	0	0	0	0	0		0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0		0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0		0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0		0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0		0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0		0	0	0	0	0	0
Piloerection i)	0	0	0	0	0		0	0	0	0	0	0
Pupil size j)	0	0	0	0	0		0	0	0	0	0	0
Salivation k)	0	0	0	0	0		0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0		0	0	0	0	0	0
Vocalization m)	0	0	0	0	0		0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0		0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-110 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 o)	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
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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-111 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7 o)	8	9	10	11	12 D
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
o) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-113 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	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	1	0	0		0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0		0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-114 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 o)	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
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	1	1	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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-115 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D				o)				D	D
Ease of removal from cage a)	0	0		0	0	0		0	0	0		
Fur condition b)	0	0		0	0	0		0	0	0		
Skin c)	0	0		0	0	0		0	0	0		
Secretions-Eye, Nose d)	0	0		0	0	0		0	0	0		
Exophthalmos e)	0	0		0	0	0		0	0	0		
Palpebral closure f)	0	0		0	0	0		0	0	0		
Mucosal membranes g)	0	0		0	0	0		0	0	0		
Lacrimation h)	0	0		0	0	0		0	0	0		
Piloerection i)	0	0		0	0	0		0	0	0		
Pupil size j)	0	0		0	0	0		0	0	0		
Salivation k)	0	0		0	1	0		0	0	0		
Abnormal respiration l)	0	0		0	0	0		0	0	0		
Vocalization m)	0	0		0	0	0		0	0	0		
Reactivity to handling n)	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) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-117 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	12
Ease of removal from cage a)	0	0	0	0	0		0	0	0	0	0	0
Fur condition b)	0	0	0	0	0		0	0	0	0	0	0
Skin c)	0	0	0	0	0		0	0	0	0	0	0
Secretions-Eye, Nose d)	0	0	0	0	0		0	0	0	0	0	0
Exophthalmos e)	0	0	0	0	0		0	0	0	0	0	0
Palpebral closure f)	0	0	0	0	0		0	0	0	0	0	0
Mucosal membranes g)	0	0	0	0	0		0	0	0	0	0	0
Lacrimation h)	0	0	0	0	0		0	0	0	0	0	0
Piloerection i)	0	0	0	0	0		0	0	0	0	0	0
Pupil size j)	0	0	0	0	0		0	0	0	0	0	0
Salivation k)	0	0	0	0	0		0	0	0	0	0	0
Abnormal respiration l)	0	0	0	0	0		0	0	0	0	0	0
Vocalization m)	0	0	0	0	0		0	0	0	0	0	0
Reactivity to handling n)	0	0	0	0	0		0	0	0	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
NP: Non-pregnant

Appendix 2-118 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 o)	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
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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-119 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D			D	o)				D	D
Ease of removal from cage a)	0	0		0	0			1	0	0		
Fur condition b)	0	0		0	0			0	0	0		
Skin c)	0	0		0	0			0	0	0		
Secretions-Eye, Nose d)	0	0		0	0			0	0	0		
Exophthalmos e)	0	0		0	0			0	0	0		
Palpebral closure f)	0	0		0	0			0	0	0		
Mucosal membranes g)	0	0		0	0			0	0	0		
Lacrimation h)	0	0		0	0			0	0	0		
Piloerection i)	0	0		0	0			0	0	0		
Pupil size j)	0	0		0	0			0	0	0		
Salivation k)	0	0		0	0			0	0	0		
Abnormal respiration l)	0	0		0	0			0	0	0		
Vocalization m)	0	0		0	0			1	0	0		
Reactivity to handling n)	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) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-121 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7 o)	8	9	10	11	12
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
o) Sacrificed on day 2 of lactation because all pups died
NP: Non-pregnant

Appendix 2-122 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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 2-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): 150

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 2-124 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D			D					D	D
Ease of removal from cage a)	0	0		0	0		0	0	0	0		
Fur condition b)	0	0		0	0		0	0	0	0		
Skin c)	0	0		0	0		0	0	0	0		
Secretions-Eye, Nose d)	0	0		0	0		0	0	0	0		
Exophthalmos e)	0	0		0	0		0	0	0	0		
Palpebral closure f)	0	0		0	0		0	0	0	0		
Mucosal membranes g)	0	0		0	0		0	0	0	0		
Lacrimation h)	0	0		0	0		0	0	0	0		
Piloerection i)	0	0		0	0		0	0	0	0		
Pupil size j)	0	0		0	0		0	0	0	0		
Salivation k)	0	0		0	0		0	0	0	0		
Abnormal respiration l)	0	0		0	0		0	0	0	0		
Vocalization m)	0	0		0	0		0	0	0	0		
Reactivity to handling n)	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
D: Dead

Appendix 2-125 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

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	1	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 2-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)	1	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 2-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): 500

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	2	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 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16 D	17	18 D	19	20	21	22
Ease of removal from cage a)	0	0	0		0		0	0	0	0
Fur condition b)	0	0	0		0		0	0	0	0
Skin c)	0	0	0		0		0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0		0	0	0	0
Exophthalmos e)	0	0	0		0		0	0	0	0
Palpebral closure f)	0	0	0		0		0	0	0	0
Mucosal membranes g)	0	0	0		0		0	0	0	0
Lacrimation h)	0	0	0		0		0	0	0	0
Piloerection i)	0	0	0		0		0	0	0	0
Pupil size j)	0	0	0		0		0	0	0	0
Salivation k)	0	0	0		0		0	0	0	0
Abnormal respiration l)	0	0	0		0		0	0	0	0
Vocalization m)	0	1	0		1		1	0	0	0
Reactivity to handling n)	0	0	0		0		1	0	0	0

a) -1: Atypically docile, 0: Easy, 1: Some resistance/avoidance, 2: Difficult, 3: Very difficult
b) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
c) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
d) 0: Absent, 1: Present
e) 0: Absent, 1: Present
f) 0: Normal, 1: Slightly closed, 2: Half closed, 3: Completely closed
g) 0: Normal, 1: Slight, 2: Moderate, 3: Marked
h) 0: Normal, 1: Present
i) 0: Absent, 1: Present
j) -1: Miosis, 0: Normal, 1: Half opened pupil, 2: Mydriasis
k) 0: None, 1: Slight, 2: Moderate, 3: Marked
l) 0: Absent, 1: Slight, 2: Moderate, 3: Marked
m) 0: None, 1: Soft, 2: Moderate, 3: Loud/aggressive
n) -1: Atypically docile, 0: Easy, 1: Slightly awkward, 2: Difficult, 3: Very difficult
D: Dead

Appendix 2-131 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D				
Ease of removal from cage a)	0	0	0		0		0	0	0	0
Fur condition b)	0	0	0		0		0	0	0	0
Skin c)	0	0	0		0		0	0	0	0
Secretions-Eye, Nose d)	0	0	0		0		0	0	0	0
Exophthalmos e)	0	0	0		0		0	0	0	0
Palpebral closure f)	0	0	0		0		0	0	0	0
Mucosal membranes g)	0	0	0		0		0	0	0	0
Lacrimation h)	0	0	0		0		0	0	0	0
Piloerection i)	0	0	0		0		0	0	0	0
Pupil size j)	0	0	0		0		0	0	0	0
Salivation k)	0	0	0		0		2	0	0	0
Abnormal respiration l)	0	0	0		0		0	0	0	0
Vocalization m)	0	0	0		0		0	0	0	0
Reactivity to handling n)	0	0	0		0		2	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
D: Dead

Appendix 2-133 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D		D		
Ease of removal from cage a)	0	0	0		0		0		0	0
Fur condition b)	0	0	0		0		0		0	0
Skin c)	0	0	0		0		0		0	0
Secretions-Eye, Nose d)	0	0	0		0		0		0	0
Exophthalmos e)	0	0	0		0		0		0	0
Palpebral closure f)	0	0	0		0		0		0	0
Mucosal membranes g)	0	0	0		0		0		0	0
Lacrimation h)	0	0	0		0		0		0	0
Piloerection i)	0	0	0		0		0		0	0
Pupil size j)	0	0	0		0		0		0	0
Salivation k)	0	0	0		0		0		0	0
Abnormal respiration l)	0	0	0		0		0		0	0
Vocalization m)	0	0	0		0		0		0	0
Reactivity to handling n)	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
D: Dead

Appendix 2-135 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)	1	0	0	0	0	0	0	1	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 2-136 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D		D		
Ease of removal from cage a)	0	0	0		0		0		0	0
Fur condition b)	0	0	0		0		0		0	0
Skin c)	0	0	0		0		0		0	0
Secretions-Eye, Nose d)	0	0	0		0		0		0	0
Exophthalmos e)	0	0	0		0		0		0	0
Palpebral closure f)	0	0	0		0		0		0	0
Mucosal membranes g)	0	0	0		0		0		0	0
Lacrimation h)	0	0	0		0		0		0	0
Piloerection i)	0	0	0		0		0		0	0
Pupil size j)	0	0	0		0		0		0	0
Salivation k)	0	0	0		0		0		0	0
Abnormal respiration l)	0	0	0		0		0		0	0
Vocalization m)	0	0	0		0		0		0	0
Reactivity to handling n)	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
D: Dead

Appendix 2-137 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

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 2-139 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

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 2-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 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Ease of removal from cage a)		0		0	0
Fur condition b)		0		0	0
Skin c)		0		0	0
Secretions-Eye, Nose d)		0		0	0
Exophthalmos e)		0		0	0
Palpebral closure f)		0		0	0
Mucosal membranes g)		0		0	0
Lacrimation h)		0		0	0
Piloerection i)		0		0	0
Pupil size j)		0		0	0
Salivation k)		0		0	0
Abnormal respiration l)		0		0	0
Vocalization m)		0		0	0
Reactivity to handling n)		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
D: Dead

Appendix 2-143 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Ease of removal from cage a)		0		0	0
Fur condition b)		0		0	0
Skin c)		0		0	0
Secretions-Eye, Nose d)		0		0	0
Exophthalmos e)		0		0	0
Palpebral closure f)		0		0	0
Mucosal membranes g)		0		0	0
Lacrimation h)		0		0	0
Piloerection i)		0		0	0
Pupil size j)		0		0	0
Salivation k)		0		0	0
Abnormal respiration l)		0		0	0
Vocalization m)		0		0	0
Reactivity to handling n)		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
D: Dead

Appendix 2-145 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6	7	4	7	2	4	7	2	8	4	0	2
Defecation count	0	0	0	0	0	0	0	0	0	0	2	4
Urination h)	1	0	0	0	1	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 2-146 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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	1	5	6	7	2	4	4	2	2	4	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 2-147 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	3	5	8	4	4	3	7	3	2	5	3
Defecation count	0	0	0	0	0	1	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	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 2-148 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	7	5	3	4	4	4	1	3	9	4	3	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-149 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6	4	2	4	2	5	5	4	7	2	3	2
Defecation count	0	0	2	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-150 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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	U	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	3	5	4	4	5	6	3	0	3	5	2
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-151 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	5	7	6	4	2	5	3	3	3	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	1
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 2-152 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	4	6	2	8	5	3	2	7	1	1	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	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 2-153 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	7	3	4	2	3	8	1	6	4	0	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	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 2-154 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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	4	6	4	3	5	3	1	6	6	1
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	1	0	0	0	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-155 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	U	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	4	5	8	6	3	0	7	5	4	3	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	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-156 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	0	2	5	1	4	7	5	6	7	3	2	5
Defecation count	3	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-157 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	4	5	3	3	3	3	5	3	8	3	5	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	1	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 2-158 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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	3	7	7	7	4	5	5	2	5	4	5
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	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 2-159 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	6	5	7	3	3	5	6	5	7	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	1	0	0	0	1	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 2-160 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	4	6	2	2	4	4	7	5	3	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	1	0	1	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-161 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	3	2	4	2	3	4	6	4	10	5	4	4
Defecation count	0	0	0	0	0	0	0	0	0	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 2-162 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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	4	6	5	6	4	5	4	0	4	6	3
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-163 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	7	3	8	5	3	0	7	5	2	4	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-164 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4001-4012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	1	3	7	0	5	6	7	4	7	4	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	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 2-165 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	4	7	3	6	4	5	8	6	9	4	3	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-166 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2001-2012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	6	3	7	8	8	5	5	7	3	5	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 2-167 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

Parameter	Animal number (3001-3012)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	4	6	5	7	8	6	3	5	6	6	4	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	1	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-168 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	8	2	5	8	3	7	8	4	2	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	1	1	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 2-169 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6	8	11	4	3	3	7	7	7	6	7	11
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 2-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): 50

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	13	6	10	10	7	4	10	6	7	7	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 2-171 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	5	6	8	9	3	6	7	8	5	5	5	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-172 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	8	6	9	6	11	5	6	0	6	7	9	6
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-173 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	4	7	7	5	5	5	7	7	6	5	9	11
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 2-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): 50

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	14	9	10	5	9	9	10	6	6	7	4	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-175 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	7	8	5	7	5	11	5	4	4	7
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-176 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12 D
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	8	7	8	6	9	6	6	7	6	
Defecation count	0	0	0	0	0	0	0	0	0	0	0	
Urination h)	0	0	0	0	0	0	0	0	0	1	0	

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
D: Dead

Appendix 2-177 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	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	6	7	6	11	5	12	5	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-178 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 i)	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	9	6	11		4	7	8	6	8	8	5	7
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) The signs of copulation were overlooked on the day of copulation.

Appendix 2-179 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	8	8	4	8	4	9	7	6	7	5	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	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 2-180 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7 i)	8	9	10	11	12 D
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	4	8	8	9	7		7	10	6	5	
Defecation count	0	0	0	0	0	0		0	0	0	0	
Urination h)	0	1	0	0	0	0		0	0	1	0	

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-181 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	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	5	7	10	5	8		7	7	6	5	8	8
Defecation count	0	0	0	0	0		0	0	0	0	0	0
Urination h)	0	0	0	0	0		0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-182 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 i)	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	9	5	6		7	7	9	6	5	6	4	6
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) The signs of copulation were overlooked on the day of copulation.

Appendix 2-183 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	6	4	9	9	8	8	6	5	6	4	9
Defecation count	0	0	0	0	0	0	0	0	0	1	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 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7 i)	8	9	10	11	12 D
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	7	11	9	9	7		7	5	8	7	
Defecation count	0	0	0	0	0	0		0	0	0	0	
Urination h)	1	0	0	0	0	0		0	0	1	0	

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-185 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	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	7	7	2	5		4	6	4	4	6	5
Defecation count	0	0	0	0	0		0	0	0	0	0	0
Urination h)	0	0	0	0	0		0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-186 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 i)	5	6	7	8	9	10	11	12
Arousal a)	0	0	0		0	0	0	0	0	0	0	0
Convulsion b)	0	0	0		0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0		0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0		0	0	0	0	0	0	0	0
Gait e)	0	0	0		0	0	0	0	0	0	0	0
Posture f)	N	N	N		N	N	N	N	N	N	N	N
Grooming g)	0	0	0		0	0	0	0	0	0	0	0
Rearing	9	5	8		6	8	7	6	4	5	3	6
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		1	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) The signs of copulation were overlooked on the day of copulation.

Appendix 2-187 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	5	6	4	9	5	5	8	5	4	6	9	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 2-188 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D				i)				D	D
Arousal a)	0	0		0	0	0		0	0	0		
Convulsion b)	0	0		0	0	0		0	0	0		
Abnormal behavior c)	0	0		0	0	0		0	0	0		
Stereotypy d)	0	0		0	0	0		0	0	0		
Gait e)	0	0		0	0	0		0	0	0		
Posture f)	N	N		N	N	N		N	N	N		
Grooming g)	0	0		0	0	0		0	0	0		
Rearing	7	3		8	13	10		8	8	7		
Defecation count	0	0		0	0	0		0	0	0		
Urination h)	0	0		0	0	0		0	1	0		

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-189 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7	8	9	10	11	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	7	6	4	5		5	5	10	6	11	5
Defecation count	0	0	0	0	0		0	0	0	0	0	0
Urination h)	0	0	0	0	0		0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
NP: Non-pregnant

Appendix 2-190 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4 i)	5	6	7	8	9	10	11	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	5	6	9		3	11	9	5	4	7	4	5
Defecation count	0	0	0		0	0	0	0	0	0	0	0
Urination h)	0	0	0		0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount
i) The signs of copulation were overlooked on the day of copulation.

Appendix 2-191 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	5	5	6	3	3	3	6	6	4	4	5	4
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-192 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D			D	i)				D	D
Arousal a)	0	0		0	0			0	0	0		
Convulsion b)	0	0		0	0			0	0	0		
Abnormal behavior c)	0	0		0	0			0	0	0		
Stereotypy d)	0	0		0	0			0	0	0		
Gait e)	0	0		0	0			0	0	0		
Posture f)	N	N		N	N			N	N	N		
Grooming g)	0	0		0	0			0	0	0		
Rearing	5	4		5	7			6	6	6		
Defecation count	0	0		0	0			0	0	0		
Urination h)	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) The signs of copulation were overlooked on the day of copulation.
D: Dead

Appendix 2-193 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 NP	7 i)	8	9	10	11	12
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	8	6	5			5	5	5	10	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
i) Sacrificed on day 2 of lactation because all pups died
NP: Non-pregnant

Appendix 2-194 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Parameter	Animal number (2101-2112)											
	1	2	3	4	5	6	7	8	9	10	11	12
Arousal a)	0	0	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0	0	0
Rearing	7	10	11	6	5	8	8	4	9	6	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 2-195 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

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	5	5	7	11	7	7	7	7	3	6	7	9
Defecation count	0	0	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-196 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4101-4112)											
	1	2	3	4	5	6	7	8	9	10	11	12
			D			D					D	D
Arousal a)	0	0		0	0		0	0	0	0		
Convulsion b)	0	0		0	0		0	0	1i)	0		
Abnormal behavior c)	0	0		0	0		0	0	0	0		
Stereotypy d)	0	0		0	0		0	0	0	0		
Gait e)	0	0		0	0		0	0	0	0		
Posture f)	N	N		N	N		N	N	N	N		
Grooming g)	0	0		0	0		0	0	0	0		
Rearing	5	6		10	11		4	7	5	5		
Defecation count	0	0		0	0		0	0	0	0		
Urination h)	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) Clonic convulsion
D: Dead

Appendix 2-197 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	4	8	3	9	7	4	3	5	5	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 2-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): 500

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	7	3	5	8	6	11	5	14	4
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	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 2-199 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	2	10	3	7	6	4	1	6	4	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 2-200 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
Arousal a)	0	0	0	0	0	0	0	0	0	0
Convulsion b)	0	0	0	0	0	0	0	0	0	0
Abnormal behavior c)	0	0	0	0	0	0	0	0	0	0
Stereotypy d)	0	0	0	0	0	0	0	0	0	0
Gait e)	0	0	0	0	0	0	0	0	0	0
Posture f)	N	N	N	N	N	N	N	N	N	N
Grooming g)	0	0	0	0	0	0	0	0	0	0
Rearing	6	7	2	6	6	6	9	8	12	4
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 2-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	10	6	6	8	8	5	3	6	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 2-202 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D				
Arousal a)	0	0	0		0		0	0	0	0
Convulsion b)	0	0	0		1i)		0	0	0	0
Abnormal behavior c)	0	0	0		0		0	0	0	0
Stereotypy d)	0	0	0		0		0	0	0	0
Gait e)	0	0	0		0		0	0	0	0
Posture f)	N	N	N		N		N	N	N	N
Grooming g)	0	0	0		0		0	0	0	0
Rearing	5	7	6		3		6	7	9	11
Defecation count	0	0	0		0		0	0	0	0
Urination h)	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
i) Clonic convulsion
D: Dead

Appendix 2-203 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	7	10	7	10	6	4	11	7	6	5
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-204 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D				
Arousal a)	0	0	0		0		0	0	0	0
Convulsion b)	0	0	0		0		0	0	0	0
Abnormal behavior c)	0	0	0		0		0	0	0	0
Stereotypy d)	0	0	0		0		0	0	0	0
Gait e)	0	0	0		0		0	0	0	0
Posture f)	N	N	N		N		N	N	N	N
Grooming g)	0	0	0		0		0	0	0	0
Rearing	9	8	5		10		6	4	10	7
Defecation count	0	0	0		0		0	0	0	0
Urination h)	0	1	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
D: Dead

Appendix 2-205 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	10	8	8	4	11	7	5	9	6	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	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 2-206 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D		D		
Arousal a)	0	0	0		0		0		0	0
Convulsion b)	0	0	0		0		0		0	0
Abnormal behavior c)	0	0	0		0		0		0	0
Stereotypy d)	0	0	0		0		0		0	0
Gait e)	0	0	0		0		0		0	0
Posture f)	N	N	N		N		N		N	N
Grooming g)	0	0	0		0		0		0	0
Rearing	10	8	6		9		13		10	12
Defecation count	0	0	0		0		0		0	0
Urination h)	0	1	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
D: Dead

Appendix 2-207 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	9	6	6	8	7	8	10	7	8
Defecation count	0	0	0	0	0	0	0	0	0	0
Urination h)	0	0	0	0	0	0	0	0	0	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 2-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): 500

Parameter	Animal number (4113-4122)									
	13	14	15	16	17	18	19	20	21	22
				D		D		D		
Arousal a)	0	0	0		0		0		0	0
Convulsion b)	0	0	0		0		0		0	0
Abnormal behavior c)	0	0	0		0		0		0	0
Stereotypy d)	0	0	0		0		0		0	0
Gait e)	0	0	0		0		0		0	0
Posture f)	N	N	N		N		N		N	N
Grooming g)	0	0	0		0		0		0	0
Rearing	11	7	6		9		14		6	7
Defecation count	0	0	0		0		0		0	0
Urination h)	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
D: Dead

Appendix 2-209 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1	4	3	2	4
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 2-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): 500

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	5	2	2	5
Defecation count	0	0	0	0	0
Urination h)	0	0	0	1	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-211 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	2	7	2	3	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 2-212 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	8	7	3	6	8
Defecation count	0	0	0	0	0
Urination h)	0	0	0	0	0

a) -2: Unconscious/semi-conscious, -1: Reduced awareness, 0: Normal, 1: Increased alertness, 2: Markedly alert
b) 0: None, 1: Minor, 2: Moderate, 3: Severe
c) 0: None, 1: Minor, 2: Moderate, 3: Severe
d) 0: None, 1: Minor, 2: Moderate, 3: Severe
e) U: No/minimal location, 0: Normal, 1: Slight, 2: Moderate, 3: Markedly
f) N: Normal, F: Flattened, H: Hunched
g) 0: None, 1: Occasional bouts (up to four), 2: Numerous bouts (more than four)
h) 0: None, 1: Small amount, 2: Moderate amount, 3: Large/excessive amount

Appendix 2-213 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6	7	10	6	6
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 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Arousal a)		0		0	0
Convulsion b)		0		0	0
Abnormal behavior c)		0		0	0
Stereotypy d)		0		0	0
Gait e)		0		0	0
Posture f)		N		N	N
Grooming g)		0		0	0
Rearing		9		8	11
Defecation count		0		0	0
Urination h)		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
D: Dead

Appendix 2-215 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	9	7	6	6	7
Defecation count	0	0	0	0	0
Urination h)	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 2-216 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Arousal a)		0		0	0
Convulsion b)		0		0	0
Abnormal behavior c)		0		0	0
Stereotypy d)		0		0	0
Gait e)		0		0	0
Posture f)		N		N	N
Grooming g)		0		0	0
Rearing		15		11	10
Defecation count		0		0	0
Urination h)		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
D: Dead

Appendix 2-217 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)	60	60	45	55	57

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 50

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)	69	87	68	56	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 2-219 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 150

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)	72	53	61	51	76

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 6 of administration)
Dose (mg/kg): 500

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)	45	51	82	48	55

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 2-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 (1101-1111)				
	1	2	3	5	11
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	56	67	46	41

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 50

Parameter	Animal number (2104-2111)				
	4	5	6	8	11
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)	62	33	52	25	84

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-223 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 150

Parameter	Animal number (3104-3111)				
	4	5	6	10	11
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)	45	55	45	45	74

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Main group, Lactation day 4)
Dose (mg/kg): 500

Parameter	Animal number (4102-4108)				
	2	4	5	7	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)	56	44	53	59	54

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 2-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)	59	48	76	38	53

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-226 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Auditory response a)		0		0	0
Approach response b)		0		0	0
Touch response c)		0		0	0
Tail pinch response d)		0		0	0
Pupillary reflex e)		P		P	P
Aerial righting reflex (Total score)		0		0	0
Landing foot splay (mm)		60		25	48

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
D: Dead

Appendix 2-227 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)	89	68	44	66	44

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of male rats (Week 2 of recovery)
Dose (mg/kg): 500

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)	30	67	111	55	60

a) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
b) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
c) -1: No reaction/ignores, 0: Normal, 1: Abnormality fearful/aggressive reaction
d) -2: None, -1: Weak, 0: Normal, 1: Exaggerate
e) P: Pass, both, F: Failed, neither, L: Left pupil responds, R: Right pupil responds

Appendix 2-229 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)	57	65	81	41	57

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual manipulative test of female rats (Week 2 of recovery)
Dose (mg/kg): 500

Parameter	Animal number (4118-4122)				
	18	19	20	21	22
	D		D		
Auditory response a)		0		0	0
Approach response b)		0		0	0
Touch response c)		0		0	0
Tail pinch response d)		0		0	0
Pupillary reflex e)		P		P	P
Aerial righting reflex (Total score)		0		0	0
Landing foot splay (mm)		47		31	80

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
D: Dead

Appendix 2-231 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1017	500
1009	1286	531
1010	1408	554
1011	1679	590
1012	1550	491
Mean	1388	533
S.D.	255	40

Appendix 2-232 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 50

Animal number	Fore limb g	Hind limb g
2008	1039	515
2009	1329	512
2010	1236	657
2011	1302	534
2012	1088	529
Mean	1199	549
S.D.	129	61

Appendix 2-233 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 150

Animal number	Fore limb g	Hind limb g
3008	1693	753
3009	1182	480
3010	1370	523
3011	1002	395
3012	1646	719
Mean	1379	574
S.D.	296	155

Appendix 2-234 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 6 of administration)
Dose (mg/kg): 500

Animal number	Fore limb g	Hind limb g
4008	1113	647
4009	1399	561
4010	1611	471
4011	1080	531
4012	1451	524
Mean	1331	547
S.D.	228	65

Appendix 2-235 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1240	507
1102	1559	759
1103	1453	827
1105	1143	497
1111	1250	628
Mean	1329	644
S.D.	171	148

Appendix 2-236 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 50

Animal number	Fore limb g	Hind limb g
2104	1201	443
2105	1042	564
2106	1078	664
2108	1134	710
2111	1180	494
Mean	1127	575
S.D.	67	112

Appendix 2-237 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 150

Animal number	Fore limb g	Hind limb g
3104	932	382
3105	1183	582
3106	1162	467
3110	1344	555
3111	1237	629
Mean	1172	523
S.D.	151	98

Appendix 2-238 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Main group, Lactation day 4)
Dose (mg/kg): 500

Animal number	Fore limb g	Hind limb g
4102	1141	577
4104	1339	520
4105	997	528
4107	1356	572
4108	1143	497
Mean	1195	539
S.D.	151	35

Appendix 2-239 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1304	469
1119	995	553
1120	1420	556
1121	1043	483
1122	1303	501
Mean	1213	512
S.D.	184	40

Appendix 2-240 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Animal number	Fore limb g	Hind limb g
4118D		
4119	883	534
4120D		
4121	795	484
4122	1469	596
Mean	1049	538
S.D.	366	56

D: Dead

Appendix 2-241 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1016	577
1009	1231	738
1010	1529	668
1011	1589	759
1012	1107	684
Mean	1294	685
S.D.	254	71

Appendix 2-242 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of male rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	Fore limb g	Hind limb g
4008	1048	683
4009	1253	513
4010	1438	538
4011	937	551
4012	1299	559
Mean	1195	569
S.D.	201	66

Appendix 2-243 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1344	803
1119	1215	585
1120	1279	647
1121	1066	536
1122	1231	478
Mean	1227	610
S.D.	103	125

Appendix 2-244 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual grip strength of female rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	Fore limb g	Hind limb g
4118D		
4119	1198	700
4120D		
4121	1054	466
4122	974	674
Mean	1075	613
S.D.	114	128

D: Dead

Appendix 2-245 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	372	335	304	176	27	112	1326
1009	345	293	264	207	242	136	1487
1010	396	363	236	271	67	109	1442
1011	419	216	198	0	38	59	930
1012	475	419	227	5	10	113	1249
Mean	401	325	246	132	77	106	1287
S.D.	50	76	40	123	95	28	220

Unit: Count

Appendix 2-246 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 50

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2008	431	385	296	79	34	15	1240
2009	387	343	245	155	295	181	1606
2010	374	277	232	147	121	84	1235
2011	423	374	372	289	106	144	1708
2012	383	184	293	276	110	219	1465
Mean	400	313	288	189	133	129	1451
S.D.	26	83	55	90	97	81	213

Unit: Count

Appendix 2-247 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 150

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3008	402	345	102	305	24	36	1214
3009	472	237	148	322	274	245	1698
3010	416	357	43	94	317	108	1335
3011	418	290	215	305	195	88	1511
3012	449	366	142	216	304	144	1621
Mean	431	319	130	248	223	124	1476
S.D.	28	55	63	96	121	78	200

Unit: Count

Appendix 2-248 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 6 of administration)
Dose (mg/kg): 500

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	317	284	94	166	90	163	1114
4009	428	342	379	225	234	213	1821
4010	461	359	290	323	289	150	1872
4011	417	431	356	339	117	131	1791
4012	445	451	456	371	45	77	1845
Mean	414	373	315	285	155	147	1689
S.D.	57	68	137	86	102	49	323

Unit: Count

Appendix 2-249 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	395	19	7	9	1	17	448
1102	376	168	37	33	12	28	654
1103	461	396	286	223	173	101	1640
1105	348	376	245	11	5	38	1023
1111	378	260	240	145	137	17	1177
Mean	392	244	163	84	66	40	988
S.D.	42	156	130	96	83	35	465

Unit: Count

Appendix 2-250 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 50

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
2104	502	186	382	271	338	270	1949
2105	371	265	219	137	28	37	1057
2106	366	277	55	5	100	20	823
2108	331	338	234	85	67	10	1065
2111	460	355	92	11	103	13	1034
Mean	406	284	196	102	127	70	1186
S.D.	72	67	130	109	122	112	438

Unit: Count

Appendix 2-251 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 150

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
3104	356	238	206	216	113	54	1183
3105	392	399	323	53	183	323	1673
3106	343	66	13	118	189	116	845
3110	324	18	24	77	14	7	464
3111	394	85	1	44	15	33	572
Mean	362	161	113	102	103	107	947
S.D.	31	156	144	70	86	127	492

Unit: Count

Appendix 2-252 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Main group, Lactation day 4)
Dose (mg/kg): 500

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4102	358	197	257	44	205	224	1285
4104	405	270	241	231	260	269	1676
4105	326	107	87	86	224	18	848
4107	378	249	24	232	310	252	1445
4108	94	11	18	5	4	21	153
Mean	312	167	125	120	201	157	1081
S.D.	125	107	116	106	117	126	601

Unit: Count

Appendix 2-253 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	446	489	390	391	433	283	2432
1119	441	378	442	345	281	20	1907
1120	459	421	390	324	335	337	2266
1121	436	343	319	300	152	8	1558
1122	367	296	247	250	253	151	1564
Mean	430	385	358	322	291	160	1945
S.D.	36	74	76	52	104	149	399

Unit: Count

Appendix 2-254 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118D							
4119	409	401	375	348	346	405	2284
4120D							
4121	401	349	287	306	261	294	1898
4122	305	398	329	377	84	176	1669
Mean	372	383	330	344	230	292	1950
S.D.	58	29	44	36	134	115	311

Unit: Count
D: Dead

Appendix 2-255 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	389	359	277	335	266	98	1724
1009	378	342	274	302	328	50	1674
1010	392	363	353	328	354	371	2161
1011	425	309	204	246	239	139	1562
1012	392	337	332	53	4	2	1120
Mean	395	342	288	253	238	132	1648
S.D.	18	21	58	117	139	143	373

Unit: Count

Appendix 2-256 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of male rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4008	350	243	293	277	183	260	1606
4009	353	328	126	0	95	229	1131
4010	381	376	371	248	148	84	1608
4011	422	358	314	337	290	317	2038
4012	477	428	378	108	24	31	1446
Mean	397	347	296	194	148	184	1566
S.D.	53	68	102	137	99	121	328

Unit: Count

Appendix 2-257 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	384	282	247	305	131	283	1632
1119	427	355	415	311	132	18	1658
1120	400	241	332	297	237	420	1927
1121	403	293	331	266	199	238	1730
1122	301	307	288	254	239	205	1594
Mean	383	296	323	287	188	233	1708
S.D.	48	41	62	25	54	145	132

Unit: Count

Appendix 2-258 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual motor activity of female rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	Interval (minutes) 0-10	10-20	20-30	30-40	40-50	50-60	Total(0-60)
4118D							
4119	433	275	252	252	217	334	1763
4120D							
4121	379	277	272	262	28	23	1241
4122	416	310	358	322	265	301	1972
Mean	409	287	294	279	170	219	1659
S.D.	28	20	56	38	125	171	377

Unit: Count
D: Dead

Appendix 3-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	395	409	424	437	457	476	483	88
1002	386	409	421	430	450	475	485	99
1003	405	425	439	453	472	496	509	104
1004	384	408	433	444	460	479	487	103
1005	360	388	414	439	466	492	513	153
1006	429	450	475	505	529	558	573	144
1007	359	366	380	395	412	437	449	90
1008	399	424	445	452	471	496	511	112
1009	373	393	418	431	451	474	487	114
1010	372	391	415	431	451	471	487	115
1011	432	463	496	518	549	577	590	158
1012	382	402	431	433	456	473	491	109
Mean	390	411	433	447	469	492	505	116
S.D.	24	27	30	33	37	39	39	23

Unit: g

Appendix 3-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 50

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
2001	416	440	457	475	495	510	520	104
2002	370	388	415	431	454	472	485	115
2003	388	408	427	441	459	476	485	97
2004	378	400	423	448	469	484	505	127
2005	465	496	515	521	542	558	571	106
2006	391	401	422	445	474	505	510	119
2007	382	417	457	473	503	532	555	173
2008	401	426	450	465	504	531	547	146
2009	357	371	386	406	428	449	455	98
2010	377	402	432	457	488	512	524	147
2011	365	383	400	414	434	456	468	103
2012	394	413	440	460	488	498	518	124
Mean	390	412	435	453	478	499	512	122
S.D.	28	32	33	30	32	33	35	23

Unit: g

Appendix 3-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 150

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
3001	387	410	436	448	464	488	492	105
3002	410	424	442	457	470	486	501	91
3003	369	385	405	416	442	459	474	105
3004	423	465	493	517	541	569	579	156
3005	365	377	401	414	433	449	457	92
3006	407	438	460	490	509	533	545	138
3007	434	464	484	499	517	540	552	118
3008	392	416	439	456	488	523	533	141
3009	375	405	426	440	463	489	506	131
3010	387	399	411	429	448	472	475	88
3011	386	415	439	447	479	500	499	113
3012	368	388	410	428	449	468	477	109
Mean	392	416	437	453	475	498	508	116
S.D.	22	29	30	33	33	36	37	22

Unit: g

Appendix 3-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Administration period)
Dose (mg/kg): 500

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4001	402	413	438	449	467	495	507	105
4002	376	391	412	425	450	474	477	101
4003	411	410	428	447	455	467	473	62
4004	366	377	401	417	438	461	467	101
4005	395	398	418	430	455	474	501	106
4006	380	390	405	418	432	449	456	76
4007	353	365	384	384	396	410	418	65
4008	376	390	409	417	436	453	467	91
4009	366	374	402	405	422	438	444	78
4010	458	472	505	516	546	575	588	130
4011	397	423	451	465	486	503	510	113
4012	413	438	454	462	493	528	546	133
Mean	391	403	426	436	456	477	488	97
S.D.	28	30	33	34	39	44	46	23

Unit: g

Appendix 3-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	252	262	278	26
1102	262	280	297	35
1103	242	261	268	26
1104	258	265	271	13
1105	237	248	258	21
1106	246	250	253	7
1107	232	243	244	12
1108	243	258	272	29
1109	274	287	295	21
1110	234	246	255	21
1111	256	265	271	15
1112	257	267	276	19
Mean	249	261	270	20
S.D.	13	13	16	8

Unit: g

Appendix 3-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Animal number	Day of administration 1	8	15	Gain 1-15
2101	266	283	285	19
2102	245	263	268	23
2103	278	292	298	20
2104	235	255	258	23
2105	258	267	274	16
2106	240	243	254	14
2107	247	265	281	34
2108	227	247	260	33
2109	243	242	247	4
2110	244	254	261	17
2111	247	269	280	33
2112	256	271	273	17
Mean	249	263	270	21
S.D.	14	15	15	9

Unit: g

Appendix 3-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

Animal number	Day of administration 1	8	15	Gain 1-15
3101	258	267	267	9
3102	234	241	251	17
3103	242	243	246	4
3104	250	254	266	16
3105	265	277	279	14
3106	246	255	261	15
3107	276	280	281	5
3108	253	262	270	17
3109	246	252	245	-1
3110	226	250	260	34
3111	256	259	265	9
3112	267	267	287	20
Mean	252	259	265	13
S.D.	14	12	13	9

Unit: g

Appendix 3-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Animal number	Day of administration 1	8	15	Gain 1-15
4101	262	261	260	-2
4102	242	248	259	17
4103	235	239	255	20
4104	244	244	265	21
4105	247	274	281	34
4106	249	246	253	4
4107	257	251	261	4
4108	252	264	278	26
4109	245	255	264	19
4110	269	281	294	25
4111	260	265	276	16
4112a)	260	271		
Mean	252	258	268	17
S.D.	10	13	13	11

Unit: g
a): Died on day 10 of administration

Appendix 3-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	284	303	336	417	133
1102	295	334	372	449	154
1103	272	303	346	433	161
1104	283	298	331	410	127
1105	267	289	330	416	149
1106	Non-pregnant				
1107	254	277	321	398	144
1108	268	297	323	397	129
1109	301	332	364	455	154
1110	269	297	337	411	142
1111	285	316	353	436	151
1112	282	315	361	455	173
Mean	278	306	343	425	147
S.D.	14	17	17	22	14

Unit: g
a): Gestation day

Appendix 3-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 50

Dam number	Administration 0	7	14	20a)	Gain 0-20
2101	292	320	367	436	144
2102	278	304	341	417	139
2103	308	334	375	448	140
2104b)					
2105	279	302	330	408	129
2106	263	296	334	413	150
2107	286	312	351	433	147
2108	267	289	333	420	153
2109	247	284	309	391	144
2110	273	305	342	415	142
2111	285	327	367	464	179
2112	278	297	331	404	126
Mean	278	306	344	423	145
S.D.	16	16	20	21	14

Unit: g
a): Gestation day
b): Excluded from data because the signs of copulation were overlooked on the day of copulation.

Appendix 3-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 150

Dam number	Administration 0	7	14	20a)	Gain 0-20
3101	276	309	342	435	159
3102	260	290	318	404	144
3103	263	297	324	401	138
3104	271	304	347	436	165
3105	267	300	344	411	144
3106	263	293	322	416	153
3107	293	311	343	418	125
3108	279	303	345	416	137
3109	253	277	304	378	125
3110	268	307	347	433	165
3111	279	305	336	431	152
3112	295	318	352	418	123
Mean	272	301	335	416	144
S.D.	13	11	15	17	15

Unit: g
a): Gestation day

Appendix 3-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the gestation period (Main group)
Dose (mg/kg): 500

Dam number	Administration 0	7	14	20a)	Gain 0-20
4101	275	291	331	387	112
4102	264	287	299	348	84
4103b)	260	280			
4104	268	297	329	398	130
4105	292	320	356	428	136
4106c)	253	276	304		
4107d)					
4108	281	297	328	382	101
4109	273	306	346	409	136
4110	310	330	363	429	119
4111e)	279	306			
4112f)					
Mean	276	299	332	397	117
S.D.	16	17	23	28	19

Unit: g
a): Gestation day
b): Died on gestation day 13
c): Died on gestation day 17
d): Excluded from data because the signs of copulation were overlooked on the day of copulation.
e): Died on gestation day 12
f): Died on day 10 of administration

Appendix 3-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	316	328	12
1102	343	381	38
1103	316	350	34
1104	304	313	9
1105	311	328	17
1106	Non-pregnant		
1107b)	251		
1108	316	342	26
1109	330	331	1
1110	330	340	10
1111	354	352	-2
1112	321	357	36
Mean	317	342	18
S.D.	26	19	15

Unit: g
a): Lactation day
b): Sacrificed on day 2 of lactation because all pups died

Appendix 3-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 50

Dam number	Administration 0	Administration 4a)	Gain 0-4
2101	333	342	9
2102	340	355	15
2103	352	357	5
2104	295	352	57
2105	309	336	27
2106	331	342	11
2107	326	337	11
2108	321	325	4
2109	286	298	12
2110	325	337	12
2111	370	371	1
2112	272	310	38
Mean	322	339	17
S.D.	28	20	16

Unit: g
a): Lactation day

Appendix 3-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 150

Dam number	Administration 0	Administration 4a)	Gain 0-4
3101	309	338	29
3102	300	325	25
3103	300	333	33
3104	313	336	23
3105	321	336	15
3106	306	322	16
3107	317	347	30
3108	312	327	15
3109	268	237	-31
3110	332	334	2
3111	332	332	0
3112	334	347	13
Mean	312	326	14
S.D.	18	29	18

Unit: g
a): Lactation day

Appendix 3-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of dams during the lactation period (Main group)
Dose (mg/kg): 500

Dam number	Administration 0	Administration 4a)	Gain 0-4
4101	286	288	2
4102	279	297	18
4103b)			
4104	325	341	16
4105	331	351	20
4106c)			
4107	282	302	20
4108	289	328	39
4109	328	339	11
4110	357	363	6
4111d)			
4112e)			
Mean	310	326	17
S.D.	29	27	11

Unit: g
a): Lactation day
b): Died on gestation day 13
c): Died on gestation day 17
d): Died on gestation day 12
e): Died on day 10 of administration

Appendix 3-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	227	238	246	256	256	268	275	48
1114	254	269	278	277	293	301	293	39
1115	242	243	245	260	271	279	283	41
1116	269	277	280	283	293	296	300	31
1117	255	268	288	293	302	309	322	67
1118	271	277	295	308	322	325	343	72
1119	241	249	256	257	270	274	271	30
1120	243	264	266	283	288	297	298	55
1121	253	256	266	269	272	281	282	29
1122	280	285	288	297	302	308	311	31
Mean	254	263	271	278	287	294	298	44
S.D.	16	16	18	18	20	18	22	16

Unit: g

Appendix 3-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats (Satellite group, Administration period)
Dose (mg/kg): 500

Animal number	Day of administration 1	8	15	22	29	36	42	Gain 1-42
4113	277	284	300	317	348	347	346	69
4114	238	239	241	259	253	262	264	26
4115	246	260	267	277	286	295	291	45
4116a)	261	285	304					
4117	248	256	260	265	282	300	297	49
4118a)	237	246	262					
4119	235	257	264	280	293	305	315	80
4120b)	249	273	285	303				
4121	255	251	265	278	293	285	299	44
4122	260	258	270	275	277	286	288	28
Mean	251	261	272	282	290	297	300	49
S.D.	13	15	19	19	29	26	25	20

Unit: g
a): Died on day 15 of administration
b): Died on day 29 of administration

Appendix 3-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	516	509	525	9
1009	491	498	509	18
1010	489	493	507	18
1011	597	600	610	13
1012	495	498	503	8
Mean	518	520	531	13
S.D.	46	45	45	5

Unit: g

Appendix 3-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of male rats (Recovery period)
Dose (mg/kg): 500

Animal number	Day of recovery 1	8	14	Gain 1-14
4008	467	479	497	30
4009	442	469	476	34
4010	588	602	627	39
4011	510	525	527	17
4012	543	558	579	36
Mean	510	527	541	31
S.D.	58	55	62	9

Unit: g

Appendix 3-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	337	346	340	3
1119	273	268	274	1
1120	304	304	302	-2
1121	281	279	279	-2
1122	310	312	313	3
Mean	301	302	302	1
S.D.	25	31	27	3

Unit: g

Appendix 3-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of female rats (Recovery period)
Dose (mg/kg): 500

Animal number	Day of recovery 1	8	14	Gain 1-14
4118a)				
4119	311	326	325	14
4120b)				
4121	296	295	297	1
4122	290	289	295	5
Mean	299	303	306	7
S.D.	11	20	17	7

Unit: g
a): Died on day 15 of administration
b): Died on day 29 of administration

Appendix 4-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	20	15	18	20	16
1002	26	25	22	22	23	21
1003	21	22	23	23	25	26
1004	22	22	21	17	20	20
1005	22	21	21	20	20	23
1006	25	22	22	24	27	27
1007	20	18	16	18	20	19
1008	22	22	22	21	22	26
1009	19	21	21	21	21	20
1010	21	20	20	21	19	21
1011	28	27	25	23	24	26
1012	17	16	19	21	18	21
Mean	22	21	21	21	22	22
S.D.	3	3	3	2	3	3

Unit: g/rat/day

Appendix 4-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 50

Animal number	Day of administration 2	8	15	30	36	42
2001	22	24	22	19	23	22
2002	18	18	21	17	18	20
2003	22	19	19	19	18	21
2004	24	24	22	22	23	25
2005	29	25	22	19	23	23
2006	18	17	21	21	23	19
2007	23	22	23	23	23	24
2008	24	24	22	19	24	24
2009	19	16	18	22	21	21
2010	24	22	23	24	24	24
2011	20	18	19	18	19	18
2012	24	24	20	19	20	19
Mean	22	21	21	20	22	22
S.D.	3	3	2	2	2	2

Unit: g/rat/day

Appendix 4-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 150

Animal number	Day of administration 2	8	15	30	36	42
3001	27	21	22	20	21	20
3002	24	19	20	19	20	21
3003	18	20	22	19	18	22
3004	25	28	27	25	24	25
3005	19	18	23	21	20	23
3006	25	27	20	24	25	23
3007	30	27	24	24	23	23
3008	25	22	20	22	20	21
3009	27	25	23	22	24	24
3010	22	20	20	21	20	21
3011	24	22	24	23	24	21
3012	21	22	22	22	27	28
Mean	24	23	22	22	22	23
S.D.	3	3	2	2	3	2

Unit: g/rat/day

Appendix 4-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Administration period)
Dose (mg/kg): 500

Animal number	Day of administration 2	8	15	30	36	42
4001	17	24	24	25	25	24
4002	14	17	19	18	22	21
4003	11	19	22	20	21	24
4004	19	20	19	20	21	22
4005	13	21	23	23	25	22
4006	14	22	22	22	19	23
4007	19	16	20	21	15	20
4008	16	23	22	22	23	24
4009	18	19	23	21	22	20
4010	24	26	30	30	29	29
4011	19	23	23	24	24	24
4012	21	28	23	24	27	27
Mean	17	22	23	23	23	23
S.D.	4	4	3	3	4	3

Unit: g/rat/day

Appendix 4-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	20	15	18
1102	20	18	20
1103	18	16	17
1104	16	18	17
1105	17	18	17
1106	15	17	13
1107	11	20	16
1108	16	18	16
1109	15	22	18
1110	17	17	14
1111	17	18	15
1112	12	19	14
Mean	16	18	16
S.D.	3	2	2

Unit: g/rat/day

Appendix 4-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

Animal number	Day of administration 2	8	15
2101	18	20	16
2102	16	19	14
2103	15	20	22
2104	17	17	19
2105	15	16	16
2106	16	14	15
2107	17	18	16
2108	20	17	17
2109	11	16	16
2110	9	17	16
2111	16	19	15
2112	17	17	16
Mean	16	18	17
S.D.	3	2	2

Unit: g/rat/day

Appendix 4-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 150

Animal number	Day of administration 2	8	15
3101	12	18	15
3102	18	14	16
3103	17	17	12
3104	18	14	16
3105	18	18	15
3106	16	15	14
3107	16	18	15
3108	14	17	16
3109	10	18	12
3110	16	18	16
3111	17	13	16
3112	18	10	19
Mean	16	16	15
S.D.	3	3	2

Unit: g/rat/day

Appendix 4-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Animal number	Day of administration 2	8	15
4101	11	14	13
4102	10	15	15
4103	10	14	17
4104	10	14	18
4105	13	18	14
4106	15	12	15
4107	15	12	15
4108	10	15	18
4109	16	15	15
4110	13	15	16
4111	12	16	15
4112a)	8	20	
Mean	12	15	16
S.D.	3	2	2

Unit: g/rat/day
a): Died on day 10 of administration

Appendix 4-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	21	20	18
1102	17	25	24	21
1103	16	18	24	19
1104	14	15	18	19
1105	19	18	23	20
1106	Non-pregnant			
1107	17	21	20	16
1108	14	20	20	20
1109	12	24	20	19
1110	15	20	21	21
1111	16	25	26	20
1112	16	24	22	19
Mean	16	21	22	19
S.D.	2	3	2	1

Unit: g/rat/day
a): Gestation day

Appendix 4-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 50

Dam number	Administration 1	7	14	20a)
2101	17	20	24	20
2102	15	20	23	18
2103	13	20	21	18
2104b)				
2105	13	20	16	18
2106	15	22	22	19
2107	16	18	20	18
2108	17	15	23	17
2109	15	20	15	16
2110	13	20	21	15
2111	20	24	24	25
2112	17	19	24	18
Mean	16	20	21	18
S.D.	2	2	3	3

Unit: g/rat/day
a): Gestation day
b): Excluded from data because the signs of copulation were overlooked on the day of copulation.

Appendix 4-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 150

Dam number	Administration 1	7	14	20a)
3101	17	21	19	20
3102	18	19	21	19
3103	14	21	17	18
3104	17	21	23	22
3105	13	21	22	21
3106	17	19	16	19
3107	19	21	22	19
3108	15	22	26	15
3109	14	19	18	17
3110	17	22	24	18
3111	18	19	23	17
3112	18	22	21	17
Mean	16	21	21	19
S.D.	2	1	3	2

Unit: g/rat/day
a): Gestation day

Appendix 4-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the gestation period (Main group)
Dose (mg/kg): 500

Dam number	Administration 1	7	14	20a)
4101	14	18	20	19
4102	14	17	19	15
4103b)	14	23		
4104	15	18	19	19
4105	19	23	24	19
4106c)	18	18	16	
4107d)				
4108	15	16	18	14
4109	20	17	26	20
4110	19	22	26	22
4111e)	18	26		
4112f)				
Mean	17	20	21	18
S.D.	2	3	4	3

Unit: g/rat/day
a): Gestation day
b): Died on gestation day 13
c): Died on gestation day 17
d): Excluded from data because the signs of copulation were overlooked on the day of copulation.
e): Died on gestation day 12
f): Died on day 10 of administration

Appendix 4-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	Administration 4a)
1101	11	36
1102	27	44
1103	31	44
1104	6	29
1105	21	32
1106	Non-pregnant	
1107b)		
1108	29	36
1109	8	26
1110	12	30
1111	16	31
1112	23	46
Mean	18	35
S.D.	9	7

Unit: g/rat/day
a): Lactation day
b): Sacrificed on day 2 of lactation because all pups died

Appendix 4-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 50

Dam number	Administration 2	4a)
2101	15	43
2102	22	38
2103	21	32
2104	31	40
2105	22	34
2106	26	39
2107	21	34
2108	16	34
2109	19	31
2110	20	37
2111	18	39
2112	11	35
Mean	20	36
S.D.	5	4

Unit: g/rat/day
a): Lactation day

Appendix 4-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 150

Dam number	Administration 2	4a)
3101	15	41
3102	27	49
3103	27	45
3104	15	43
3105	23	34
3106	17	35
3107	28	39
3108	26	38
3109	0	13
3110	19	32
3111	22	34
3112	30	38
Mean	21	37
S.D.	8	9

Unit: g/rat/day
a): Lactation day

Appendix 4-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of dams during the lactation period (Main group)
Dose (mg/kg): 500

Dam number	Administration 2	4a)
4101	31	28
4102	22	36
4103b)		
4104	18	33
4105	24	37
4106c)		
4107	21	32
4108	28	42
4109	23	38
4110	27	39
4111d)		
4112e)		
Mean	24	36
S.D.	4	4

Unit: g/rat/day
a): Lactation day
b): Died on gestation day 13
c): Died on gestation day 17
d): Died on gestation day 12
e): Died on day 10 of administration

Appendix 4-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	13	15	14	14	13	15
1114	14	17	15	8	18	12
1115	13	15	13	16	17	18
1116	18	16	12	16	17	16
1117	21	18	18	18	18	22
1118	19	13	18	18	11	20
1119	11	18	15	11	16	12
1120	18	17	13	17	17	14
1121	15	15	15	17	15	15
1122	15	17	15	14	14	16
Mean	16	16	15	15	16	16
S.D.	3	2	2	3	2	3

Unit: g/rat/day

Appendix 4-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats (Satellite group, Administration period)
Dose (mg/kg): 500

Animal number	Day of administration 2	8	15	30	36	42
4113	12	16	17	19	18	18
4114	12	14	14	13	18	14
4115	15	15	16	14	17	13
4116a)	11	18	19			
4117	10	16	17	18	22	14
4118a)	14	14	17			
4119	8	16	15	21	18	22
4120b)	7	17	18			
4121	18	17	18	16	12	17
4122	14	15	16	9	16	17
Mean	12	16	17	16	17	16
S.D.	3	1	1	4	3	3

Unit: g/rat/day
a): Died on day 15 of administration
b): Died on day 29 of administration

Appendix 4-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 1	8	14
1008	24	27	30
1009	20	26	27
1010	19	27	28
1011	25	27	30
1012	21	23	23
Mean	22	26	28
S.D.	3	2	3

Unit: g/rat/day

Appendix 4-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of male rats (Recovery period)
Dose (mg/kg): 500

Animal number	Day of recovery 1	8	14
4008	22	29	31
4009	18	30	28
4010	27	36	39
4011	20	32	31
4012	24	32	32
Mean	22	32	32
S.D.	3	3	4

Unit: g/rat/day

Appendix 4-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 1	8	14
1118	17	23	18
1119	11	13	19
1120	14	19	20
1121	16	16	19
1122	15	22	18
Mean	15	19	19
S.D.	2	4	1

Unit: g/rat/day

Appendix 4-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual food consumption of female rats (Recovery period)
Dose (mg/kg): 500

Animal number	Day of recovery 1	8	14
4118a)			
4119	20	29	25
4120b)			
4121	14	17	22
4122	17	21	21
Mean	17	22	23
S.D.	3	6	2

Unit: g/rat/day
a): Died on day 15 of administration
b): Died on day 29 of administration

Appendix 5-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	7.0	++	+	-	+-	++	+	Y
1009	>=9.0	++	+	-	-	-	+-	Y
1010	7.5	++	+	-	+-	+	+-	Y
1011	>=9.0	++	+	-	+-	-	+-	Y
1012	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 5-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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	38	9.0	1892	0.95	2.74	1.12
1009	43	15.5	1226	0.87	3.03	1.18
1010	32	6.1	2502	0.73	2.49	1.09
1011	35	14.0	1802	1.32	4.35	1.85
1012	53	21.0	1010	0.92	3.24	1.22
Mean	40	13.1	1686	0.96	3.17	1.29
S.D.	8	5.8	590	0.22	0.72	0.32

Appendix 5-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 50

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
2008	>=9.0	++	+	-	-	-	+-	Y
2009	>=9.0	++	+	-	-	-	+-	Y
2010	7.5	-	+-	-	+-	-	+-	Y
2011	8.0	+	+	-	+-	-	+-	Y
2012	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 5-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 50

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 2-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): 50

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
2008	34	7.3	2300	0.80	2.63	1.18
2009	42	8.4	2032	0.94	2.39	1.02
2010	51	15.8	1824	1.67	4.85	1.96
2011	32	13.0	1726	1.30	3.70	1.69
2012	33	13.0	1542	0.73	3.56	1.17
Mean	38	11.5	1885	1.09	3.43	1.40
S.D.	8	3.5	292	0.39	0.98	0.40

Appendix 5-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 150

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
3008	8.5	+-	+-	-	+-	-	+-	Y
3009	7.0	++	++	-	-	+	+-	Y
3010	7.5	++	+	-	-	-	+-	Y
3011	7.0	++	+	-	+++	-	+-	Y
3012	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 5-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 150

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 2-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): 150

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
3008	51	26.8	860	1.07	4.21	1.66
3009	39	12.8	1834	1.02	3.62	1.51
3010	31	9.5	1938	1.01	3.02	1.41
3011	43	13.2	1576	1.08	3.20	1.50
3012	40	16.1	1416	1.29	3.48	1.67
Mean	41	15.7	1525	1.09	3.51	1.55
S.D.	7	6.6	425	0.11	0.46	0.11

Appendix 5-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 500

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4008	7.0	+	+	-	-	-	+-	Y
4009	7.0	+-	-	-	-	-	+-	Y
4010	7.0	+	+-	-	-	-	+-	Y
4011	7.0	+	+	-	+++	-	+-	Y
4012	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 5-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 6 of administration)
Dose (mg/kg): 500

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 2-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): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	52	11.0	1466	0.62	2.15	1.17
4009	43	19.2	1872	2.00	4.77	2.57
4010	51	23.7	1396	1.80	4.49	2.09
4011	55	25.8	1216	1.60	4.26	2.06
4012	59	24.4	1270	1.42	4.05	2.00
Mean	52	20.8	1444	1.49	3.94	1.98
S.D.	6	6.0	259	0.53	1.04	0.51

Appendix 5-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6.5	+	+-	-	-	-	+-	Y
1119	8.0	++	+	-	-	+	+-	Y
1120	6.0	+	+-	-	-	+	+-	Y
1121	6.5	+	+-	-	-	+	+-	Y
1122	6.0	+	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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	30	8.0	1708	0.88	2.30	1.22
1119	23	4.3	2236	0.45	1.52	0.71
1120	27	4.1	2404	0.34	1.58	0.48
1121	20	6.5	2308	1.03	2.27	1.08
1122	36	13.5	1386	1.03	2.94	1.16
Mean	27	7.3	2008	0.75	2.12	0.93
S.D.	6	3.8	440	0.33	0.59	0.32

Appendix 5-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 500

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118D								
4119	6.0	+-	+-	-	-	-	+-	Y
4120D								
4121	6.0	-	-	-	-	-	+-	Y
4122	6.5	+	+-	-	-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow
D: Dead

Appendix 5-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Satellite group, Week 6 of administration)
Dose (mg/kg): 500

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118D							
4119	-	-	+-	-	-	-	-
4120D							
4121	-	-	+-	-	-	-	-
4122	-	-	+-	-	-	-	-

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

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

D: Dead

Appendix 5-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118D						
4119	47	16.2	810	0.78	1.89	0.84
4120D						
4121	42	11.7	1180	0.87	2.00	1.26
4122	27	7.8	1564	0.70	1.65	0.80
Mean	39	11.9	1185	0.78	1.85	0.97
S.D.	10	4.2	377	0.09	0.18	0.25

D: Dead

Appendix 5-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	8.5	++	+	-	+-	+	+-	Y
1009	8.0	+	+	-	+-	-	+-	Y
1010	8.5	+	+	-	-	-	+-	Y
1011	8.0	++	+	-	+-	-	+-	Y
1012	8.0	+-	-	-	+-	-	+-	Y

1) - : 0 mg/dL +- : 15 mg/dL + : 30 mg/dL ++ : 100 mg/dL +++ : >=300 mg/dL
2) - : 0 mg/dL +- : 5 mg/dL + : 15 mg/dL ++ : 40 mg/dL +++ : 80 mg/dL
3) - : 0 mg/dL + : 100 mg/dL ++ : 250 mg/dL +++ : 500 mg/dL ++++ : >=1000 mg/dL
4) - : 0 mg/dL +- : 0.015 mg/dL + : 0.062 mg/dL ++ : 0.135 mg/dL +++ : 0.405 mg/dL
5) - : 0 mg/dL + : 0.8 mg/dL ++ : 1.6 mg/dL +++ : 3.2 mg/dL
6) +- : 0.1-1.0 E.U./dL + : 2.0 E.U./dL ++ : 4.0 E.U./dL +++ : >=8.0 E.U./dL
7) LY : Light yellow Y : Yellow DY : Dark yellow

Appendix 5-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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	52	14.9	1732	1.19	4.47	1.61
1009	40	14.9	1682	1.19	4.16	1.55
1010	37	11.5	2208	1.40	3.59	1.61
1011	45	17.4	2056	1.50	5.97	2.19
1012	55	21.1	1500	1.27	5.25	2.03
Mean	46	16.0	1836	1.31	4.69	1.80
S.D.	8	3.6	289	0.14	0.93	0.29

Appendix 5-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4008	>=9.0	+-	+-	-	-	-	+-	Y
4009	8.5	+-	+-	-	-	-	+-	Y
4010	8.5	+	+	-	-	-	+-	Y
4011	7.5	+	+	-	+++	-	+-	Y
4012	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 5-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of male rats (Week 2 of recovery)
Dose (mg/kg): 500

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 2-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): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4008	49	17.2	1714	1.20	4.88	2.03
4009	45	18.7	1904	1.98	5.85	2.66
4010	60	26.4	1554	1.90	6.71	2.69
4011	59	25.9	1364	1.66	5.65	2.33
4012	64	24.8	1476	1.34	6.00	2.28
Mean	55	22.6	1602	1.62	5.82	2.40
S.D.	8	4.3	211	0.34	0.66	0.28

Appendix 5-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6.5	+-	-	-	-	-	+-	Y
1121	7.5	+	+-	-	-	-	+-	Y
1122	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 5-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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	39	11.6	1648	1.00	3.32	1.42
1119	30	4.6	3270	0.98	2.31	1.19
1120	27	3.9	3766	0.68	2.21	0.89
1121	36	5.4	2200	0.50	2.11	0.78
1122	36	9.3	2098	1.04	3.11	1.15
Mean	34	7.0	2596	0.84	2.61	1.09
S.D.	5	3.3	884	0.24	0.56	0.25

Appendix 5-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	pH	1) Protein	2) Ketone body	3) Glucose	4) Occult blood	5) Bilirubin	6) Urobilinogen	7) Color
4118D								
4119	>=9.0	+	+-	-	-	-	+-	Y
4120D								
4121	8.5	+-	+-	-	-	-	+-	Y
4122	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
D: Dead

Appendix 5-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual urinalysis of female rats (Week 2 of recovery)
Dose (mg/kg): 500

Animal number	URINE SEDIMENT						
						CRYSTALLIZATION	
	RBC	WBC	SEC	SREC	Cast	PS	CO
4118D							
4119	-	-	+-	-	-	+-	-
4120D							
4121	-	-	+-	-	-	+-	-
4122	-	-	+-	-	-	+-	-

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

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

D: Dead

Appendix 5-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

Animal number	Water intake mL/24h	Urine volume mL/24h	Osmotic Pressure mOsm/kg	Na mmol/24h	K mmol/24h	Cl mmol/24h
4118D						
4119	30	10.9	1866	1.20	2.99	1.35
4120D						
4121	34	9.7	1942	0.95	2.95	1.28
4122	28	7.0	2746	1.05	3.00	1.12
Mean	31	9.2	2185	1.07	2.98	1.25
S.D.	3	2.0	488	0.13	0.03	0.12

D: Dead

Appendix 6-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	859	14.4	41.7	48.6	16.8	34.6	2.4	103.8	16.4	23.0	236
1002	894	15.5	45.0	50.3	17.3	34.4	2.4	118.5	14.4	23.6	244
1003	842	14.9	42.4	50.4	17.7	35.0	2.1	97.2	13.6	19.3	233
1004	878	15.3	43.8	49.8	17.4	34.9	1.9	91.9	14.5	15.9	255
1005	842	14.8	43.1	51.1	17.6	34.4	2.2	87.3	14.0	20.7	244
Mean	863	15.0	43.2	50.0	17.4	34.7	2.2	99.7	14.6	20.5	242
S.D.	23	0.4	1.3	0.9	0.4	0.3	0.2	12.2	1.1	3.1	9

Appendix 6-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	107.3	79.3	16.9	0.7	0.4	1.9	0.7	85.1	18.2	0.8	0.4	2.1	0.8
1002	64.2	76.7	18.0	1.2	0.3	2.7	1.2	49.2	11.6	0.8	0.2	1.7	0.7
1003	80.3	66.6	27.8	2.1	0.3	1.9	1.2	53.5	22.3	1.7	0.3	1.6	1.0
1004	61.8	63.3	32.1	1.3	0.3	2.5	0.4	39.2	19.8	0.8	0.2	1.6	0.3
1005	89.5	75.5	22.0	0.6	0.2	1.0	0.7	67.6	19.7	0.5	0.2	0.9	0.6
Mean	80.6	72.3	23.4	1.2	0.3	2.0	0.8	58.9	18.3	0.9	0.3	1.6	0.7
S.D.	18.8	6.9	6.5	0.6	0.1	0.7	0.4	17.8	4.0	0.5	0.1	0.4	0.3

LUC: Large unstained cells

Appendix 6-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 50

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	821	14.4	41.1	50.0	17.5	35.0	2.2	92.3	12.8	15.1	256
2002	845	14.8	43.5	51.5	17.5	33.9	1.9	110.6	15.8	21.3	219
2003	850	15.2	43.1	50.6	17.8	35.2	2.0	110.3	16.7	18.9	342
2004	850	15.0	43.2	50.8	17.6	34.7	1.8	109.4	15.2	16.8	259
2005	879	15.5	44.0	50.1	17.7	35.3	2.0	106.9	14.5	14.5	294
Mean	849	15.0	43.0	50.6	17.6	34.8	2.0	105.9	15.0	17.3	274
S.D.	21	0.4	1.1	0.6	0.1	0.6	0.1	7.7	1.5	2.8	46

Appendix 6-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 50

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	57.9	74.6	21.3	1.1	0.4	1.7	1.0	43.2	12.3	0.6	0.2	1.0	0.6
2002	59.1	72.1	22.1	1.5	0.3	3.3	0.7	42.6	13.1	0.9	0.2	1.9	0.4
2003	51.2	60.0	34.5	2.5	0.2	2.0	0.9	30.7	17.7	1.3	0.1	1.0	0.5
2004	63.7	72.5	20.1	1.7	0.3	4.1	1.3	46.1	12.8	1.1	0.2	2.6	0.8
2005	75.7	73.3	22.5	1.6	0.3	1.8	0.4	55.5	17.1	1.2	0.2	1.3	0.3
Mean	61.5	70.5	24.1	1.7	0.3	2.6	0.9	43.6	14.6	1.0	0.2	1.6	0.5
S.D.	9.1	5.9	5.9	0.5	0.1	1.1	0.3	8.9	2.6	0.3	0.0	0.7	0.2

LUC: Large unstained cells

Appendix 6-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 150

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	807	14.7	42.3	52.4	18.2	34.7	2.2	100.5	21.7	21.6	261
3002	765	14.5	41.5	54.2	18.9	34.9	2.5	130.6	13.7	16.8	237
3003	845	14.9	43.5	51.5	17.6	34.2	2.7	115.8	17.7	19.6	316
3004	835	14.8	43.2	51.7	17.8	34.3	2.5	100.0	13.4	18.9	243
3005	846	15.2	43.9	51.8	17.9	34.6	2.1	94.2	18.3	21.7	277
Mean	820	14.8	42.9	52.3	18.1	34.5	2.4	108.2	17.0	19.7	267
S.D.	34	0.3	1.0	1.1	0.5	0.3	0.2	14.8	3.5	2.0	32

Appendix 6-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 150

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	128.6	79.3	17.1	1.2	0.4	1.5	0.6	101.9	22.0	1.5	0.5	1.9	0.8
3002	116.5	77.2	20.1	0.6	0.4	1.1	0.7	89.9	23.4	0.7	0.5	1.3	0.8
3003	83.4	74.4	20.1	1.5	0.4	2.2	1.4	62.0	16.8	1.2	0.3	1.8	1.1
3004	57.5	63.7	30.0	2.1	0.2	2.8	1.2	36.6	17.2	1.2	0.1	1.6	0.7
3005	75.2	74.7	22.3	0.5	0.3	1.8	0.3	56.2	16.8	0.4	0.2	1.3	0.3
Mean	92.2	73.9	21.9	1.2	0.3	1.9	0.8	69.3	19.2	1.0	0.3	1.6	0.7
S.D.	29.5	6.0	4.9	0.7	0.1	0.7	0.5	26.4	3.2	0.4	0.2	0.3	0.3

LUC: Large unstained cells

Appendix 6-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 500

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	848*	14.4*	43.0*	50.7*	17.0*	33.6*	2.2*	124.3*	17.2	20.5	305
4002	889	14.8	44.1	49.5	16.6	33.5	1.5	98.8	20.1	22.1	306
4003	816	13.9	39.9	48.8	17.1	34.9	1.3	107.4	16.1	22.1	359
4004	860	15.2	44.0	51.2	17.6	34.4	2.0	93.8	20.3	18.5	303
4005	809	13.6	39.3	48.6	16.8	34.5	2.7	112.1	18.1	26.0	346
Mean	844	14.4	42.1	49.8	17.0	34.2	1.9	107.3	18.4	21.8	324
S.D.	33	0.6	2.3	1.2	0.4	0.6	0.6	11.9	1.8	2.8	27

*: Re-analyzed value

Appendix 6-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of administration)
Dose (mg/kg): 500

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	99.8*	79.8*	16.6*	1.2*	0.3*	1.6*	0.5*	79.6*	16.6*	1.2*	0.3*	1.6*	0.5*
4002	69.5	78.9	17.4	0.9	0.4	1.8	0.5	54.8	12.1	0.7	0.3	1.2	0.4
4003	67.0	75.6	20.0	1.4	0.3	2.2	0.4	50.7	13.4	0.9	0.2	1.5	0.3
4004	80.7	66.8	28.2	1.2	0.4	2.3	1.2	53.9	22.7	0.9	0.3	1.8	1.0
4005	92.9	82.5	14.9	0.6	0.2	1.3	0.5	76.7	13.9	0.6	0.2	1.2	0.4
Mean	82.0	76.7	19.4	1.1	0.3	1.8	0.6	63.1	15.7	0.9	0.3	1.5	0.5
S.D.	14.3	6.1	5.2	0.3	0.1	0.4	0.3	13.8	4.2	0.2	0.1	0.3	0.3

LUC: Large unstained cells
*: Re-analyzed value

Appendix 6-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	691	12.3	36.2	52.4	17.8	34.1	8.4	162.1	10.6	12.7	268
1102	710	13.4	39.7	55.9	18.9	33.7	8.5	136.7	10.5	13.1	282
1103	738	13.6	40.2	54.5	18.4	33.8	6.2	144.7	11.6	14.4	390
1105	746	13.9	41.4	55.5	18.6	33.6	7.7	133.1	12.1	10.7	337
1106a)	771Z	15.1Z	43.5Z	56.4Z	19.6Z	34.8Z	3.4Z	137.0Z	12.8Z	16.0Z	206Z
1107b)	537Z	9.6Z	28.6Z	53.3Z	17.9Z	33.6Z	8.3Z	191.9Z	9.3Z	12.7Z	323Z
1111	682	12.9	37.9	55.7	18.9	33.9	7.1	183.6	11.2	13.7	203
Mean	713	13.2	39.1	54.8	18.5	33.8	7.6	152.0	11.2	12.9	296
S.D.	28	0.6	2.0	1.4	0.5	0.2	1.0	20.9	0.7	1.4	71

a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 6-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	131.3	62.4	34.3	0.4	0.3	1.9	0.8	81.9	45.0	0.5	0.3	2.5	1.1
1102	116.4	64.0	27.9	0.7	0.5	4.6	2.4	74.4	32.4	0.8	0.5	5.3	2.8
1103	58.1	56.4	40.3	0.9	0.1	1.7	0.6	32.8	23.4	0.5	0.0	1.0	0.3
1105	156.6	38.9	57.2	0.4	0.3	2.4	0.9	60.9	89.6	0.5	0.4	3.7	1.4
1106a)	126.6Z	66.7Z	28.8Z	1.4Z	0.4Z	1.5Z	1.2Z	84.4Z	36.5Z	1.8Z	0.5Z	1.9Z	1.5Z
1107b)	223.8Z	36.0Z	56.1Z	0.3Z	0.2Z	6.8Z	0.6Z	80.5Z	125.6Z	0.7Z	0.5Z	15.2Z	1.3Z
1111	100.4	64.0	32.7	0.3	0.2	2.2	0.7	64.3	32.9	0.3	0.2	2.2	0.7
Mean	112.6	57.1	38.5	0.5	0.3	2.6	1.1	62.9	44.7	0.5	0.3	2.9	1.3
S.D.	36.8	10.7	11.4	0.3	0.1	1.2	0.7	18.7	26.3	0.2	0.2	1.6	1.0

LUC: Large unstained cells
a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 6-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 50

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
2104	738	13.1	38.5	52.2	17.8	34.1	6.8	150.1	11.2	13.8	379
2105	731	13.9	40.9	55.9	19.0	33.9	7.9	148.6	11.3	12.5	262
2106	707	14.1	42.4	59.9	19.9	33.2	8.9	154.9	11.9	16.8	344
2108	710	13.4	39.8	56.0	18.9	33.8	8.3	162.8	11.7	13.8	295
2111	699	12.5	36.7	52.6	17.9	34.1	7.6	168.2	12.5	16.7	219
Mean	717	13.4	39.7	55.3	18.7	33.8	7.9	156.9	11.7	14.7	300
S.D.	17	0.6	2.2	3.1	0.9	0.4	0.8	8.4	0.5	1.9	64

Appendix 6-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 50

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
2104	122.6	60.8	36.2	1.0	0.4	1.0	0.5	74.6	44.4	1.2	0.5	1.2	0.7
2105	93.1	51.9	44.3	0.4	0.3	2.8	0.4	48.3	41.2	0.3	0.3	2.6	0.4
2106	111.9	50.8	45.0	0.6	0.2	2.7	0.6	56.8	50.4	0.7	0.3	3.0	0.7
2108	116.5	58.1	37.7	0.3	0.3	2.6	1.0	67.7	44.0	0.4	0.3	3.0	1.2
2111	94.4	57.6	37.7	0.6	0.3	3.0	0.9	54.4	35.5	0.5	0.3	2.8	0.8
Mean	107.7	55.8	40.2	0.6	0.3	2.4	0.7	60.4	43.1	0.6	0.3	2.5	0.8
S.D.	13.3	4.3	4.1	0.3	0.1	0.8	0.3	10.6	5.4	0.4	0.1	0.8	0.3

LUC: Large unstained cells

Appendix 6-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 150

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
3104	724	13.0	38.3	53.0	17.9	33.8	5.9	160.3	10.8	15.5	247
3105	743	14.0	41.3	55.6	18.9	33.9	7.0	133.0	11.7	15.9	220
3106	704	13.1	39.4	55.9	18.7	33.4	7.3	169.4	13.0	16.8	283
3110	757	14.2	41.4	54.7	18.7	34.3	6.6	147.3	11.8	15.7	256
3111	723	13.8	40.2	55.7	19.1	34.3	5.8	137.2	12.3	15.1	198
Mean	730	13.6	40.1	55.0	18.7	33.9	6.5	149.4	11.9	15.8	241
S.D.	20	0.5	1.3	1.2	0.5	0.4	0.7	15.3	0.8	0.6	33

Appendix 6-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 150

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
3104	86.2	42.2	52.8	0.3	0.2	4.2	0.4	36.4	45.5	0.3	0.1	3.6	0.3
3105	64.8	64.3	30.0	0.4	0.2	4.1	1.0	41.7	19.5	0.3	0.1	2.6	0.7
3106	95.0	59.5	35.9	0.9	0.3	2.6	0.9	56.5	34.1	0.8	0.2	2.5	0.8
3110	112.5	54.2	40.9	0.9	0.2	3.1	0.7	61.0	46.0	1.0	0.2	3.5	0.8
3111	107.7	61.8	33.5	0.9	0.3	2.9	0.7	66.5	36.1	1.0	0.3	3.1	0.7
Mean	93.2	56.4	38.6	0.7	0.2	3.4	0.7	52.4	36.2	0.7	0.2	3.1	0.7
S.D.	19.0	8.8	8.9	0.3	0.1	0.7	0.2	12.8	10.8	0.4	0.1	0.5	0.2

LUC: Large unstained cells

Appendix 6-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 500

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
4102	605	12.2	37.5	61.9	20.1	32.5	11.4	196.0	10.9	11.7	246
4104	711	13.3	38.8	54.5	18.8	34.4	6.1	158.1	10.6	13.6	231
4105	703	13.4	38.2	54.4	19.0	35.0	5.1	159.1	11.7	17.6	250
4107	681	13.3	38.5	56.5	19.5	34.5	5.1	170.3	11.2	14.0	214
4108	677	12.6	36.9	54.5	18.7	34.2	8.4	135.8	11.7	14.3	277
Mean	675	13.0	38.0	56.4	19.2	34.1	7.2	163.9	11.2	14.2	244
S.D.	42	0.5	0.8	3.2	0.6	1.0	2.7	21.9	0.5	2.1	23

Appendix 6-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Lactation day 5)
Dose (mg/kg): 500

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
4102	95.7	65.5	27.9	0.4	0.2	4.4	1.7	62.7	26.7	0.3	0.2	4.2	1.6
4104	127.1	54.0	42.0	0.4	0.3	2.4	0.9	68.7	53.4	0.5	0.3	3.1	1.2
4105	124.5	60.5	31.7	0.4	0.3	5.1	2.0	75.4	39.5	0.5	0.4	6.3	2.5
4107	164.6	50.8	43.6	0.3	0.4	3.6	1.3	83.7	71.7	0.5	0.7	5.9	2.2
4108	100.5	61.1	36.5	0.2	0.2	1.4	0.7	61.3	36.6	0.2	0.2	1.4	0.7
Mean	122.5	58.4	36.3	0.3	0.3	3.4	1.3	70.4	45.6	0.4	0.4	4.2	1.6
S.D.	27.4	5.9	6.7	0.1	0.1	1.5	0.5	9.3	17.4	0.1	0.2	2.0	0.7

LUC: Large unstained cells

Appendix 6-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	850	15.8	46.1	54.3	18.6	34.3	2.0	95.5	11.9	17.4	192
1114	832	15.2	43.2	51.9	18.3	35.3	2.1	103.7	10.9	13.2	192
1115	787	13.8	40.2	51.0	17.6	34.5	2.9	108.5	11.7	17.9	184
1116	839	15.5	44.6	53.2	18.5	34.8	2.8	102.9	11.7	17.6	204
1117	796	14.7	42.5	53.4	18.5	34.6	2.1	111.3	10.9	13.6	208
Mean	821	15.0	43.3	52.8	18.3	34.7	2.4	104.4	11.4	15.9	196
S.D.	28	0.8	2.2	1.3	0.4	0.4	0.4	6.0	0.5	2.3	10

Appendix 6-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	64.1	85.5	11.1	1.7	0.3	1.0	0.3	54.8	7.1	1.1	0.2	0.7	0.2
1114	83.6	83.9	13.5	0.7	0.3	1.2	0.4	70.1	11.3	0.6	0.3	1.0	0.4
1115	60.0	78.8	17.2	1.1	0.2	1.5	1.2	47.3	10.3	0.7	0.1	0.9	0.7
1116	49.0	73.0	23.7	1.1	0.2	1.6	0.5	35.8	11.6	0.5	0.1	0.8	0.2
1117	33.9	75.3	19.9	1.9	0.3	2.3	0.4	25.5	6.7	0.6	0.1	0.8	0.1
Mean	58.1	79.3	17.1	1.3	0.3	1.5	0.6	46.7	9.4	0.7	0.2	0.8	0.3
S.D.	18.4	5.4	5.0	0.5	0.1	0.5	0.4	17.2	2.3	0.2	0.1	0.1	0.2

LUC: Large unstained cells

Appendix 6-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

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	745	14.7	42.2	56.6	19.8	34.9	2.5	108.7	10.4	15.1	218
4114	792	13.8	39.4	49.8	17.4	34.9	2.8	128.2	10.8	14.5	226
4115	793	15.2	43.9	55.4	19.1	34.5	1.9	92.0	10.8	16.9	205
4116D											
4117	749	14.3	40.1	53.5	19.1	35.7	1.9	126.7	11.6	15.3	188
Mean	770	14.5	41.4	53.8	18.9	35.0	2.3	113.9	10.9	15.5	209
S.D.	26	0.6	2.0	3.0	1.0	0.5	0.5	17.1	0.5	1.0	17

D: Dead

Appendix 6-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

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	72.4	77.7	18.2	1.4	0.3	1.9	0.5	56.2	13.2	1.0	0.2	1.4	0.3
4114	102.7	78.5	17.5	1.0	0.3	1.7	1.0	80.6	17.9	1.1	0.3	1.7	1.1
4115	68.5	79.6	15.7	1.1	0.2	2.5	0.8	54.5	10.8	0.8	0.2	1.7	0.5
4116D													
4117	61.1	82.8	12.9	1.9	0.2	1.8	0.4	50.6	7.9	1.2	0.1	1.1	0.2
Mean	76.2	79.7	16.1	1.4	0.3	2.0	0.7	60.5	12.5	1.0	0.2	1.5	0.5
S.D.	18.3	2.2	2.4	0.4	0.1	0.4	0.3	13.6	4.2	0.2	0.1	0.3	0.4

LUC: Large unstained cells
D: Dead

Appendix 6-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	898	15.8	46.0	51.2	17.6	34.3	1.9	90.5	17.3	21.9	331
1009	944	16.0	46.5	49.3	16.9	34.4	1.6	83.6	15.6	22.6	283
1010	942	15.8	45.8	48.6	16.8	34.5	1.9	95.8	16.6	19.6	273
1011	960	15.6	45.1	47.0	16.3	34.6	1.4	86.6	18.2	22.1	314
1012	954	16.0	46.8	49.0	16.7	34.1	1.7	97.1	17.4	20.3	273
Mean	940	15.8	46.0	49.0	16.9	34.4	1.7	90.7	17.0	21.3	295
S.D.	24	0.2	0.7	1.5	0.5	0.2	0.2	5.8	1.0	1.3	26

Appendix 6-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	99.9	76.8	17.4	2.7	0.4	2.1	0.5	76.8	17.4	2.7	0.4	2.1	0.5
1009	80.9	82.4	12.7	0.7	0.5	1.6	2.2	66.7	10.2	0.5	0.4	1.3	1.8
1010	55.7	76.9	18.2	1.5	0.4	2.0	1.1	42.9	10.1	0.8	0.2	1.1	0.6
1011	53.2	61.7	33.6	0.8	0.2	3.2	0.4	32.8	17.9	0.4	0.1	1.7	0.2
1012	52.0	77.2	17.7	1.3	0.5	2.1	1.3	40.2	9.2	0.7	0.2	1.1	0.7
Mean	68.3	75.0	19.9	1.4	0.4	2.2	1.1	51.9	13.0	1.0	0.3	1.5	0.8
S.D.	21.3	7.8	8.0	0.8	0.1	0.6	0.7	18.9	4.3	1.0	0.1	0.4	0.6

LUC: Large unstained cells

Appendix 6-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 500

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	931	15.5	46.0	49.4	16.6	33.7	1.7	97.9	20.2	23.5	292
4009	934	16.2	47.2	50.5	17.4	34.4	1.8	86.7	17.2	23.7	260
4010	887	15.1	43.4	48.9	17.0	34.7	2.0	105.4	14.2	19.9	305
4011	891	15.2	43.7	49.0	17.0	34.8	1.9	103.3	16.9	23.7	268
4012	877	15.0	44.1	50.2	17.2	34.2	2.2	99.4	17.6	21.8	301
Mean	904	15.4	44.9	49.6	17.0	34.4	1.9	98.5	17.2	22.5	285
S.D.	27	0.5	1.6	0.7	0.3	0.4	0.2	7.3	2.1	1.7	20

Appendix 6-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of male rats (End of recovery)
Dose (mg/kg): 500

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	88.6	77.9	17.9	1.5	0.3	1.6	0.7	69.0	15.8	1.3	0.3	1.5	0.6
4009	72.2	86.7	9.5	1.4	0.4	0.8	1.2	62.6	6.9	1.0	0.3	0.6	0.9
4010	116.5	78.2	16.5	1.5	0.7	2.5	0.7	91.1	19.2	1.7	0.8	2.9	0.8
4011	52.7	64.3	30.1	2.0	0.2	2.2	1.2	33.9	15.8	1.0	0.1	1.2	0.6
4012	85.0	71.1	22.8	2.9	0.2	2.2	0.6	60.5	19.4	2.5	0.2	1.9	0.6
Mean	83.0	75.6	19.4	1.9	0.4	1.9	0.9	63.4	15.4	1.5	0.3	1.6	0.7
S.D.	23.4	8.4	7.7	0.6	0.2	0.7	0.3	20.5	5.1	0.6	0.3	0.9	0.1

LUC: Large unstained cells

Appendix 6-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	852	15.7	44.9	52.6	18.4	35.0	1.4	101.3	11.6	17.1	171
1119	882	15.9	45.9	52.0	18.0	34.7	1.8	97.2	12.4	19.7	170
1120	891	16.0	45.2	50.8	17.9	35.3	1.3	129.7	12.8	15.9	188
1121	920	15.9	46.3	50.4	17.3	34.2	2.0	100.0	11.6	17.8	198
1122	851	16.3	46.2	54.2	19.2	35.4	1.9	86.5	11.9	15.5	172
Mean	879	16.0	45.7	52.0	18.2	34.9	1.7	102.9	12.1	17.2	180
S.D.	29	0.2	0.6	1.5	0.7	0.5	0.3	16.1	0.5	1.7	13

Appendix 6-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	47.0	71.9	22.5	2.4	0.2	2.5	0.5	33.8	10.6	1.1	0.1	1.2	0.2
1119	40.8	85.6	11.6	0.9	0.3	0.8	0.9	34.9	4.7	0.4	0.1	0.3	0.4
1120	66.2	77.9	16.7	2.7	0.4	1.5	0.9	51.6	11.1	1.8	0.2	1.0	0.6
1121	53.9	64.7	31.1	1.1	0.3	2.2	0.7	34.9	16.8	0.6	0.2	1.2	0.4
1122	74.4	75.0	20.7	1.4	0.4	2.0	0.5	55.9	15.4	1.0	0.3	1.5	0.4
Mean	56.5	75.0	20.5	1.7	0.3	1.8	0.7	42.2	11.7	1.0	0.2	1.0	0.4
S.D.	13.8	7.7	7.2	0.8	0.1	0.7	0.2	10.6	4.8	0.5	0.1	0.5	0.1

LUC: Large unstained cells

Appendix 6-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 500

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
4118D											
4119	814	15.6	44.2	54.3	19.1	35.3	1.9	119.6	11.0	17.2	221
4120D											
4121	852	15.5	43.2	50.8	18.2	35.9	2.2	106.7	11.4	14.3	180
4122	904	15.8	44.5	49.2	17.4	35.4	1.1	109.2	12.0	14.3	205
Mean	857	15.6	44.0	51.4	18.2	35.5	1.7	111.8	11.5	15.3	202
S.D.	45	0.2	0.7	2.6	0.9	0.3	0.6	6.8	0.5	1.7	21

D: Dead

Appendix 6-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hematology of female rats (End of recovery)
Dose (mg/kg): 500

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
4118D													
4119	67.3	62.9	31.5	1.9	0.4	2.8	0.5	42.3	21.2	1.3	0.2	1.9	0.3
4120D													
4121	85.2	84.4	12.1	0.9	0.4	1.1	1.0	71.9	10.4	0.8	0.3	0.9	0.9
4122	43.4	71.7	22.9	2.5	0.2	1.7	1.0	31.1	9.9	1.1	0.1	0.8	0.4
Mean	65.3	73.0	22.2	1.8	0.3	1.9	0.8	48.4	13.8	1.1	0.2	1.2	0.5
S.D.	21.0	10.8	9.7	0.8	0.1	0.9	0.3	21.1	6.4	0.3	0.1	0.6	0.3

LUC: Large unstained cells
D: Dead

Appendix 7-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	45	24	48	0	243	5.1	40	44	71	0.1	162
1002	61	33	44	1	326	23.5	55	32	91	0.1	156
1003	60	29	44	0	440	18.2	42	34	80	0.1	152
1004	58	24	47	1	359	6.6	39	49	72	0.0	140
1005	54	23	32	1	389	21.8	47	34	79	0.1	169
Mean	56	27	43	1	351	15.0	45	39	79	0.1	156
S.D.	7	4	6	1	74	8.6	7	7	8	0.0	11

Appendix 7-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	11	0.36	142	4.7	104	9.4	6.1	5.5	3.1	1.29
1002	13	0.32	144	4.6	107	9.7	5.7	5.7	3.2	1.28
1003	12	0.31	142	4.5	108	9.6	5.5	5.5	3.3	1.50
1004	16	0.28	143	4.9	108	10.0	6.9	5.4	3.0	1.25
1005	14	0.35	144	4.7	108	9.1	6.3	5.5	3.2	1.39
Mean	13	0.32	143	4.7	107	9.6	6.1	5.5	3.2	1.34
S.D.	2	0.03	1	0.1	2	0.3	0.5	0.1	0.1	0.10

Appendix 7-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 50

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	54	27	41	1	274	8.9	48	27	78	0.1	162
2002	59	27	41	0	497	3.2	50	23	79	0.1	126
2003	56	21	40	1	357	4.6	33	16	54	0.1	122
2004	55	27	46	0	353	3.7	53	45	85	0.1	129
2005	58	20	52	1	309	17.8	51	42	81	0.1	152
Mean	56	24	44	1	358	7.6	47	31	75	0.1	138
S.D.	2	4	5	1	85	6.1	8	12	12	0.0	18

Appendix 7-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 50

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	13	0.32	141	4.8	105	9.5	6.1	5.3	3.1	1.41
2002	12	0.34	144	4.7	107	9.7	6.0	5.7	3.2	1.28
2003	13	0.35	145	4.2	108	9.6	5.6	5.8	3.0	1.07
2004	12	0.23	143	4.8	104	10.4	6.4	5.5	3.1	1.29
2005	15	0.33	143	5.0	106	10.3	6.5	5.6	3.2	1.33
Mean	13	0.31	143	4.7	106	9.9	6.1	5.6	3.1	1.28
S.D.	1	0.05	1	0.3	2	0.4	0.4	0.2	0.1	0.13

Appendix 7-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 150

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	53	28	53	1	463	5.2	46	38	79	0.1	152
3002	60	28	63	1	570	3.3	48	48	84	0.1	159
3003	76	34	52	1	328	8.1	57	26	83	0.1	129
3004	53	20	40	1	339	11.0	52	65	90	0.0	130
3005	57	27	44	1	406	2.3	39	29	64	0.0	130
Mean	60	27	50	1	421	6.0	48	41	80	0.1	140
S.D.	10	5	9	0	99	3.6	7	16	10	0.1	14

Appendix 7-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 150

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	10	0.31	142	5.2	106	9.8	6.2	5.7	3.2	1.28
3002	12	0.34	139	4.7	103	9.2	6.1	5.2	2.8	1.17
3003	14	0.33	143	4.8	107	9.3	6.3	5.4	3.0	1.25
3004	14	0.27	143	4.6	103	10.4	6.6	5.7	3.0	1.11
3005	13	0.21	143	4.8	107	9.9	7.0	5.5	3.0	1.20
Mean	13	0.29	142	4.8	105	9.7	6.4	5.5	3.0	1.20
S.D.	2	0.05	2	0.2	2	0.5	0.4	0.2	0.1	0.07

Appendix 7-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 500

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	54	25	53	1	491	3.8	53	40	83	0.0	124
4002	61	33	57	1	397	6.6	58	29	91	0.1	129
4003	59	27	64	1	524	2.4	37	23	69	0.1	108
4004	59	29	35	1	370	3.8	30	10	50	0.1	130
4005	49	26	40	1	380	3.8	53	57	81	0.0	101
Mean	56	28	50	1	432	4.1	46	32	75	0.1	118
S.D.	5	3	12	0	70	1.5	12	18	16	0.1	13

Appendix 7-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of administration)
Dose (mg/kg): 500

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	14	0.37	143	4.4	103	9.5	6.0	5.9	3.1	1.11
4002	13	0.37	144	5.1	105	9.4	7.5	5.8	3.2	1.23
4003	13	0.33	143	4.5	105	9.9	6.4	6.0	3.2	1.14
4004	12	0.29	144	4.5	106	9.9	6.1	5.8	3.2	1.23
4005	13	0.26	144	4.7	104	10.9	7.6	6.1	3.4	1.26
Mean	13	0.32	144	4.6	105	9.9	6.7	5.9	3.2	1.19
S.D.	1	0.05	1	0.3	1	0.6	0.8	0.1	0.1	0.07

Appendix 7-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	67	50	42	1	276	25.1	64	65	118	0.1	111
1102	84	70	48	1	386	10.2	59	148	126	0.1	119
1103	77	52	82	0	245	10.1	53	40	108	0.0	117
1105	94	51	55	1	245	29.0	43	66	90	0.1	129
1106a)	59Z	50Z	62Z	1Z	949Z	63.9Z	53Z	89Z	116Z	0.0Z	165Z
1107b)	58Z	50Z	48Z	1Z	444Z	19.9Z	78Z	126Z	165Z	0.1Z	129Z
1111	74	43	40	1	487	12.1	57	23	104	0.1	111
Mean	79	53	53	1	328	17.3	55	68	109	0.1	117
S.D.	10	10	17	0	106	9.0	8	48	14	0.0	7

a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 7-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	0.32	143	4.1	105	10.3	7.9	6.0	3.4	1.31
1102	13	0.34	140	3.9	110	9.8	5.4	5.9	3.5	1.46
1103	16	0.36	143	3.9	109	10.5	6.6	6.5	3.6	1.24
1105	18	0.34	141	3.8	107	10.0	6.0	5.8	3.0	1.07
1106a)	27Z	0.40Z	141Z	4.3Z	105Z	10.5Z	6.2Z	5.8Z	3.5Z	1.52Z
1107b)	32Z	0.40Z	139Z	4.2Z	103Z	11.8Z	7.8Z	6.2Z	3.5Z	1.30Z
1111	16	0.37	139	4.1	107	10.0	5.6	6.0	3.4	1.31
Mean	15	0.35	141	4.0	108	10.1	6.3	6.0	3.4	1.28
S.D.	2	0.02	2	0.1	2	0.3	1.0	0.3	0.2	0.14

a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 7-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 50

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
2104	110	69	48	1	495	11.1	47	21	90	0.1	109
2105	66	40	53	0	246	9.8	63	39	110	0.1	128
2106	73	52	54	1	164	17.8	66	45	133	0.1	111
2108	70	53	41	1	238	18.4	48	45	99	0.0	113
2111	90	52	81	0	195	12.9	34	71	77	0.1	131
Mean	82	53	55	1	268	14.0	52	44	102	0.1	118
S.D.	18	10	15	1	131	3.9	13	18	21	0.0	10

Appendix 7-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 50

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
2104	17	0.38	141	4.1	107	9.8	6.7	5.8	3.2	1.23
2105	14	0.34	142	4.0	109	10.5	7.2	5.9	3.5	1.46
2106	15	0.33	142	4.2	107	10.7	6.2	6.5	3.8	1.41
2108	15	0.35	139	4.5	105	10.3	7.4	5.7	3.3	1.38
2111	14	0.36	142	3.8	105	10.5	6.8	6.0	3.5	1.40
Mean	15	0.35	141	4.1	107	10.4	6.9	6.0	3.5	1.38
S.D.	1	0.02	1	0.3	2	0.3	0.5	0.3	0.2	0.09

Appendix 7-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 150

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
3104	81	59	42	1	244	9.8	47	21	90	0.1	119
3105	66	38	35	1	274	15.9	46	61	100	0.1	110
3106	94	55	134	1	225	28.3	56	25	104	0.1	120
3110	72	55	74	0	221	34.7	55	25	98	0.1	115
3111	83	41	58	0	229	26.4	51	16	89	0.1	127
Mean	79	50	69	1	239	23.0	51	30	96	0.1	118
S.D.	11	9	40	1	22	10.0	5	18	6	0.0	6

Appendix 7-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 150

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
3104	11	0.33	139	4.5	105	9.9	7.1	5.8	3.2	1.23
3105	14	0.27	140	4.5	106	10.3	7.0	6.4	3.5	1.21
3106	14	0.35	141	4.6	107	10.1	6.1	5.9	3.4	1.36
3110	13	0.36	140	4.8	106	10.1	6.6	6.2	3.4	1.21
3111	13	0.36	140	4.4	107	10.4	7.0	6.1	3.4	1.26
Mean	13	0.33	140	4.6	106	10.2	6.8	6.1	3.4	1.25
S.D.	1	0.04	1	0.2	1	0.2	0.4	0.2	0.1	0.06

Appendix 7-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 500

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
4102	62	49	34	1	154	20.7	67	58	127	0.1	111
4104	74	40	63	1	160	6.7	65	29	109	0.1	123
4105	84	51	52	1	160	16.6	62	51	114	0.0	114
4107	66	39	34	1	276	11.1	77	25	126	0.0	117
4108	79	57	44	1	237	50.5	63	51	119	0.1	116
Mean	73	47	45	1	197	21.1	67	43	119	0.1	116
S.D.	9	8	12	0	56	17.3	6	15	8	0.1	4

Appendix 7-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Lactation day 5)
Dose (mg/kg): 500

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
4102	10	0.30	142	4.4	107	10.1	7.0	6.1	3.4	1.26
4104	15	0.33	139	4.4	104	10.4	6.6	6.5	3.7	1.32
4105	11	0.30	143	4.1	104	10.9	7.2	6.6	3.5	1.13
4107	12	0.31	143	4.0	107	10.2	6.3	6.0	3.3	1.22
4108	19	0.29	143	4.4	102	10.7	7.4	6.0	3.4	1.31
Mean	13	0.31	142	4.3	105	10.5	6.9	6.2	3.5	1.25
S.D.	4	0.02	2	0.2	2	0.3	0.4	0.3	0.2	0.08

Appendix 7-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	61	27	51	2	479	15.2	47	17	96	0.1	120
1114	69	21	60	1	189	11.3	76	12	137	0.1	121
1115	68	29	49	2	234	11.2	44	12	87	0.1	143
1116	76	41	68	1	466	11.1	56	13	109	0.1	157
1117	59	24	54	1	362	13.3	78	31	146	0.1	134
Mean	67	28	56	1	346	12.4	60	17	115	0.1	135
S.D.	7	8	8	1	132	1.8	16	8	26	0.0	16

Appendix 7-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	14	0.36	140	4.0	107	9.6	3.8	5.6	3.3	1.43
1114	12	0.38	140	4.4	106	9.7	4.2	6.6	3.7	1.28
1115	15	0.38	140	4.3	105	9.3	4.6	6.0	3.5	1.40
1116	16	0.37	142	4.2	109	9.5	3.3	6.0	3.6	1.50
1117	14	0.36	142	4.0	110	9.9	3.1	6.3	3.8	1.52
Mean	14	0.37	141	4.2	107	9.6	3.8	6.1	3.6	1.43
S.D.	1	0.01	1	0.2	2	0.2	0.6	0.4	0.2	0.10

Appendix 7-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

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	49	19	68	1	173	3.5	78	44	133	0.1	148
4114	43	28	48	1	174	9.5	66	25	120	0.1	118
4115	55	21	35	1	186	3.8	52	16	97	0.0	136
4116D											
4117	53	25	69	1	155	8.8	67	38	127	0.0	96
Mean	50	23	55	1	172	6.4	66	31	119	0.1	125
S.D.	5	4	16	0	13	3.2	11	13	16	0.1	23

D: Dead

Appendix 7-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

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	16	0.38	142	4.1	103	10.2	5.8	6.4	3.7	1.37
4114	15	0.33	141	4.7	105	10.0	4.8	6.5	3.6	1.24
4115	14	0.32	140	4.4	106	9.6	4.4	6.2	3.6	1.38
4116D										
4117	17	0.39	142	4.5	106	10.6	4.7	6.3	3.8	1.52
Mean	16	0.36	141	4.4	105	10.1	4.9	6.4	3.7	1.38
S.D.	1	0.04	1	0.3	1	0.4	0.6	0.1	0.1	0.11

D: Dead

Appendix 7-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	33	49	0	357	8.8	42	40	75	0.0	128
1009	71	38	44	0	343	6.5	47	20	75	0.1	116
1010	64	35	39	0	345	5.2	38	29	64	0.1	111
1011	64	34	39	1	365	6.1	59	72	111	0.1	108
1012	54	28	42	0	358	39.0	43	33	80	0.1	119
Mean	64	34	43	0	354	13.1	46	39	81	0.1	116
S.D.	6	4	4	0	9	14.5	8	20	18	0.0	8

Appendix 7-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	0.32	142	4.7	105	9.7	6.2	5.9	3.1	1.11
1009	17	0.38	144	4.7	108	9.7	5.5	6.2	3.1	1.00
1010	15	0.37	144	4.5	108	9.6	5.4	5.8	3.1	1.15
1011	16	0.35	143	4.7	105	9.8	6.5	6.2	3.2	1.07
1012	17	0.34	145	4.4	108	9.9	6.0	6.2	3.3	1.14
Mean	16	0.35	144	4.6	107	9.7	5.9	6.1	3.2	1.09
S.D.	1	0.02	1	0.1	2	0.1	0.5	0.2	0.1	0.06

Appendix 7-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 500

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	69	39	45	1	556	7.2	45	42	82	0.1	126
4009	58	27	48	0	245	4.7	41	22	73	0.1	123
4010	70	33	60	1	333	12.4	66	70	109	0.0	119
4011	62	25	47	0	254	2.6	50	36	80	0.0	128
4012	88	30	53	1	371	3.6	44	15	68	0.0	122
Mean	69	31	51	1	352	6.1	49	37	82	0.0	124
S.D.	12	5	6	1	126	3.9	10	21	16	0.1	4

Appendix 7-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of male rats (End of recovery)
Dose (mg/kg): 500

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	16	0.32	143	4.3	107	9.0	5.8	5.4	3.1	1.35
4009	13	0.29	142	4.7	106	9.3	5.7	5.8	3.0	1.07
4010	17	0.37	143	4.4	107	10.1	5.9	6.6	3.3	1.00
4011	16	0.33	144	4.4	108	9.2	5.6	5.8	3.0	1.07
4012	18	0.36	144	4.5	108	9.7	7.1	6.2	3.2	1.07
Mean	16	0.33	143	4.5	107	9.5	6.0	6.0	3.1	1.11
S.D.	2	0.03	1	0.2	1	0.4	0.6	0.5	0.1	0.14

Appendix 7-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	102	57	75	1	251	13.5	88	16	139	0.1	124
1119	74	39	46	1	129	7.4	55	9	102	0.1	131
1120	72	35	70	0	207	7.9	63	17	126	0.1	124
1121	65	21	29	1	141	6.5	67	16	126	0.1	126
1122	75	29	43	1	181	13.7	69	16	130	0.1	132
Mean	78	36	53	1	182	9.8	68	15	125	0.1	127
S.D.	14	13	19	0	50	3.5	12	3	14	0.0	4

Appendix 7-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	18	0.45	141	4.8	109	9.7	4.8	6.1	3.5	1.35
1119	18	0.41	143	4.3	110	9.8	5.4	6.5	3.6	1.24
1120	16	0.35	142	4.8	108	9.5	5.4	6.1	3.5	1.35
1121	17	0.40	145	4.3	109	10.1	5.9	6.4	3.5	1.21
1122	22	0.40	143	4.8	109	10.1	5.0	6.6	3.9	1.44
Mean	18	0.40	143	4.6	109	9.8	5.3	6.3	3.6	1.32
S.D.	2	0.04	1	0.3	1	0.3	0.4	0.2	0.2	0.09

Appendix 7-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 500

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
4118D											
4119	121	77	90	1	153	10.4	77	18	138	0.1	132
4120D											
4121	68	28	53	1	186	5.5	80	15	134	0.1	128
4122	70	28	55	1	179	6.0	70	18	119	0.1	124
Mean	86	44	66	1	173	7.3	76	17	130	0.1	128
S.D.	30	28	21	0	17	2.7	5	2	10	0.0	4

D: Dead

Appendix 7-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual blood chemistry of female rats (End of recovery)
Dose (mg/kg): 500

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
4118D										
4119	18	0.42	141	4.6	106	10.0	5.3	6.6	3.6	1.20
4120D										
4121	17	0.41	142	4.6	110	9.8	5.4	6.3	3.4	1.17
4122	20	0.42	143	4.7	106	10.0	5.4	6.6	3.5	1.13
Mean	18	0.42	142	4.6	107	9.9	5.4	6.5	3.5	1.17
S.D.	2	0.01	1	0.1	2	0.1	0.1	0.2	0.1	0.04

D: Dead

Appendix 7-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of male rats (End of administration)
Dose (mg/kg): 0

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
1001	64.3	5.0	15.44
1002	82.6	5.6	9.03
1003	88.5	7.3	25.68
1004	64.9	4.0	8.81
1005	55.4	2.7	6.45
Mean	71.1	4.9	13.08
S.D.	13.8	1.7	7.79

Appendix 7-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of male rats (End of administration)
Dose (mg/kg): 50

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
2001	70.0	4.8	12.11
2002	69.0	5.4	29.72
2003	64.4	5.2	4.68
2004	61.7	6.3	19.38
2005	88.9	5.9	61.64
Mean	70.8	5.5	25.51
S.D.	10.7	0.6	22.22

Appendix 7-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of male rats (End of administration)
Dose (mg/kg): 150

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
3001	61.9	4.4	24.46
3002	50.3	3.9	37.09
3003	95.1	5.7	24.93
3004	82.0	6.3	11.74
3005	86.1	5.6	14.08
Mean	75.1	5.2	22.46
S.D.	18.4	1.0	10.12

Appendix 7-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of male rats (End of administration)
Dose (mg/kg): 500

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
4001	74.5	3.8	20.84
4002	62.7	4.4	32.21
4003	73.4	5.4	7.37
4004	79.2	4.3	38.03
4005	76.0	4.6	22.67
Mean	73.2	4.5	24.22
S.D.	6.2	0.6	11.75

Appendix 7-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (Lactation day 5)
Dose (mg/kg): 0

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
1101	68.2	4.4	36.06
1102	51.9	2.6	15.98
1103	59.7	3.6	19.59
1105	91.6	4.2	15.77
1111	82.8	3.1	38.33
Mean	70.8	3.6	25.15
S.D.	16.3	0.7	11.13

Appendix 7-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (Lactation day 5)
Dose (mg/kg): 50

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
2104	62.1	4.8	19.86
2105	88.7	3.7	30.58
2106	95.9	6.0	27.94
2108	62.1	3.1	20.33
2111	69.8	3.7	12.99
Mean	75.7	4.3	22.34
S.D.	15.7	1.2	7.02

Appendix 7-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (Lactation day 5)
Dose (mg/kg): 150

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
3104	60.1	2.4	6.07
3105	69.3	3.7	17.18
3106	52.0	2.5	8.29
3110	70.8	3.5	7.19
3111	82.8	4.5	15.62
Mean	67.0	3.3	10.87
S.D.	11.6	0.9	5.14

Appendix 7-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (Lactation day 5)
Dose (mg/kg): 500

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
4102	58.0	3.9	39.77
4104	57.7	3.6	21.80
4105	80.5	4.0	22.22
4107	61.4	3.6	23.06
4108	51.2	3.1	8.32
Mean	61.8	3.6	23.03
S.D.	11.1	0.4	11.17

Appendix 7-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (Satellite group, End of administration)
Dose (mg/kg): 0

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
1113	69.7	3.4	1.29
1114	60.4	3.0	1.19
1115	56.9	4.4	6.94
1116	73.4	4.7	3.42
1117	72.5	3.8	7.99
Mean	66.6	3.9	4.17
S.D.	7.5	0.7	3.16

Appendix 7-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
4113	57.1	4.7	3.67
4114	52.7	3.7	6.63
4115	76.4	3.5	3.17
4116D			
4117	51.7	3.1	5.02
Mean	59.5	3.8	4.62
S.D.	11.5	0.7	1.55

D: Dead

Appendix 7-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of male rats (End of recovery)
Dose (mg/kg): 0

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
1008	77.3	5.2	19.91
1009	64.2	5.1	18.08
1010	66.2	4.8	8.60
1011	65.4	5.2	8.69
1012	83.9	5.2	16.79
Mean	71.4	5.1	14.41
S.D.	8.7	0.2	5.38

Appendix 7-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of male rats (End of recovery)
Dose (mg/kg): 500

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
4008	50.5	5.0	6.29
4009	61.5	5.0	14.53
4010	73.3	5.7	67.80
4011	65.9	5.0	17.30
4012	73.7	4.0	10.07
Mean	65.0	4.9	23.20
S.D.	9.6	0.6	25.29

Appendix 7-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (End of recovery)
Dose (mg/kg): 0

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
1118	90.2	3.0	4.24
1119	83.4	2.8	20.36
1120	74.9	2.4	8.05
1121	111.0	2.9	6.51
1122	100.0	3.4	9.09
Mean	91.9	2.9	9.65
S.D.	14.1	0.4	6.26

Appendix 7-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual hormones of female rats (End of recovery)
Dose (mg/kg): 500

Animal number	T^3 ng/dL	T^4 µg/dL	TSH ng/mL
4118D			
4119	71.5	2.6	20.81
4120D			
4121	106.0	4.1	18.27
4122	110.0	3.6	9.73
Mean	95.8	3.4	16.27
S.D.	21.2	0.8	5.80

D: Dead

Appendix 8-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	460	1.97	10.7	9.2	10.2	19.4	243
	1002	453	2.11	13.0	12.5	11.3	23.8	267
	1003	477	2.21	11.8	9.4	13.2	22.6	273
	1004	466	2.09	14.8	15.5	10.7	26.2	175
	1005	485	2.12	14.4	12.1	11.1	23.2	404
	1006	546	2.17	17.0	13.5	10.4	23.9	218
	1007	425	2.03	10.5	13.3	10.7	24.0	209
	Mean	473	2.10	13.2	12.2	11.1	23.3	256
	S.D.	37	0.08	2.4	2.3	1.0	2.1	74
Relative	1001		0.43	2.3	2.0	2.2	4.2	53
	1002		0.47	2.9	2.8	2.5	5.3	59
	1003		0.46	2.5	2.0	2.8	4.7	57
	1004		0.45	3.2	3.3	2.3	5.6	38
	1005		0.44	3.0	2.5	2.3	4.8	83
	1006		0.40	3.1	2.5	1.9	4.4	40
	1007		0.48	2.5	3.1	2.5	5.6	49
	Mean		0.45	2.8	2.6	2.4	4.9	54
	S.D.		0.03	0.3	0.5	0.3	0.6	15

Appendix 8-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1.44	11.08	0.63	1.50	1.58	3.08
	1002	1.43	11.82	0.96	1.52	1.54	3.06
	1003	1.46	11.86	0.75	1.66	1.65	3.31
	1004	1.46	11.99	0.72	1.51	1.58	3.09
	1005	1.35	11.57	0.78	1.52	1.54	3.06
	1006	1.46	14.46	0.78	1.69	1.76	3.45
	1007	1.27	11.05	0.61	1.46	1.47	2.93
	Mean	1.41	11.98	0.75	1.55	1.59	3.14
	S.D.	0.07	1.16	0.12	0.09	0.09	0.18
Relative	1001	0.31	2.41	0.14	0.33	0.34	0.67
	1002	0.32	2.61	0.21	0.34	0.34	0.68
	1003	0.31	2.49	0.16	0.35	0.35	0.69
	1004	0.31	2.57	0.15	0.32	0.34	0.66
	1005	0.28	2.39	0.16	0.31	0.32	0.63
	1006	0.27	2.65	0.14	0.31	0.32	0.63
	1007	0.30	2.60	0.14	0.34	0.35	0.69
	Mean	0.30	2.53	0.16	0.33	0.34	0.66
	S.D.	0.02	0.10	0.02	0.02	0.01	0.03

Appendix 8-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1001	28	27	55	1.46	1.47	2.93
	1002	30	33	63	1.66	1.63	3.29
	1003	23	26	49	1.62	1.61	3.23
	1004	28	27	55	1.92	1.90	3.82
Absolute	1005	31	36	67	1.76	1.78	3.54
	1006	37	41	78	1.73	1.73	3.46
	1007	29	31	60	1.52	1.51	3.03
	Mean	29	32	61	1.67	1.66	3.33
	S.D.	4	6	10	0.15	0.15	0.31
	1001	6	6	12	0.32	0.32	0.64
	1002	7	7	14	0.37	0.36	0.73
	1003	5	5	10	0.34	0.34	0.68
	1004	6	6	12	0.41	0.41	0.82
Relative	1005	6	7	14	0.36	0.37	0.73
	1006	7	8	14	0.32	0.32	0.63
	1007	7	7	14	0.36	0.36	0.71
	Mean	6	7	13	0.35	0.35	0.71
	S.D.	1	1	2	0.03	0.03	0.06

Appendix 8-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1001	620	585	1205	1.69	1.12
	1002	669	723	1392	1.67	1.05
	1003	633	620	1253	1.78	1.32
	1004	750	751	1501	1.71	1.15
Absolute	1005	715	744	1459	1.98	1.51
	1006	674	658	1332	2.09	1.74
	1007	669	666	1335	1.79	1.21
	Mean	676	678	1354	1.82	1.30
	S.D.	45	64	106	0.16	0.25
	1001	135	127	262	0.37	0.24
	1002	148	160	307	0.37	0.23
	1003	133	130	263	0.37	0.28
	1004	161	161	322	0.37	0.25
Relative	1005	147	153	301	0.41	0.31
	1006	123	121	244	0.38	0.32
	1007	157	157	314	0.42	0.28
	Mean	143	144	288	0.38	0.27
	S.D.	14	17	31	0.02	0.03

Appendix 8-5 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 50

	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	2001	501	2.12	14.7	12.7	16.0	28.7	310
	2002	458	2.12	13.8	13.7	12.2	25.9	311
	2003	464	1.99	13.5	10.5	9.3	19.8	241
	2004	481	2.18	13.6	11.5	9.4	20.9	290
	2005	545	2.10	16.8	11.9	12.8	24.7	279
	2006	493	2.20	14.5	8.5	12.4	20.9	352
	2007	527	2.25	14.6	11.1	10.7	21.8	292
	2008	521	2.19	12.2	9.4	11.2	20.6	255
	2009	435	2.12	12.5	12.7	7.5	20.2	274
	2010	501	2.14	15.3	13.1	11.2	24.3	226
	2011	447	2.05	11.6	8.0	7.0	15.0	184
	2012	499	2.25	15.6	15.0	14.4	29.4	404
	Mean	489	2.14	14.1	11.5	11.2	22.7	285
	S.D.	33	0.08	1.5	2.1	2.6	4.1	58
Relative	2001		0.42	2.9	2.5	3.2	5.7	62
	2002		0.46	3.0	3.0	2.7	5.7	68
	2003		0.43	2.9	2.3	2.0	4.3	52
	2004		0.45	2.8	2.4	2.0	4.3	60
	2005		0.39	3.1	2.2	2.3	4.5	51
	2006		0.45	2.9	1.7	2.5	4.2	71
	2007		0.43	2.8	2.1	2.0	4.1	55
	2008		0.42	2.3	1.8	2.1	4.0	49
	2009		0.49	2.9	2.9	1.7	4.6	63
	2010		0.43	3.1	2.6	2.2	4.9	45
	2011		0.46	2.6	1.8	1.6	3.4	41
	2012		0.45	3.1	3.0	2.9	5.9	81
	Mean		0.44	2.9	2.4	2.3	4.6	58
	S.D.		0.03	0.2	0.5	0.5	0.8	12

Appendix 8-6 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 50

	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	1.39	14.40	0.68	1.73	1.79	3.52
	2002	1.37	12.38	0.69	1.61	1.69	3.30
	2003	1.44	11.95	0.78	1.65	1.59	3.24
	2004	1.67	14.07	0.65	1.86	1.92	3.78
	2005	1.59	14.45	0.85	1.99	1.92	3.91
	2006	1.60	13.54	0.72	1.85	1.89	3.74
	2007	1.43	15.22	0.78	2.05	1.96	4.01
	2008	1.60	15.81	0.61	1.79	1.76	3.55
	2009	1.39	12.01	0.69	1.54	1.66	3.20
	2010	1.44	15.00	0.75	1.82	1.82	3.64
	2011	1.29	10.73	0.69	1.23	1.21	2.44
	2012	1.33	14.48	0.69	1.73	1.64	3.37
	Mean	1.46	13.67	0.72	1.74	1.74	3.48
	S.D.	0.12	1.56	0.07	0.22	0.21	0.42
Relative	2001	0.28	2.87	0.14	0.35	0.36	0.70
	2002	0.30	2.70	0.15	0.35	0.37	0.72
	2003	0.31	2.58	0.17	0.36	0.34	0.70
	2004	0.35	2.93	0.14	0.39	0.40	0.79
	2005	0.29	2.65	0.16	0.37	0.35	0.72
	2006	0.32	2.75	0.15	0.38	0.38	0.76
	2007	0.27	2.89	0.15	0.39	0.37	0.76
	2008	0.31	3.03	0.12	0.34	0.34	0.68
	2009	0.32	2.76	0.16	0.35	0.38	0.74
	2010	0.29	2.99	0.15	0.36	0.36	0.73
	2011	0.29	2.40	0.15	0.28	0.27	0.55
	2012	0.27	2.90	0.14	0.35	0.33	0.68
	Mean	0.30	2.79	0.15	0.36	0.35	0.71
	S.D.	0.02	0.18	0.01	0.03	0.03	0.06

Appendix 8-7 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 50

	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	31	34	65	1.65	1.61	3.26
	2002	33	38	71	1.88	1.85	3.73
	2003	29	31	60	1.58	1.62	3.20
	2004	34	35	69	1.73	1.74	3.47
	2005	34	37	71	2.15	2.16	4.31
	2006	30	32	62	1.73	1.68	3.41
	2007	35	39	74	1.61	1.60	3.21
Absolute	2008	26	31	57	1.57	1.63	3.20
	2009	34	27	61	1.63	1.58	3.21
	2010	31	33	64	1.66	1.65	3.31
	2011	25	27	52	1.54	1.53	3.07
	2012	38	41	79	1.84	1.93	3.77
	Mean	32	34	65	1.71	1.72	3.43
	S.D.	4	4	8	0.17	0.18	0.35
	2001	6	7	13	0.33	0.32	0.65
	2002	7	8	16	0.41	0.40	0.81
	2003	6	7	13	0.34	0.35	0.69
	2004	7	7	14	0.36	0.36	0.72
	2005	6	7	13	0.39	0.40	0.79
	2006	6	6	13	0.35	0.34	0.69
	2007	7	7	14	0.31	0.30	0.61
Relative	2008	5	6	11	0.30	0.31	0.61
	2009	8	6	14	0.37	0.36	0.74
	2010	6	7	13	0.33	0.33	0.66
	2011	6	6	12	0.34	0.34	0.69
	2012	8	8	16	0.37	0.39	0.76
	Mean	7	7	14	0.35	0.35	0.70
	S.D.	1	1	1	0.03	0.03	0.06

Appendix 8-8 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 50

	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)
	2001	653	625	1278	2.19	1.33
	2002	720	684	1404	2.06	1.30
	2003	690	682	1372	2.05	1.29
	2004	694	681	1375	1.63	1.32
	2005	855	816	1671	1.70	1.07
	2006	642	580	1222	1.83	1.37
	2007	664	618	1282	1.60	1.50
Absolute	2008	668	640	1308	1.71	1.52
	2009	693	659	1352	1.56	1.00
	2010	737	713	1450	2.23	1.34
	2011	608	599	1207	1.44	0.99
	2012	724	752	1476	1.34	1.12
	Mean	696	671	1366	1.78	1.26
	S.D.	62	67	127	0.29	0.18
	2001	130	125	255	0.44	0.27
	2002	157	149	307	0.45	0.28
	2003	149	147	296	0.44	0.28
	2004	144	142	286	0.34	0.27
	2005	157	150	307	0.31	0.20
	2006	130	118	248	0.37	0.28
	2007	126	117	243	0.30	0.28
Relative	2008	128	123	251	0.33	0.29
	2009	159	151	311	0.36	0.23
	2010	147	142	289	0.45	0.27
	2011	136	134	270	0.32	0.22
	2012	145	151	296	0.27	0.22
	Mean	142	137	280	0.37	0.26
	S.D.	12	13	25	0.06	0.03

Appendix 8-9 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 150

	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	469	2.09	12.0	11.5	7.2	18.7	331
	3002	487	2.11	12.0	11.6	10.0	21.6	288
	3003	451	2.01	12.4	12.1	14.0	26.1	240
	3004	544	2.10	15.4	12.1	16.2	28.3	194
	3005	432	2.10	11.0	11.4	10.9	22.3	320
	3006	513	2.33	15.6	14.7	12.0	26.7	299
	3007	518	2.11	15.9	15.0	14.9	29.9	304
	3008	503	2.17	14.3	7.4	8.7	16.1	262
	3009	482	2.11	13.8	13.4	12.4	25.8	264
	3010	457	2.04	13.9	11.5	10.9	22.4	211
	3011	472	2.04	11.9	10.1	9.0	19.1	293
	3012	455	2.14	13.8	14.7	11.0	25.7	248
	Mean	482	2.11	13.5	12.1	11.4	23.6	271
	S.D.	33	0.08	1.6	2.2	2.6	4.2	42
Relative	3001		0.45	2.6	2.5	1.5	4.0	71
	3002		0.43	2.5	2.4	2.1	4.4	59
	3003		0.45	2.7	2.7	3.1	5.8	53
	3004		0.39	2.8	2.2	3.0	5.2	36
	3005		0.49	2.5	2.6	2.5	5.2	74
	3006		0.45	3.0	2.9	2.3	5.2	58
	3007		0.41	3.1	2.9	2.9	5.8	59
	3008		0.43	2.8	1.5	1.7	3.2	52
	3009		0.44	2.9	2.8	2.6	5.4	55
	3010		0.45	3.0	2.5	2.4	4.9	46
	3011		0.43	2.5	2.1	1.9	4.0	62
	3012		0.47	3.0	3.2	2.4	5.6	55
	Mean		0.44	2.8	2.5	2.4	4.9	57
	S.D.		0.03	0.2	0.4	0.5	0.8	10

Appendix 8-10 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 150

	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	1.63	13.66	0.60	1.76	1.67	3.43
	3002	1.42	12.59	0.72	1.71	1.73	3.44
	3003	1.50	13.07	0.68	1.67	1.73	3.40
	3004	1.65	17.24	0.68	2.12	2.05	4.17
	3005	1.39	13.51	0.69	1.70	1.82	3.52
	3006	1.39	12.35	0.74	1.50	1.61	3.11
	3007	1.68	16.03	0.81	2.13	2.01	4.14
	3008	1.51	13.38	0.65	1.70	1.69	3.39
	3009	1.61	13.41	0.71	2.13	2.10	4.23
	3010	1.24	12.30	0.56	1.55	1.60	3.15
	3011	1.35	14.15	0.53	1.83	1.78	3.61
	3012	1.36	13.99	0.73	1.85	1.88	3.73
	Mean	1.48	13.81	0.68	1.80	1.81	3.61
	S.D.	0.14	1.47	0.08	0.22	0.17	0.38
Relative	3001	0.35	2.91	0.13	0.38	0.36	0.73
	3002	0.29	2.59	0.15	0.35	0.36	0.71
	3003	0.33	2.90	0.15	0.37	0.38	0.75
	3004	0.30	3.17	0.13	0.39	0.38	0.77
	3005	0.32	3.13	0.16	0.39	0.42	0.81
	3006	0.27	2.41	0.14	0.29	0.31	0.61
	3007	0.32	3.09	0.16	0.41	0.39	0.80
	3008	0.30	2.66	0.13	0.34	0.34	0.67
	3009	0.33	2.78	0.15	0.44	0.44	0.88
	3010	0.27	2.69	0.12	0.34	0.35	0.69
	3011	0.29	3.00	0.11	0.39	0.38	0.76
	3012	0.30	3.07	0.16	0.41	0.41	0.82
	Mean	0.31	2.87	0.14	0.38	0.38	0.75
	S.D.	0.02	0.24	0.02	0.04	0.04	0.07

Appendix 8-11 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 150

	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	20	21	41	1.52	1.51	3.03
	3002	26	29	55	1.73	1.77	3.50
	3003	22	25	47	1.57	1.63	3.20
	3004	42	47	89	1.91	1.84	3.75
	3005	36	35	71	1.59	1.63	3.22
	3006	35	37	72	1.63	1.67	3.30
	3007	29	31	60	1.61	1.63	3.24
Absolute	3008	32	37	69	1.62	1.63	3.25
	3009	35	39	74	1.66	1.64	3.30
	3010	32	38	70	1.43	1.41	2.84
	3011	29	30	59	1.63	1.65	3.28
	3012	38	40	78	1.83	1.87	3.70
	Mean	31	34	65	1.64	1.66	3.30
	S.D.	6	7	14	0.13	0.13	0.25
	3001	4	4	9	0.32	0.32	0.65
	3002	5	6	11	0.36	0.36	0.72
	3003	5	6	10	0.35	0.36	0.71
	3004	8	9	16	0.35	0.34	0.69
	3005	8	8	16	0.37	0.38	0.75
	3006	7	7	14	0.32	0.33	0.64
	3007	6	6	12	0.31	0.31	0.63
Relative	3008	6	7	14	0.32	0.32	0.65
	3009	7	8	15	0.34	0.34	0.68
	3010	7	8	15	0.31	0.31	0.62
	3011	6	6	13	0.35	0.35	0.69
	3012	8	9	17	0.40	0.41	0.81
	Mean	6	7	14	0.34	0.34	0.69
	S.D.	1	1	3	0.03	0.03	0.06

Appendix 8-12 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 150

	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)
	3001	552	589	1141	1.56	1.11
	3002	671	643	1314	1.76	1.21
	3003	632	635	1267	1.60	1.29
	3004	709	664	1373	2.19	1.04
	3005	658	666	1324	2.01	1.17
	3006	628	556	1184	1.73	1.01
	3007	674	693	1367	1.70	1.54
Absolute	3008	508	548	1056	1.14	0.92
	3009	668	658	1326	2.01	1.49
	3010	644	635	1279	2.01	1.67
	3011	776	772	1548	2.04	1.32
	3012	742	798	1540	2.28	1.36
	Mean	655	655	1310	1.84	1.26
	S.D.	74	75	144	0.32	0.23
	3001	118	126	243	0.33	0.24
	3002	138	132	270	0.36	0.25
	3003	140	141	281	0.35	0.29
	3004	130	122	252	0.40	0.19
	3005	152	154	306	0.47	0.27
	3006	122	108	231	0.34	0.20
	3007	130	134	264	0.33	0.30
Relative	3008	101	109	210	0.23	0.18
	3009	139	137	275	0.42	0.31
	3010	141	139	280	0.44	0.37
	3011	164	164	328	0.43	0.28
	3012	163	175	338	0.50	0.30
	Mean	137	137	273	0.38	0.27
	S.D.	18	20	38	0.07	0.06

Appendix 8-13 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 500

	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	478	2.11	13.7	10.7	14.8	25.5	262
	4002	450	2.20	14.9	9.7	11.4	21.1	251
	4003	452	2.10	12.4	10.8	14.7	25.5	201
	4004	440	2.03	12.2	11.4	15.2	26.6	176
	4005	456	2.20	14.5	8.3	6.2	14.5	271
	4006	426	2.04	13.1	14.3	14.4	28.7	164
	4007	389	2.08	13.4	8.1	16.2	24.3	168
	Mean	442	2.11	13.5	10.5	13.3	23.7	213
	S.D.	28	0.07	1.0	2.1	3.5	4.7	47
Relative	4001		0.44	2.9	2.2	3.1	5.3	55
	4002		0.49	3.3	2.2	2.5	4.7	56
	4003		0.46	2.7	2.4	3.3	5.6	44
	4004		0.46	2.8	2.6	3.5	6.0	40
	4005		0.48	3.2	1.8	1.4	3.2	59
	4006		0.48	3.1	3.4	3.4	6.7	38
	4007		0.53	3.4	2.1	4.2	6.2	43
	Mean		0.48	3.1	2.4	3.1	5.4	48
	S.D.		0.03	0.3	0.5	0.9	1.2	9

Appendix 8-14 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 500

	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	1.56	14.80	0.70	1.96	1.98	3.94
	4002	1.39	13.88	0.55	1.76	1.74	3.50
	4003	1.22	13.50	0.56	1.75	1.78	3.53
	4004	1.32	14.49	0.75	1.97	1.84	3.81
	4005	1.44	13.69	0.71	2.62	2.56	5.18
	4006	1.38	13.17	0.64	1.74	1.78	3.52
	4007	1.12	12.14	0.65	1.62	1.57	3.19
	Mean	1.35	13.67	0.65	1.92	1.89	3.81
	S.D.	0.14	0.88	0.08	0.33	0.32	0.65
Relative	4001	0.33	3.10	0.15	0.41	0.41	0.82
	4002	0.31	3.08	0.12	0.39	0.39	0.78
	4003	0.27	2.99	0.12	0.39	0.39	0.78
	4004	0.30	3.29	0.17	0.45	0.42	0.87
	4005	0.32	3.00	0.16	0.57	0.56	1.14
	4006	0.32	3.09	0.15	0.41	0.42	0.83
	4007	0.29	3.12	0.17	0.42	0.40	0.82
	Mean	0.31	3.10	0.15	0.43	0.43	0.86
	S.D.	0.02	0.10	0.02	0.06	0.06	0.13

Appendix 8-15 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 500

	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	42	78	1.53	1.52	3.05
	4002	27	28	55	1.70	1.62	3.32
	4003	42	40	82	1.52	1.51	3.03
	4004	29	33	62	1.33	1.33	2.66
	4005	34	38	72	1.71	1.71	3.42
	4006	29	30	59	1.64	1.61	3.25
	4007	32	32	64	1.61	1.59	3.20
	Mean	33	35	67	1.58	1.56	3.13
	S.D.	5	5	10	0.13	0.12	0.25
Relative	4001	8	9	16	0.32	0.32	0.64
	4002	6	6	12	0.38	0.36	0.74
	4003	9	9	18	0.34	0.33	0.67
	4004	7	8	14	0.30	0.30	0.60
	4005	7	8	16	0.38	0.38	0.75
	4006	7	7	14	0.38	0.38	0.76
	4007	8	8	16	0.41	0.41	0.82
	Mean	7	8	15	0.36	0.35	0.71
	S.D.	1	1	2	0.04	0.04	0.08

Appendix 8-16 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of administration)
Dose (mg/kg): 500

	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	639	622	1261	1.70	1.12
	4002	638	613	1251	1.73	1.48
	4003	565	554	1119	1.61	1.35
	4004	545	548	1093	1.50	1.15
	4005	698	710	1408	1.99	1.22
	4006	687	715	1402	1.62	1.06
	4007	697	686	1383	1.71	1.40
	Mean	638	635	1274	1.69	1.25
	S.D.	63	70	131	0.15	0.16
Relative	4001	134	130	264	0.36	0.23
	4002	142	136	278	0.38	0.33
	4003	125	123	248	0.36	0.30
	4004	124	125	248	0.34	0.26
	4005	153	156	309	0.44	0.27
	4006	161	168	329	0.38	0.25
	4007	179	176	356	0.44	0.36
	Mean	145	145	290	0.39	0.29
	S.D.	20	22	42	0.04	0.05

Appendix 8-17 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
Absolute	1101	297	1.98	20.1	6.7	8.2	14.9	156
	1102	348	2.00	15.5	8.1	11.1	19.2	261
	1103	307	1.95	17.7	7.2	8.0	15.2	166
	1104	288	2.02	17.8	7.1	5.5	12.6	130
	1105	293	2.00	12.5	8.2	9.4	17.6	187
	1106a)	325Z	1.87Z	11.5Z	7.4Z	7.3Z	14.7Z	424Z
	1107b)	270Z	1.90Z	13.8Z	7.1Z	6.5Z	13.6Z	59Z
	1108	307	1.96	17.3	7.9	9.3	17.2	158
	1109	310	1.98	16.7	11.8	11.2	23.0	163
	1110	316	2.01	16.0	7.9	8.4	16.3	242
	1111	331	1.99	17.2	7.1	7.1	14.2	325
	1112	321	1.95	20.8	6.5	6.5	13.0	202
	Mean	312	1.98	17.2	7.9	8.5	16.3	199
	S.D.	18	0.02	2.3	1.5	1.8	3.1	60
Relative	1101		0.67	6.8	2.3	2.8	5.0	53
	1102		0.57	4.5	2.3	3.2	5.5	75
	1103		0.64	5.8	2.3	2.6	5.0	54
	1104		0.70	6.2	2.5	1.9	4.4	45
	1105		0.68	4.3	2.8	3.2	6.0	64
	1106a)		0.58Z	3.5Z	2.3Z	2.2Z	4.5Z	130Z
	1107b)		0.70Z	5.1Z	2.6Z	2.4Z	5.0Z	217Z
	1108		0.64	5.6	2.6	3.0	5.6	51
	1109		0.64	5.4	3.8	3.6	7.4	53
	1110		0.64	5.1	2.5	2.7	5.2	77
	1111		0.60	5.2	2.1	2.1	4.3	98
	1112		0.61	6.5	2.0	2.0	4.0	63
	Mean		0.64	5.5	2.5	2.7	5.2	63
	S.D.		0.04	0.8	0.5	0.6	1.0	16

a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-18 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1101	0.99	9.67	0.60	0.93	0.96	1.89
	1102	1.13	10.28	0.58	0.98	0.92	1.90
	1103	0.95	10.21	0.60	1.04	1.07	2.11
	1104	0.99	8.89	0.60	1.01	0.99	2.00
	1105	1.00	9.73	0.99	0.93	0.99	1.92
	1106a)	0.98Z	11.50Z	0.65Z	1.67Z	0.15Z	1.82Z
	1107b)	0.82Z	9.75Z	0.39Z	0.92Z	0.90Z	1.82Z
Absolute	1108	1.03	9.92	0.73	1.07	1.14	2.21
	1109	0.87	10.39	0.62	1.12	1.07	2.19
	1110	0.95	9.26	0.59	1.01	0.98	1.99
	1111	1.03	9.14	0.53	1.07	1.04	2.11
	1112	1.16	10.22	0.63	1.02	1.01	2.03
	Mean	1.01	9.77	0.65	1.02	1.02	2.04
	S.D.	0.09	0.53	0.13	0.06	0.06	0.12
	1101	0.33	3.26	0.20	0.31	0.32	0.64
	1102	0.32	2.95	0.17	0.28	0.26	0.55
	1103	0.31	3.33	0.20	0.34	0.35	0.69
	1104	0.34	3.09	0.21	0.35	0.34	0.69
	1105	0.34	3.32	0.34	0.32	0.34	0.66
	1106a)	0.30Z	3.54Z	0.20Z	0.51Z	0.05Z	0.56Z
	1107b)	0.30Z	3.61Z	0.14Z	0.34Z	0.33Z	0.67Z
Relative	1108	0.34	3.23	0.24	0.35	0.37	0.72
	1109	0.28	3.35	0.20	0.36	0.35	0.71
	1110	0.30	2.93	0.19	0.32	0.31	0.63
	1111	0.31	2.76	0.16	0.32	0.31	0.64
	1112	0.36	3.18	0.20	0.32	0.31	0.63
	Mean	0.32	3.14	0.21	0.33	0.33	0.66
	S.D.	0.02	0.20	0.05	0.02	0.03	0.05

a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-19 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	31	37	68	47.4	58.8	106.2	805
	1102	34	35	69	43.7	48.9	92.6	624
	1103	39	43	82	59.6	42.7	102.3	681
	1104	33	34	67	57.7	46.8	104.5	919
	1105	36	38	74	52.7	43.4	96.1	633
	1106a)	33Z	31Z	64Z	47.3Z	38.0Z	85.3Z	1045Z
	1107b)	34Z	34Z	68Z	56.5Z	39.1Z	95.6Z	1304Z
Absolute	1108	34	36	70	43.6	57.3	100.9	609
	1109	35	37	72	44.9	60.0	104.9	592
	1110	35	39	74	60.5	45.9	106.4	586
	1111	31	33	64	47.9	40.8	88.7	1047
	1112	35	31	66	50.2	56.5	106.7	925
	Mean	34	36	71	50.8	50.1	100.9	742
	S.D.	2	3	5	6.5	7.3	6.4	169
	1101	10	12	23	16.0	19.8	35.8	271
	1102	10	10	20	12.6	14.1	26.6	179
	1103	13	14	27	19.4	13.9	33.3	222
	1104	11	12	23	20.0	16.3	36.3	319
	1105	12	13	25	18.0	14.8	32.8	216
	1106a)	10Z	10Z	20Z	14.6Z	11.7Z	26.2Z	322Z
	1107b)	13Z	13Z	25Z	20.9Z	14.5Z	35.4Z	483Z
Relative	1108	11	12	23	14.2	18.7	32.9	198
	1109	11	12	23	14.5	19.4	33.8	191
	1110	11	12	23	19.1	14.5	33.7	185
	1111	9	10	19	14.5	12.3	26.8	316
	1112	11	10	21	15.6	17.6	33.2	288
	Mean	11	12	23	16.4	16.1	32.5	239
	S.D.	1	1	2	2.6	2.6	3.3	55

a): Non-pregnant
b): Sacrificed on day 2 of lactation because all pups died
Z: Data was excluded from statistical analysis.

Appendix 8-20 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 50

	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	304	2.01	18.4	9.2	8.8	18.0	127
	2102	309	1.95	17.5	10.4	10.3	20.7	215
	2103	339	2.06	20.4	9.8	7.9	17.7	225
	2104	297	1.98	17.0	9.3	5.7	15.0	241
	2105	305	1.97	19.3	8.8	8.0	16.8	144
	2106	313	1.94	20.0	8.4	8.6	17.0	238
	2107	303	1.96	18.4	7.6	6.7	14.3	137
	2108	303	1.97	18.1	7.2	8.1	15.3	167
	2109	279	1.99	16.6	10.1	9.4	19.5	109
	2110	299	1.91	19.3	9.4	10.8	20.2	109
	2111	340	2.03	18.2	8.7	6.4	15.1	205
	2112	285	1.90	16.3	9.5	7.3	16.8	77
	Mean	306	1.97	18.3	9.0	8.2	17.2	166
	S.D.	18	0.05	1.3	1.0	1.5	2.1	57
Relative	2101		0.66	6.1	3.0	2.9	5.9	42
	2102		0.63	5.7	3.4	3.3	6.7	70
	2103		0.61	6.0	2.9	2.3	5.2	66
	2104		0.67	5.7	3.1	1.9	5.1	81
	2105		0.65	6.3	2.9	2.6	5.5	47
	2106		0.62	6.4	2.7	2.7	5.4	76
	2107		0.65	6.1	2.5	2.2	4.7	45
	2108		0.65	6.0	2.4	2.7	5.0	55
	2109		0.71	5.9	3.6	3.4	7.0	39
	2110		0.64	6.5	3.1	3.6	6.8	36
	2111		0.60	5.4	2.6	1.9	4.4	60
	2112		0.67	5.7	3.3	2.6	5.9	27
	Mean		0.65	6.0	3.0	2.7	5.6	54
	S.D.		0.03	0.3	0.4	0.6	0.8	17

Appendix 8-21 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 50

	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	10.77	0.66	1.14	1.10	2.24
	2102	0.88	10.27	0.75	1.03	1.00	2.03
	2103	1.00	10.31	0.75	1.03	1.03	2.06
	2104	1.10	9.99	0.78	1.02	1.07	2.09
	2105	0.97	10.99	0.69	1.07	1.07	2.14
	2106	1.03	10.67	0.73	1.06	1.04	2.10
	2107	0.97	9.43	0.54	1.10	1.05	2.15
	2108	0.94	10.04	0.75	1.10	1.10	2.20
	2109	0.90	9.00	0.44	1.04	0.98	2.02
	2110	0.98	9.62	0.59	1.02	0.96	1.98
	2111	1.08	11.03	0.63	1.07	1.05	2.12
	2112	0.97	10.15	0.58	1.03	1.04	2.07
	Mean	0.99	10.19	0.66	1.06	1.04	2.10
	S.D.	0.07	0.63	0.10	0.04	0.04	0.08
Relative	2101	0.35	3.54	0.22	0.38	0.36	0.74
	2102	0.28	3.32	0.24	0.33	0.32	0.66
	2103	0.29	3.04	0.22	0.30	0.30	0.61
	2104	0.37	3.36	0.26	0.34	0.36	0.70
	2105	0.32	3.60	0.23	0.35	0.35	0.70
	2106	0.33	3.41	0.23	0.34	0.33	0.67
	2107	0.32	3.11	0.18	0.36	0.35	0.71
	2108	0.31	3.31	0.25	0.36	0.36	0.73
	2109	0.32	3.23	0.16	0.37	0.35	0.72
	2110	0.33	3.22	0.20	0.34	0.32	0.66
	2111	0.32	3.24	0.19	0.31	0.31	0.62
	2112	0.34	3.56	0.20	0.36	0.36	0.73
	Mean	0.32	3.33	0.22	0.35	0.34	0.69
	S.D.	0.02	0.18	0.03	0.02	0.02	0.04

Appendix 8-22 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 50

	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	41	45	86	47.3	52.7	100.0	759
	2102	42	47	89	44.9	47.8	92.7	696
	2103	39	38	77	59.0	53.2	112.2	870
	2104	51	55	106	68.3	59.8	128.1	633
	2105	39	42	81	53.4	42.5	95.9	672
	2106	34	39	73	40.9	47.7	88.6	733
	2107	24	30	54	41.8	55.3	97.1	725
Absolute	2108	35	36	71	48.4	52.9	101.3	895
	2109	37	44	81	41.1	45.2	86.3	667
	2110	42	45	87	45.5	47.2	92.7	799
	2111	38	42	80	78.9	70.5	149.4	646
	2112	35	38	73	46.5	34.6	81.1	548
	Mean	38	42	80	51.3	50.8	102.1	720
	S.D.	6	6	12	11.8	9.0	19.4	100
	2101	13	15	28	15.6	17.3	32.9	250
	2102	14	15	29	14.5	15.5	30.0	225
	2103	12	11	23	17.4	15.7	33.1	257
	2104	17	19	36	23.0	20.1	43.1	213
	2105	13	14	27	17.5	13.9	31.4	220
	2106	11	12	23	13.1	15.2	28.3	234
	2107	8	10	18	13.8	18.3	32.0	239
Relative	2108	12	12	23	16.0	17.5	33.4	295
	2109	13	16	29	14.7	16.2	30.9	239
	2110	14	15	29	15.2	15.8	31.0	267
	2111	11	12	24	23.2	20.7	43.9	190
	2112	12	13	26	16.3	12.1	28.5	192
	Mean	13	14	26	16.7	16.5	33.2	235
	S.D.	2	2	5	3.3	2.4	5.1	30

Appendix 8-23 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 150

	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	299	1.97	19.8	10.9	9.8	20.7	134
	3102	290	2.08	25.2	10.5	8.0	18.5	173
	3103	292	1.92	16.8	9.6	8.8	18.4	160
	3104	295	2.00	18.8	8.0	8.1	16.1	110
	3105	304	1.92	16.9	8.8	9.1	17.9	157
	3106	278	1.85	15.5	6.3	9.2	15.5	134
	3107	313	2.10	23.0	12.7	11.2	23.9	250
	3108	295	1.94	15.2	13.1	12.3	25.4	166
	3109	224	1.93	15.6	6.4	6.4	12.8	56
	3110	310	2.03	16.4	8.7	5.7	14.4	248
	3111	300	1.90	17.6	7.5	7.8	15.3	268
	3112	321	2.11	23.2	9.9	10.1	20.0	246
	Mean	293	1.98	18.7	9.4	8.9	18.2	175
	S.D.	25	0.08	3.4	2.2	1.9	3.8	65
Relative	3101		0.66	6.6	3.6	3.3	6.9	45
	3102		0.72	8.7	3.6	2.8	6.4	60
	3103		0.66	5.8	3.3	3.0	6.3	55
	3104		0.68	6.4	2.7	2.7	5.5	37
	3105		0.63	5.6	2.9	3.0	5.9	52
	3106		0.67	5.6	2.3	3.3	5.6	48
	3107		0.67	7.3	4.1	3.6	7.6	80
	3108		0.66	5.2	4.4	4.2	8.6	56
	3109		0.86	7.0	2.9	2.9	5.7	25
	3110		0.65	5.3	2.8	1.8	4.6	80
	3111		0.63	5.9	2.5	2.6	5.1	89
	3112		0.66	7.2	3.1	3.1	6.2	77
	Mean		0.68	6.4	3.2	3.0	6.2	59
	S.D.		0.06	1.0	0.6	0.6	1.1	19

Appendix 8-24 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 150

	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	0.91	10.70	0.60	1.03	1.02	2.05
	3102	0.97	10.34	0.67	1.18	1.23	2.41
	3103	1.02	10.66	0.70	1.03	1.04	2.07
	3104	0.94	11.19	0.56	1.04	1.01	2.05
	3105	0.97	9.91	0.62	1.05	0.97	2.02
	3106	1.04	9.10	0.51	0.91	0.92	1.83
	3107	1.06	10.92	0.63	1.11	1.12	2.23
	3108	0.97	10.54	0.61	0.99	1.02	2.01
	3109	0.81	7.74	1.02	1.00	0.99	1.99
	3110	0.97	9.76	0.58	0.98	0.95	1.93
	3111	0.99	9.99	0.57	1.03	1.07	2.10
	3112	0.96	10.55	0.58	1.22	1.23	2.45
	Mean	0.97	10.12	0.64	1.05	1.05	2.10
	S.D.	0.06	0.94	0.13	0.09	0.10	0.18
Relative	3101	0.30	3.58	0.20	0.34	0.34	0.69
	3102	0.33	3.57	0.23	0.41	0.42	0.83
	3103	0.35	3.65	0.24	0.35	0.36	0.71
	3104	0.32	3.79	0.19	0.35	0.34	0.69
	3105	0.32	3.26	0.20	0.35	0.32	0.66
	3106	0.37	3.27	0.18	0.33	0.33	0.66
	3107	0.34	3.49	0.20	0.35	0.36	0.71
	3108	0.33	3.57	0.21	0.34	0.35	0.68
	3109	0.36	3.46	0.46	0.45	0.44	0.89
	3110	0.31	3.15	0.19	0.32	0.31	0.62
	3111	0.33	3.33	0.19	0.34	0.36	0.70
	3112	0.30	3.29	0.18	0.38	0.38	0.76
	Mean	0.33	3.45	0.22	0.36	0.36	0.72
	S.D.	0.02	0.19	0.08	0.04	0.04	0.08

Appendix 8-25 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 150

	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	36	41	77	56.8	61.3	118.1	770
	3102	40	43	83	63.9	55.5	119.4	755
	3103	42	44	86	45.3	51.2	96.5	634
	3104	46	48	94	64.3	46.4	110.7	865
	3105	35	37	72	59.0	56.4	115.4	675
	3106	30	35	65	50.3	56.8	107.1	793
	3107	45	43	88	48.7	42.2	90.9	645
	3108	35	34	69	51.0	46.7	97.7	776
	3109	43	43	86	48.3	41.7	90.0	578
	3110	41	46	87	59.7	41.3	101.0	678
	3111	40	40	80	42.5	37.7	80.2	819
	3112	34	38	72	57.1	56.4	113.5	744
	Mean	39	41	80	53.9	49.5	103.4	728
	S.D.	5	4	9	7.2	7.8	12.6	85
Relative	3101	12	14	26	19.0	20.5	39.5	258
	3102	14	15	29	22.0	19.1	41.2	260
	3103	14	15	29	15.5	17.5	33.0	217
	3104	16	16	32	21.8	15.7	37.5	293
	3105	12	12	24	19.4	18.6	38.0	222
	3106	11	13	23	18.1	20.4	38.5	285
	3107	14	14	28	15.6	13.5	29.0	206
	3108	12	12	23	17.3	15.8	33.1	263
	3109	19	19	38	21.6	18.6	40.2	258
	3110	13	15	28	19.3	13.3	32.6	219
	3111	13	13	27	14.2	12.6	26.7	273
	3112	11	12	22	17.8	17.6	35.4	232
	Mean	13	14	27	18.5	16.9	35.4	249
	S.D.	2	2	4	2.6	2.7	4.6	29

Appendix 8-26 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 500

	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	273	2.06	18.6	8.8	11.4	20.2	62
	4102	264	1.91	14.2	8.9	6.6	15.5	97
	4103D	287Z	1.90Z	18.7Z	10.8Z	10.3Z	21.1Z	247Z
	4104	294	2.01	15.5	8.9	8.1	17.0	135
	4105	312	1.97	19.3	8.9	8.4	17.3	108
	4106D	305Z	1.96Z	15.9Z	15.0Z	10.6Z	25.6Z	143Z
	4107	260	1.94	14.6	6.2	7.7	13.9	68
	4108	286	2.03	17.1	9.5	8.9	18.4	98
	4109	303	1.94	17.6	7.5	7.4	14.9	191
	4110	330	2.02	15.6	12.7	9.5	22.2	154
	4111D	321Z	1.90Z	19.0Z	11.0Z	10.4Z	21.4Z	317Z
	4112D	280Z	2.02Z	23.5Z	11.5Z	10.0Z	21.5Z	390Z
	Mean	290	1.99	16.6	8.9	8.5	17.4	114
	S.D.	24	0.05	1.9	1.9	1.5	2.8	44
Relative	4101		0.75	6.8	3.2	4.2	7.4	23
	4102		0.72	5.4	3.4	2.5	5.9	37
	4103D		0.66Z	6.5Z	3.8Z	3.6Z	7.4Z	86Z
	4104		0.68	5.3	3.0	2.8	5.8	46
	4105		0.63	6.2	2.9	2.7	5.5	35
	4106D		0.64Z	5.2Z	4.9Z	3.5Z	8.4Z	47Z
	4107		0.75	5.6	2.4	3.0	5.3	26
	4108		0.71	6.0	3.3	3.1	6.4	34
	4109		0.64	5.8	2.5	2.4	4.9	63
	4110		0.61	4.7	3.8	2.9	6.7	47
	4111D		0.59Z	5.9Z	3.4Z	3.2Z	6.7Z	99Z
	4112D		0.72Z	8.4Z	4.1Z	3.6Z	7.7Z	139Z
	Mean		0.69	5.7	3.1	3.0	6.0	39
	S.D.		0.05	0.6	0.5	0.6	0.8	13

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-27 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 500

	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	0.84	9.73	0.55	1.03	1.00	2.03
	4102	0.87	10.04	0.74	1.05	1.02	2.07
	4103D	1.25Z	16.40Z	0.48Z	1.09Z	1.08Z	2.17Z
	4104	0.99	11.85	0.71	1.14	1.05	2.19
	4105	1.07	11.60	0.58	1.11	1.15	2.26
	4106D	1.52Z	14.33Z	0.39Z	1.27Z	1.22Z	2.49Z
	4107	0.89	9.77	0.42	0.92	0.96	1.88
	4108	0.90	11.15	0.55	1.09	1.05	2.14
	4109	0.93	11.50	0.59	1.07	1.06	2.13
	4110	1.07	12.96	0.74	1.21	1.20	2.41
	4111D	1.23Z	19.49Z	0.75Z	1.35Z	1.26Z	2.61Z
	4112D	1.10Z	16.17Z	0.53Z	1.31Z	1.24Z	2.55Z
	Mean	0.95	11.08	0.61	1.08	1.06	2.14
	S.D.	0.09	1.15	0.11	0.08	0.08	0.16
Relative	4101	0.31	3.56	0.20	0.38	0.37	0.74
	4102	0.33	3.80	0.28	0.40	0.39	0.78
	4103D	0.44Z	5.71Z	0.17Z	0.38Z	0.38Z	0.76Z
	4104	0.34	4.03	0.24	0.39	0.36	0.74
	4105	0.34	3.72	0.19	0.36	0.37	0.72
	4106D	0.50Z	4.70Z	0.13Z	0.42Z	0.40Z	0.82Z
	4107	0.34	3.76	0.16	0.35	0.37	0.72
	4108	0.31	3.90	0.19	0.38	0.37	0.75
	4109	0.31	3.80	0.19	0.35	0.35	0.70
	4110	0.32	3.93	0.22	0.37	0.36	0.73
	4111D	0.38Z	6.07Z	0.23Z	0.42Z	0.39Z	0.81Z
	4112D	0.39Z	5.78Z	0.19Z	0.47Z	0.44Z	0.91Z
	Mean	0.33	3.81	0.21	0.37	0.37	0.74
	S.D.	0.01	0.14	0.04	0.02	0.01	0.02

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-28 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Main group, End of administration)
Dose (mg/kg): 500

	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)
	4101	54	50	104	43.3	44.8	88.1	685
	4102	47	52	99	53.0	34.8	87.8	649
	4103D	59Z	60Z	119Z	35.2Z	43.3Z	78.5Z	4828Z
	4104	45	48	93	57.2	51.7	108.9	533
	4105	50	55	105	55.3	69.1	124.4	834
	4106D	62Z	57Z	119Z	67.1Z	71.8Z	138.9Z	23422Z
	4107	46	46	92	38.4	39.6	78.0	600
Absolute	4108	44	49	93	55.8	51.6	107.4	581
	4109	37	37	74	60.3	53.8	114.1	651
	4110	53	64	117	57.7	56.5	114.2	744
	4111D	89Z	103Z	192Z	93.6Z	53.7Z	147.3Z	7081Z
	4112D	57Z	57Z	114Z	45.9Z	51.9Z	97.8Z	385Z
	Mean	47	50	97	52.6	50.2	102.9	660
	S.D.	5	8	13	7.7	10.6	16.2	96
	4101	20	18	38	15.9	16.4	32.3	251
	4102	18	20	38	20.1	13.2	33.3	246
	4103D	21Z	21Z	41Z	12.3Z	15.1Z	27.4Z	1682Z
	4104	15	16	32	19.5	17.6	37.0	181
	4105	16	18	34	17.7	22.1	39.9	267
	4106D	20Z	19Z	39Z	22.0Z	23.5Z	45.5Z	7679Z
	4107	18	18	35	14.8	15.2	30.0	231
Relative	4108	15	17	33	19.5	18.0	37.6	203
	4109	12	12	24	19.9	17.8	37.7	215
	4110	16	19	35	17.5	17.1	34.6	225
	4111D	28Z	32Z	60Z	29.2Z	16.7Z	45.9Z	2206Z
	4112D	20Z	20Z	41Z	16.4Z	18.5Z	34.9Z	138Z
	Mean	16	17	34	18.1	17.2	35.3	227
	S.D.	2	2	4	2.0	2.6	3.3	28

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-29 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	260	1.94	11.7	5.7	5.0	10.7	355
	1114	283	2.05	16.7	6.7	6.3	13.0	417
	1115	271	1.91	16.0	7.5	8.0	15.5	278
	1116	284	2.01	18.8	9.2	8.6	17.8	436
	1117	301	1.95	17.9	8.2	6.8	15.0	323
	Mean	280	1.97	16.2	7.5	6.9	14.4	362
	S.D.	15	0.06	2.7	1.3	1.4	2.7	65
Relative	1113		0.75	4.5	2.2	1.9	4.1	137
	1114		0.72	5.9	2.4	2.2	4.6	147
	1115		0.70	5.9	2.8	3.0	5.7	103
	1116		0.71	6.6	3.2	3.0	6.3	154
	1117		0.65	5.9	2.7	2.3	5.0	107
	Mean		0.71	5.8	2.7	2.5	5.1	130
	S.D.		0.04	0.8	0.4	0.5	0.9	23

Appendix 8-30 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	0.90	6.07	0.56	0.85	0.82	1.67
	1114	1.03	7.16	0.65	0.95	0.93	1.88
	1115	0.93	7.50	0.57	0.99	0.94	1.93
	1116	0.90	7.41	0.50	1.07	1.02	2.09
	1117	0.95	7.35	0.43	0.93	0.96	1.89
	Mean	0.94	7.10	0.54	0.96	0.93	1.89
	S.D.	0.05	0.59	0.08	0.08	0.07	0.15
Relative	1113	0.35	2.33	0.22	0.33	0.32	0.64
	1114	0.36	2.53	0.23	0.34	0.33	0.66
	1115	0.34	2.77	0.21	0.37	0.35	0.71
	1116	0.32	2.61	0.18	0.38	0.36	0.74
	1117	0.32	2.44	0.14	0.31	0.32	0.63
	Mean	0.34	2.54	0.20	0.35	0.34	0.68
	S.D.	0.02	0.17	0.04	0.03	0.02	0.05

Appendix 8-31 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1113	29	31	60	42.7	48.1	90.8	555
	1114	37	37	74	47.6	48.1	95.7	439
	1115	41	46	87	48.0	44.2	92.2	607
Absolute	1116	42	45	87	38.7	36.2	74.9	666
	1117	29	34	63	33.2	33.0	66.2	750
	Mean	36	39	74	42.0	41.9	84.0	603
	S.D.	6	7	13	6.2	7.0	12.7	117
	1113	11	12	23	16.4	18.5	34.9	213
	1114	13	13	26	16.8	17.0	33.8	155
	1115	15	17	32	17.7	16.3	34.0	224
Relative	1116	15	16	31	13.6	12.7	26.4	235
	1117	10	11	21	11.0	11.0	22.0	249
	Mean	13	14	27	15.1	15.1	30.2	215
	S.D.	2	3	5	2.8	3.1	5.7	36

Appendix 8-32 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

	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	322	2.07	18.5	12.7	10.0	22.7	299
	4114	245	1.99	16.0	7.5	8.1	15.6	243
	4115	270	2.07	16.8	8.1	7.0	15.1	185
	4116D	299Z	1.99Z	22.7Z	8.9Z	10.3Z	19.2Z	496Z
	4117	274	2.04	17.3	10.6	9.2	19.8	258
	Mean	278	2.04	17.2	9.7	8.6	18.3	246
	S.D.	32	0.04	1.0	2.4	1.3	3.6	47
Relative	4113		0.64	5.7	3.9	3.1	7.0	93
	4114		0.81	6.5	3.1	3.3	6.4	99
	4115		0.77	6.2	3.0	2.6	5.6	69
	4116D		0.67Z	7.6Z	3.0Z	3.4Z	6.4Z	166Z
	4117		0.74	6.3	3.9	3.4	7.2	94
	Mean		0.74	6.2	3.5	3.1	6.6	89
	S.D.		0.07	0.3	0.5	0.4	0.7	13

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-33 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

	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	1.12	10.46	0.47	1.06	1.06	2.12
	4114	0.86	7.84	0.57	0.91	0.91	1.82
	4115	1.07	8.12	0.55	1.02	1.06	2.08
	4116D	1.36Z	17.39Z	0.59Z	1.44Z	1.35Z	2.79Z
	4117	0.87	8.53	0.52	0.94	0.97	1.91
	Mean	0.98	8.74	0.53	0.98	1.00	1.98
	S.D.	0.13	1.18	0.04	0.07	0.07	0.14
Relative	4113	0.35	3.25	0.15	0.33	0.33	0.66
	4114	0.35	3.20	0.23	0.37	0.37	0.74
	4115	0.40	3.01	0.20	0.38	0.39	0.77
	4116D	0.45Z	5.82Z	0.20Z	0.48Z	0.45Z	0.93Z
	4117	0.32	3.11	0.19	0.34	0.35	0.70
	Mean	0.36	3.14	0.19	0.36	0.36	0.72
	S.D.	0.03	0.11	0.03	0.02	0.03	0.05

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-34 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (Satellite group, End of administration)
Dose (mg/kg): 500

	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)
	4113	48	46	94	41.4	52.0	93.4	685
	4114	38	41	79	53.5	45.7	99.2	668
	4115	49	57	106	57.8	56.0	113.8	418
Absolute	4116D	41Z	41Z	82Z	70.8Z	52.2Z	123.0Z	374Z
	4117	40	41	81	44.1	43.5	87.6	539
	Mean	44	46	90	49.2	49.3	98.5	578
	S.D.	6	8	13	7.7	5.7	11.2	125
	4113	15	14	29	12.9	16.1	29.0	213
	4114	16	17	32	21.8	18.7	40.5	273
	4115	18	21	39	21.4	20.7	42.1	155
Relative	4116D	14Z	14Z	27Z	23.7Z	17.5Z	41.1Z	125Z
	4117	15	15	30	16.1	15.9	32.0	197
	Mean	16	17	33	18.1	17.9	35.9	210
	S.D.	1	3	5	4.3	2.3	6.4	49

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-35 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	493	2.11	12.4	10.7	6.4	17.1	235
	1009	477	2.05	11.7	11.1	11.6	22.7	150
	1010	473	2.18	13.6	8.0	9.6	17.6	291
	1011	583	2.10	12.9	13.5	13.5	27.0	183
	1012	476	2.20	13.2	10.9	6.6	17.5	224
	Mean	500	2.13	12.8	10.8	9.5	20.4	217
	S.D.	47	0.06	0.7	2.0	3.1	4.4	54
Relative	1008		0.43	2.5	2.2	1.3	3.5	48
	1009		0.43	2.5	2.3	2.4	4.8	31
	1010		0.46	2.9	1.7	2.0	3.7	62
	1011		0.36	2.2	2.3	2.3	4.6	31
	1012		0.46	2.8	2.3	1.4	3.7	47
	Mean		0.43	2.6	2.2	1.9	4.1	44
	S.D.		0.04	0.3	0.3	0.5	0.6	13

Appendix 8-36 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1.67	13.68	0.71	1.73	1.80	3.53
	1009	1.29	11.20	0.72	1.38	1.46	2.84
	1010	1.33	11.22	0.65	1.48	1.45	2.93
	1011	1.51	13.68	0.73	1.73	2.11	3.84
	1012	1.40	10.84	0.67	1.68	1.62	3.30
	Mean	1.44	12.12	0.70	1.60	1.69	3.29
	S.D.	0.15	1.43	0.03	0.16	0.28	0.42
Relative	1008	0.34	2.77	0.14	0.35	0.37	0.72
	1009	0.27	2.35	0.15	0.29	0.31	0.60
	1010	0.28	2.37	0.14	0.31	0.31	0.62
	1011	0.26	2.35	0.13	0.30	0.36	0.66
	1012	0.29	2.28	0.14	0.35	0.34	0.69
	Mean	0.29	2.42	0.14	0.32	0.34	0.66
	S.D.	0.03	0.20	0.01	0.03	0.03	0.05

Appendix 8-37 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1008	29	30	59	1.59	1.56	3.15
	1009	31	33	64	1.55	1.50	3.05
	1010	27	31	58	1.48	1.51	2.99
Absolute	1011	24	26	50	1.69	1.71	3.40
	1012	27	32	59	1.57	1.54	3.11
	Mean	28	30	58	1.58	1.56	3.14
	S.D.	3	3	5	0.08	0.09	0.16
	1008	6	6	12	0.32	0.32	0.64
	1009	6	7	13	0.32	0.31	0.64
	1010	6	7	12	0.31	0.32	0.63
Relative	1011	4	4	9	0.29	0.29	0.58
	1012	6	7	12	0.33	0.32	0.65
	Mean	6	6	12	0.31	0.31	0.63
	S.D.	1	1	2	0.02	0.01	0.03

Appendix 8-38 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1008	663	662	1325	2.32	1.95
	1009	596	581	1177	1.56	1.29
	1010	678	648	1326	2.12	1.48
Absolute	1011	679	664	1343	1.91	1.10
	1012	667	625	1292	1.37	1.20
	Mean	657	636	1293	1.86	1.40
	S.D.	35	34	67	0.39	0.34
	1008	134	134	269	0.47	0.40
	1009	125	122	247	0.33	0.27
	1010	143	137	280	0.45	0.31
Relative	1011	116	114	230	0.33	0.19
	1012	140	131	271	0.29	0.25
	Mean	132	128	259	0.37	0.28
	S.D.	11	9	20	0.08	0.08

Appendix 8-39 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 500

	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	468	2.17	12.6	15.8	13.9	29.7	316
	4009	444	2.08	14.5	12.9	10.8	23.7	219
	4010	585	2.23	14.7	11.0	14.2	25.2	217
	4011	500	2.14	13.4	16.0	15.2	31.2	198
	4012	533	2.46	14.4	11.4	9.3	20.7	478
	Mean	506	2.22	13.9	13.4	12.7	26.1	286
	S.D.	55	0.15	0.9	2.4	2.5	4.3	117
Relative	4008		0.46	2.7	3.4	3.0	6.3	68
	4009		0.47	3.3	2.9	2.4	5.3	49
	4010		0.38	2.5	1.9	2.4	4.3	37
	4011		0.43	2.7	3.2	3.0	6.2	40
	4012		0.46	2.7	2.1	1.7	3.9	90
	Mean		0.44	2.8	2.7	2.5	5.2	57
	S.D.		0.04	0.3	0.7	0.5	1.1	22

Appendix 8-40 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 500

	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	1.52	11.57	0.64	1.70	1.90	3.60
	4009	1.39	11.54	0.68	1.74	1.81	3.55
	4010	1.55	16.97	0.96	2.10	2.12	4.22
	4011	1.51	13.67	0.80	2.12	1.99	4.11
	4012	1.48	13.68	0.78	1.91	1.78	3.69
	Mean	1.49	13.49	0.77	1.91	1.92	3.83
	S.D.	0.06	2.22	0.12	0.20	0.14	0.31
Relative	4008	0.32	2.47	0.14	0.36	0.41	0.77
	4009	0.31	2.60	0.15	0.39	0.41	0.80
	4010	0.26	2.90	0.16	0.36	0.36	0.72
	4011	0.30	2.73	0.16	0.42	0.40	0.82
	4012	0.28	2.57	0.15	0.36	0.33	0.69
	Mean	0.29	2.65	0.15	0.38	0.38	0.76
	S.D.	0.02	0.17	0.01	0.03	0.04	0.05

Appendix 8-41 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 500

	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	28	29	57	1.79	1.78	3.57
	4009	29	29	58	1.46	1.38	2.84
	4010	32	31	63	1.50	1.54	3.04
	4011	32	33	65	1.55	1.54	3.09
	4012	36	40	76	1.50	1.44	2.94
	Mean	31	32	64	1.56	1.54	3.10
	S.D.	3	5	8	0.13	0.15	0.28
Relative	4008	6	6	12	0.38	0.38	0.76
	4009	7	7	13	0.33	0.31	0.64
	4010	5	5	11	0.26	0.26	0.52
	4011	6	7	13	0.31	0.31	0.62
	4012	7	8	14	0.28	0.27	0.55
	Mean	6	7	13	0.31	0.31	0.62
	S.D.	1	1	1	0.05	0.05	0.09

Appendix 8-42 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of male rats (End of recovery)
Dose (mg/kg): 500

	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)
	4008	763	724	1487	2.05	1.56
	4009	613	603	1216	1.71	1.18
	4010	620	623	1243	1.81	1.32
Absolute	4011	670	640	1310	2.16	1.52
	4012	656	643	1299	2.61	1.42
	Mean	664	647	1311	2.07	1.40
	S.D.	60	46	106	0.35	0.15
	4008	163	155	318	0.44	0.33
	4009	138	136	274	0.39	0.27
	4010	106	106	212	0.31	0.23
Relative	4011	134	128	262	0.43	0.30
	4012	123	121	244	0.49	0.27
	Mean	133	129	262	0.41	0.28
	S.D.	21	18	39	0.07	0.04

Appendix 8-43 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	322	2.06	20.2	9.2	8.9	18.1	243
	1119	259	1.69	15.9	8.2	7.9	16.1	171
	1120	295	1.87	17.7	6.1	6.0	12.1	251
	1121	261	2.05	15.4	9.9	10.1	20.0	176
	1122	295	1.98	16.6	12.9	9.1	22.0	278
	Mean	286	1.93	17.2	9.3	8.4	17.7	224
	S.D.	27	0.15	1.9	2.5	1.6	3.8	48
Relative	1118		0.64	6.3	2.9	2.8	5.6	75
	1119		0.65	6.1	3.2	3.1	6.2	66
	1120		0.63	6.0	2.1	2.0	4.1	85
	1121		0.79	5.9	3.8	3.9	7.7	67
	1122		0.67	5.6	4.4	3.1	7.5	94
	Mean		0.68	6.0	3.3	3.0	6.2	77
	S.D.		0.07	0.3	0.9	0.7	1.5	12

Appendix 8-44 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1.01	8.05	0.54	0.99	1.08	2.07
	1119	0.84	5.92	0.51	0.95	0.97	1.92
	1120	1.02	7.09	0.44	1.06	1.06	2.12
	1121	0.82	6.74	0.54	0.91	0.91	1.82
	1122	0.99	7.46	0.56	0.86	0.85	1.71
	Mean	0.94	7.05	0.52	0.95	0.97	1.93
	S.D.	0.10	0.80	0.05	0.08	0.10	0.17
Relative	1118	0.31	2.50	0.17	0.31	0.34	0.64
	1119	0.32	2.29	0.20	0.37	0.37	0.74
	1120	0.35	2.40	0.15	0.36	0.36	0.72
	1121	0.31	2.58	0.21	0.35	0.35	0.70
	1122	0.34	2.53	0.19	0.29	0.29	0.58
	Mean	0.33	2.46	0.18	0.34	0.34	0.68
	S.D.	0.02	0.12	0.02	0.03	0.03	0.07

Appendix 8-45 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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)
	1118	43	48	91	56.1	54.2	110.3	431
	1119	33	34	67	31.8	40.6	72.4	664
	1120	34	33	67	43.7	41.9	85.6	565
Absolute	1121	37	39	76	40.8	44.4	85.2	651
	1122	32	31	63	34.4	38.1	72.5	509
	Mean	36	37	73	41.4	43.8	85.2	564
	S.D.	4	7	11	9.5	6.2	15.5	98
	1118	13	15	28	17.4	16.8	34.3	134
	1119	13	13	26	12.3	15.7	28.0	256
	1120	12	11	23	14.8	14.2	29.0	192
Relative	1121	14	15	29	15.6	17.0	32.6	249
	1122	11	11	21	11.7	12.9	24.6	173
	Mean	13	13	25	14.4	15.3	29.7	201
	S.D.	1	2	3	2.4	1.8	3.8	52

Appendix 8-46 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 500

	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	4118D	259Z	1.92Z	19.1Z	9.1Z	6.8Z	15.9Z	255Z
	4119	306	2.04	20.2	8.8	8.5	17.3	423
	4120D	310Z	2.03Z	25.5Z	10.9Z	15.3Z	26.2Z	297Z
	4121	281	1.96	15.2	6.7	6.0	12.7	327
	4122	270	2.03	16.0	8.9	9.4	18.3	238
	Mean	286	2.01	17.1	8.1	8.0	16.1	329
	S.D.	18	0.04	2.7	1.2	1.8	3.0	93
Relative	4118D		0.74Z	7.4Z	3.5Z	2.6Z	6.1Z	98Z
	4119		0.67	6.6	2.9	2.8	5.7	138
	4120D		0.65Z	8.2Z	3.5Z	4.9Z	8.5Z	96Z
	4121		0.70	5.4	2.4	2.1	4.5	116
	4122		0.75	5.9	3.3	3.5	6.8	88
	Mean		0.71	6.0	2.9	2.8	5.7	114
	S.D.		0.04	0.6	0.5	0.7	1.2	25

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-47 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 500

	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	4118D	1.12Z	12.36Z	0.46Z	0.99Z	0.96Z	1.95Z
	4119	0.99	8.35	0.52	1.00	1.02	2.02
	4120D	1.40Z	16.58Z	0.69Z	1.30Z	1.29Z	2.59Z
	4121	0.80	6.30	0.47	0.85	0.88	1.73
	4122	0.88	6.81	0.60	0.95	0.93	1.88
	Mean	0.89	7.15	0.53	0.93	0.94	1.88
	S.D.	0.10	1.07	0.07	0.08	0.07	0.15
Relative	4118D	0.43Z	4.77Z	0.18Z	0.38Z	0.37Z	0.75Z
	4119	0.32	2.73	0.17	0.33	0.33	0.66
	4120D	0.45Z	5.35Z	0.22Z	0.42Z	0.42Z	0.84Z
	4121	0.28	2.24	0.17	0.30	0.31	0.62
	4122	0.33	2.52	0.22	0.35	0.34	0.70
	Mean	0.31	2.50	0.19	0.33	0.33	0.66
	S.D.	0.03	0.25	0.03	0.03	0.02	0.04

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 8-48 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual organ weight of female rats (End of recovery)
Dose (mg/kg): 500

	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)
	4118D	46Z	51Z	97Z	51.0Z	47.5Z	98.5Z	451Z
	4119	47	50	97	49.9	33.7	83.6	556
	4120D	62Z	56Z	118Z	61.1Z	65.9Z	127.0Z	389Z
Absolute	4121	35	35	70	36.6	32.7	69.3	805
	4122	46	46	92	47.6	47.4	95.0	518
	Mean	43	44	86	44.7	37.9	82.6	626
	S.D.	7	8	14	7.1	8.2	12.9	156
	4118D	18Z	20Z	37Z	19.7Z	18.3Z	38.0Z	174Z
	4119	15	16	32	16.3	11.0	27.3	182
	4120D	20Z	18Z	38Z	19.7Z	21.3Z	41.0Z	125Z
Relative	4121	12	12	25	13.0	11.6	24.7	286
	4122	17	17	34	17.6	17.6	35.2	192
	Mean	15	15	30	15.6	13.4	29.1	220
	S.D.	3	3	5	2.4	3.6	5.5	57

D: Dead
Z: Data was excluded from statistical analysis.

Appendix 9-1(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Intestine,cecum	Cell infiltration,mucosal: minimal lymphocytic/eosinophilic
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic
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,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Liver, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-2(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic

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, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-3(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Intestine,duodenum	Regeneration,mucosal: minimal, focal
Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic
Spleen	Hematopoiesis,extramedullary: minimal
Testis	Atrophy,seminiferous tubular: minimal, unilateral

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-4(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

All tissues	Not remarkable

Histopathology:

Kidney	Cyst: minimal medullary Regeneration,tubular: minimal
Prostate	Cell infiltration: mild, lymphocytic
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Heart, Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-5(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Heart	Cell infiltration: minimal, mononuclear
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-6(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Kidney	Regeneration,tubular: minimal Cell infiltration,interstitial: minimal, lymphocytic
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic

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, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-7(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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 2-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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-9(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Kidney	Regeneration,tubular: minimal Cell infiltration,interstitial: minimal, lymphocytic
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-10(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Thyroid

Appendix 9-11(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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
Liver	Microgranuloma: mild

Following tissues : Not remarkable

Thyroid

Appendix 9-12(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Kidney, Thyroid

Appendix 9-13(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2001 Male 50 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
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-14(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2002 Male 50 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
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-15(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2003 Male 50 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

Following tissues : Not remarkable

Liver, Thyroid

Appendix 9-16(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2004 Male 50 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
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-17(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2005 Male 50 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Eosinophilic body,tubular cell: mild
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-18(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2006 Male 50 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2007 Male 50 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2008 Male 50 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2009 Male 50 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2010 Male 50 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2011 Male 50 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 3 present less than 1x1mm,less than 1x1mm,less than 1x1mm
Other 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2012 Male 50 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3001 Male 150 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
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-26(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3002 Male 150 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Eosinophilic body,tubular cell: mild
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal
Thyroid	Hypertrophy,follicular cell: minimal

Appendix 9-27(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3003 Male 150 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

Following tissues : Not remarkable

Liver, Thyroid

Appendix 9-28(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3004 Male 150 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Large: mild, bilateral
Liver	Large: mild
Other tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild, bilateral Eosinophilic body,tubular cell: moderate, bilateral
Liver	Vacuolation,hepatocyte,periportal: minimal Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal
Thyroid	Hypertrophy,follicular cell: minimal

Appendix 9-29(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3005 Male 150 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
Liver	Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-30(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3006 Male 150 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3007 Male 150 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Large: mild, bilateral
Liver	Large: mild
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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3008 Male 150 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3009 Male 150 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Large: mild, bilateral
Other 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3010 Male 150 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3011 Male 150 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3012 Male 150 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4001 Male 500 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
Kidney(PAS stain)	PAS reaction negative
Kidney(alpha2u globulin)	Alpha2u globulin immunohistochemistry positive
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic
Spleen	Hematopoiesis,extramedullary: minimal
Thyroid	Hypertrophy,follicular cell: 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, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus, Trachea
Urinary bladder

Appendix 9-38(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4002 Male 500 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 Urinary cast,granular: minimal
Kidney(PAS stain)	PAS reaction negative
Kidney(alpha2u globulin)	Alpha2u globulin immunohistochemistry positive
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic

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, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus
Trachea, Thyroid, Urinary bladder

Appendix 9-39(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4003 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Heart	Cell infiltration: minimal, mononuclear
Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: moderate Urinary cast,granular: minimal Cell infiltration,interstitial: mild, lymphocytic
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic
Thyroid	Hypertrophy,follicular cell: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Eye
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus
Trachea, Urinary bladder

Appendix 9-40(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4004 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Eye	Dysplasia,retinal: minimal
Kidney	Dilatation,tubular: minimal collecting Regeneration,tubular: minimal Eosinophilic body,tubular cell: moderate
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal
Prostate	Cell infiltration: mild lymphocytic/neutrophilic
Testis	Atrophy,seminiferous tubular: minimal, bilateral
Thyroid	Hypertrophy,follicular cell: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Epididymis, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Thymus
Trachea, Urinary bladder

Appendix 9-41(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4005 Male 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Large: mild, bilateral
Stomach	Focus,dark red,glandular stomach: 1 present 3x0.5mm
Other tissues	Not remarkable

Histopathology:

Kidney	Dilatation,tubular: mild, bilateral proximal/Henle's/distal/collecting Regeneration,tubular: moderate, bilateral Eosinophilic body,tubular cell: moderate, bilateral Urinary cast,granular: mild, bilateral Cell infiltration,interstitial: mild, bilateral, lymphocytic
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Prostate	Cell infiltration: minimal, lymphocytic
Spleen	Hematopoiesis,extramedullary: minimal
Stomach	Erosion,glandular stomach: minimal fundus

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, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Skeletal muscle,femoral, Seminal vesicle(coagulating gland), Testis, Thymus, Trachea
Thyroid, Urinary bladder

Appendix 9-42(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4006 Male 500 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4007 Male 500 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4008 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: minimal Urinary cast,granular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-45(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4009 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Kidney, Thyroid

Appendix 9-46(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4010 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Eosinophilic body,tubular cell: minimal Urinary cast,granular: minimal
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Thyroid	Hypertrophy,follicular cell: minimal

Appendix 9-47(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4011 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Urinary cast,granular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-48(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4012 Male 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Kidney	Regeneration,tubular: mild Urinary cast,granular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-49(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1101 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Eye	Dysplasia,retinal: mild
Liver	Microgranuloma: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Stomach, Skeletal muscle,femoral, 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 2-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:

Liver	Microgranuloma: minimal
Spleen	Hematopoiesis,extramedullary: mild

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Stomach, Skeletal muscle,femoral, 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 2-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:

Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Pituitary	Aberrant craniopharyngeal tissue: 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, Liver, Ovary, Parathyroid
Pancreas, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Stomach, Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder
Uterus, Vagina

Appendix 9-52(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1104 Female 0 mg/kg Day 45 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 2-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:

Intestine,duodenum	Regeneration,mucosal: minimal, focal with inflammation
Intestine,ileum(Peyer's patch)	Erosion: mild
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,jejunum, Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Liver, Ovary, Parathyroid
Pancreas, Pituitary, Salivary gland,submandibular, Spinal cord(thoracic)
Sciatic nerve, Stomach, Skeletal muscle,femoral, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-54(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1106 Female 0 mg/kg Day 41 Undelivered

Gross pathology:

Kidney	Small: moderate, left
Uterus	Retention,white material
Vagina	Atresia Retention,white material
Other tissues	Not remarkable

Histopathology:

Kidney	Cell infiltration,interstitial: minimal, lymphocytic Fibrosis: mild Pigment-laden macrophage: minimal greenish yellow
Spleen	Hematopoiesis,extramedullary: minimal
Uterus	Cell infiltration,inflammatory: minimal, bilateral No finding correlating with necropsy data.

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Stomach, Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder
Vagina

Appendix 9-55(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1107 Female 0 mg/kg Day 43 All littermates died

Gross pathology:

Spleen	Focus,white: 1 present 3x3mm
Stomach	Focus,white,forestomach: many 1x1 to 4x3mm
Other tissues	Not remarkable

Histopathology:

Intestine,colon	Atrophy,mucosal: minimal
Kidney	Vacuolation,tubular: mild proximal
Liver	Vacuolation,hepatocyte,periportal: minimal
Salivary gland,submandibular	Atrophy,acinar,diffuse: minimal
Spleen	Capsulitis: mild Atrophy,white pulp: minimal
Stomach	Ulcer,forestomach: mild Hyperplasia,squamous,forestomach: mild
Thymus	Atrophy: moderate

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,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Spinal cord(thoracic), Sciatic nerve, Skeletal muscle,femoral
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-56(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1108 Female 0 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-57(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1109 Female 0 mg/kg Day 45 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1110 Female 0 mg/kg Day 47 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1111 Female 0 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Intestine,duodenum	Erosion: minimal
Kidney	Regeneration,tubular: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: mild
Stomach	Erosion,glandular stomach: minimal pyloric

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Liver, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder, Uterus
Vagina

Appendix 9-60(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 1112 Female 0 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-61(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Kidney	Cyst: minimal medullary Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, 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 2-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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
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 2-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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, 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 2-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:

Liver Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
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 2-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:

Kidney	Regeneration,tubular: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, 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 2-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:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Stomach	Erosion,glandular stomach: mild fundus

Following tissues : Not remarkable

Adrenal, Liver, Thyroid

Appendix 9-67(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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, Thyroid

Appendix 9-68(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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, Thyroid

Appendix 9-69(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-70(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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:

Stomach	Focus,white,forestomach: 1 present 1x1mm,near limiting ridge
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal
Stomach	Cyst,inclusion: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-71(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2101 Female 50 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-72(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2102 Female 50 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-73(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2103 Female 50 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-74(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2104 Female 50 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Hypertrophy,zona fasciculata: minimal
Liver	Microgranuloma: mild

Following tissues : Not remarkable

Thyroid

Appendix 9-75(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2105 Female 50 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver, Thyroid

Appendix 9-76(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2106 Female 50 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver, Thyroid

Appendix 9-77(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2107 Female 50 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2108 Female 50 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver, Thyroid

Appendix 9-79(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2109 Female 50 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x3mm
Other 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2110 Female 50 mg/kg Day 45 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2111 Female 50 mg/kg Day 42 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

Following tissues : Not remarkable

Adrenal, Liver, Thyroid

Appendix 9-82(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 2112 Female 50 mg/kg Day 46 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3101 Female 150 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-84(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3102 Female 150 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-85(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3103 Female 150 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-86(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3104 Female 150 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-87(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3105 Female 150 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-88(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3106 Female 150 mg/kg Day 42 End of administration period (L4)

Gross pathology:

Stomach	Focus,depressed,forestomach: 1 present 1x1x0.5mm Focus,raised,glandular stomach: 1 present 1x1x0.5mm
Other tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-89(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3107 Female 150 mg/kg Day 46 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3108 Female 150 mg/kg Day 45 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-91(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3109 Female 150 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3110 Female 150 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-93(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3111 Female 150 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-94(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 3112 Female 150 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4101 Female 500 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-96(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4102 Female 500 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: mild
Intestine,cecum	Cell infiltration,mucosal: minimal lymphocytic/eosinophilic
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: 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,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder, Uterus
Vagina

Appendix 9-97(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4103 Female 500 mg/kg Day 32 Found dead

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Hypertrophy,zona fasciculata: minimal
Intestine,jejunum	Sample autolysed
Intestine,colon	Sample autolysed
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Spleen	Atrophy,white pulp: mild
Cause of demise	Test substance toxicity

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular
Lung(bronchus), Ovary, Parathyroid, Pancreas, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4104 Female 500 mg/kg Day 43 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: mild
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: mild
Thyroid	Hypertrophy,follicular cell: 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, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Stomach, Skeletal muscle,femoral, Thymus, Trachea, Urinary bladder, Uterus
Vagina

Appendix 9-99(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4105 Female 500 mg/kg Day 45 End of administration period (L4)

Gross pathology:

Kidney	Cyst: 1 present, right 2x2x2mm
Other tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: minimal
Kidney	Cyst: mild cortical Regeneration,tubular: minimal
Liver	Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Pituitary	Aberrant craniopharyngeal tissue: 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, Lymph node,mesenteric
Lymph node,submandibular, Ovary, Parathyroid, Pancreas
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder, Uterus
Vagina

Appendix 9-100(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4106 Female 500 mg/kg Day 33 Found dead

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Hypertrophy,zona fasciculata: minimal
Intestine,colon	Sample autolysed
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Salivary gland,submandibular	Atrophy,acinar,diffuse: minimal
Spleen	Hematopoiesis,extramedullary: minimal Atrophy,white pulp: mild
Cause of demise	Test substance toxicity

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, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Ovary, Parathyroid, Pancreas, Pituitary
Spinal cord(thoracic), Sciatic nerve, Stomach, Skeletal muscle,femoral, Thymus
Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-101(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4107 Female 500 mg/kg Day 44 End of administration period (L4)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Spleen	Hematopoiesis,extramedullary: minimal
Thymus	Atrophy: minimal

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Stomach, Skeletal muscle,femoral, Trachea
Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-102(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4108 Female 500 mg/kg Day 43 End of administration period (L4)

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 2x15mm
Other tissues	Not remarkable

Histopathology:

Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Spleen	Hematopoiesis,extramedullary: mild
Stomach	Erosion,glandular stomach: minimal fundus

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, Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder, Uterus
Vagina

Appendix 9-103(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4109 Female 500 mg/kg Day 46 End of administration period (L4)

Gross pathology:

Stomach	Focus,white,glandular stomach: 1 present 1x1mm Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

No tissues examined

Appendix 9-104(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4110 Female 500 mg/kg Day 46 End of administration period (L4)

Gross pathology:

All tissues Not remarkable

Histopathology:

No tissues examined

Appendix 9-105(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4111 Female 500 mg/kg Day 30 Found dead

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Hypertrophy,zona fasciculata: minimal
Eye	Dysplasia,retinal: minimal
Intestine,cecum	Cell infiltration,mucosal: minimal lymphocytic/eosinophilic
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Salivary gland,submandibular	Atrophy,acinar,diffuse: minimal
Spleen	Hematopoiesis,extramedullary: mild
Cause of demise	Test substance toxicity

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,colon
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular
Lung(bronchus), Ovary, Parathyroid, Pancreas, Pituitary, Spinal cord(thoracic)
Sciatic nerve, Stomach, Skeletal muscle,femoral, Thymus, Trachea, Thyroid
Urinary bladder, Uterus, Vagina

Appendix 9-106(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4112 Female 500 mg/kg Day 10 Found dead

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Hypertrophy,zona fasciculata: minimal
Cause of demise	Test substance toxicity

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, Liver, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
Thymus, Trachea, Thyroid, Urinary bladder, Uterus, Vagina

Appendix 9-107(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4113 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: minimal
Heart	Cell infiltration: minimal, mononuclear
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Pancreas	Atrophy,acinar,focal: minimal
Thyroid	Hypertrophy,follicular cell: minimal

Following tissues : Not remarkable

Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,colon, Intestine,rectum, Kidney, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pituitary
Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Thymus, Trachea, Urinary bladder, Uterus
Vagina

Appendix 9-108(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4114 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: minimal
Liver	Hypertrophy,hepatocytic,centrilobular: 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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4115 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: mild
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: 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), Ovary
Parathyroid, Pancreas, Pituitary, Salivary gland,submandibular
Spinal cord(thoracic), Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral
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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4116 Female 500 mg/kg Day 15 Found dead

Gross pathology:

Intestine,colon	Focus,dark red: 1 present 3x3mm,70cm above anus
Other tissues	Not remarkable

Histopathology:

Cerebellum(pons)	Hemorrhage: minimal fourth ventricle
Cerebrum	Hemorrhage: mild third ventricle/lateral ventricle/ cerebral aqueduct, fresh
Intestine,colon	Hemorrhage: mild mucosal to submucosal, with necrosis and inflammation
Salivary gland,submandibular	Atrophy,acinar,diffuse: minimal
Cause of demise	Test substance toxicity

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Eye, Heart, Intestine,duodenum
Intestine,jejunum, Intestine,ileum(Peyer's patch), Intestine,cecum
Intestine,rectum, Kidney, Lymph node,mesenteric, Lymph node,submandibular, Liver
Lung(bronchus), Ovary, Parathyroid, Pancreas, Pituitary, Spinal cord(thoracic)
Sciatic nerve, Spleen, Stomach, Skeletal muscle,femoral, 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4117 Female 500 mg/kg Day 43 End of administration period (D42)

Gross pathology:

Kidney	Dilatation,pelvic: mild, left
Other tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: minimal
Kidney	Dilatation,pelvic: mild Regeneration,tubular: minimal
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, Lymph node,mesenteric
Lymph node,submandibular, Lung(bronchus), Ovary, Parathyroid, Pancreas
Pituitary, Salivary gland,submandibular, Spinal cord(thoracic), Sciatic nerve
Spleen, Stomach, Skeletal muscle,femoral, 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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4118 Female 500 mg/kg Day 15 Found dead

Gross pathology:

All tissues	Not remarkable

Histopathology:

Cerebrum	Hemorrhage: mild third ventricle/forth ventricle, fresh
Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Lung(bronchus)	Aggregation,alveolar macrophage: minimal
Salivary gland,submandibular	Atrophy,acinar,diffuse: minimal
Spleen	Hematopoiesis,extramedullary: minimal
Cause of demise	Test substance toxicity

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,ileum(Peyer's patch)
Intestine,cecum, Intestine,colon, Intestine,rectum, Kidney
Lymph node,mesenteric, Lymph node,submandibular, Ovary, Parathyroid, Pancreas
Pituitary, Spinal cord(thoracic), Sciatic nerve, Stomach
Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder, Uterus
Vagina

Appendix 9-113(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4119 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

Stomach	Focus,dark red,glandular stomach: 1 present 1x1mm
Other tissues	Not remarkable

Histopathology:

Liver	Hypertrophy,hepatocytic,centrilobular: minimal
Stomach	Erosion,glandular stomach: minimal fundus

Following tissues : Not remarkable

Adrenal, Thyroid

Appendix 9-114(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4120 Female 500 mg/kg Day 29 Found dead

Gross pathology:

Kidney	Focus,dark red: 1 present, right 2x2mm
Other tissues	Not remarkable

Histopathology:

Intestine,ileum(Peyer's patch)	Sample autolysed
Intestine,colon	Sample autolysed
Kidney	Hemorrhage,interstitial: minimal, unilateral fresh
Liver	Microgranuloma: minimal Hypertrophy,hepatocytic,centrilobular: mild
Salivary gland,submandibular	Atrophy,acinar,diffuse: minimal
Cause of demise	Test substance toxicity

Following tissues : Not remarkable

Adrenal, Bone+Bone marrow,femoral, Cerebellum(pons), Cerebrum, Eye, Heart
Intestine,duodenum, Intestine,jejunum, Intestine,cecum, Intestine,rectum
Lymph node,mesenteric, Lymph node,submandibular, Lung(bronchus), Ovary
Parathyroid, Pancreas, Pituitary, Spinal cord(thoracic), Sciatic nerve, Spleen
Stomach, Skeletal muscle,femoral, Thymus, Trachea, Thyroid, Urinary bladder
Uterus, Vagina

Appendix 9-115(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4121 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 9-116(1/1) Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats

Individual gross and histopathological findings

Animal No. 4122 Female 500 mg/kg Day 57 End of recovery period

Gross pathology:

All tissues	Not remarkable

Histopathology:

Adrenal	Vacuolation,cortical cell: minimal
Liver	Microgranuloma: minimal

Following tissues : Not remarkable

Thyroid

Appendix 10-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
1102	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1103	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1104	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1105	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1106	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	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	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
1110	E	M	D	P	E	E	M	D	P	E	M	D	P	E	E	4	4.3	
1111	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
1112	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																3.9	4.0	
S.D.																0.3	0.1	

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 10-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 50

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	D	P	E	M	D	D	P	E	M	3	5.0	
2102	E	M	D	P	E	E	M	D	P	E	E	M	D	P	E	4	4.7	
2103	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
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	D	P	E	E	M	D	P	E	E	M	D	P	E	M	D	3	5.0	
2107	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2108	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
2109	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2110	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
2111	E	M	D	D	P	E	M	D	D	P	E	M	D	D	P	3	5.0	
2112	D	P	E	E	M	D	P	E	E	M	D	P	E	E	M	3	5.0	
Total(%)b)																		0/12(0.0)
Mean																3.7	4.4	
S.D.																0.5	0.5	

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 2-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): 150

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	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
3102	D	P	E	E	M	D	P	E	E	M	D	P	E	E	M	3	5.0	
3103	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3104	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3105	E	M	D	D	P	E	M	D	D	P	E	M	D	D	P	3	5.0	
3106	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
3107	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
3108	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	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	M	D	P	E	M	D	P	E	M	D	P	E	E	M	D	3	4.0	
3112	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
Total(%)b)																		0/12(0.0)
Mean																3.5	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

Appendix 10-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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): 500

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	D	P	E	M	D	P	E	M	D	P	E	M	D	P	E	4	4.0	
4102	E	M	D	P	E	M	D	P	E	M	D	P	E	M	D	4	4.0	
4103	P	E	M	D	D	P	E	M	D	P	E	M	D	P	E	4	4.3	
4104	M	D	D	P	E	M	D	P	E	M	D	P	E	M	D	3	4.0	
4105	E	M	D	P	E	E	M	D	P	E	M	D	P	E	M	4	4.3	
4106	M	D	P	E	M	D	P	E	M	D	P	E	M	D	P	3	4.0	
4107	M	D	P	E	E	M	D	P	E	M	D	P	E	M	D	3	4.5	
4108	D	P	E	M	D	P	E	M	D	P	E	M	D	D	P	3	4.0	
4109	M	D	D	P	E	M	D	P	E	E	M	D	P	E	E	3	4.5	
4110	P	E	M	D	D	P	E	M	D	P	E	M	D	P	E	4	4.3	
4111	P	E	M	D	P	E	M	D	P	E	M	D	P	E	M	4	4.0	
4112c)	D	D	P	E	M	D	P	E	M	D								
Total(%)b)																		0/11(0.0)
Mean																3.5	4.2	
S.D.																0.5	0.2	

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): Died on day 10 of administration

Appendix 11-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	1	P
1002	1102	C	2	P
1003	1103	C	2	P
1004	1104	C	3	P
1005	1105	C	2	P
1006	1106	C	1	NP
1007	1107	C	3	P
1008	1108	C	2	P
1009	1109	C	3	P
1010	1110	C	5	P
1011	1111	C	2	P
1012	1112	C	3	P

C: Copulated P: Pregnant NP: Non-pregnant

Appendix 11-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 50

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
2001	2101	C	4	P
2002	2102	C	4	P
2003	2103	C	3	P
2004	2104	C	-a)	P
2005	2105	C	2	P
2006	2106	C	2	P
2007	2107	C	2	P
2008	2108	C	2	P
2009	2109	C	3	P
2010	2110	C	3	P
2011	2111	C	1	P
2012	2112	C	4	P

C: Copulated P: Pregnant
a): Overlooked on the day of copulation

Appendix 11-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 150

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
3001	3101	C	3	P
3002	3102	C	3	P
3003	3103	C	4	P
3004	3104	C	1	P
3005	3105	C	1	P
3006	3106	C	1	P
3007	3107	C	4	P
3008	3108	C	3	P
3009	3109	C	3	P
3010	3110	C	2	P
3011	3111	C	2	P
3012	3112	C	1	P

C: Copulated P: Pregnant

Appendix 11-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual mating and fertility of animals
Dose (mg/kg): 500

Pairing number Male	Female	Copulated or not copulated	Days until copulation	Pregnant or non-pregnant
4001	4101	C	4	P
4002	4102	C	2	P
4003	4103	C	4	P
4004	4104	C	2	P
4005	4105	C	3	P
4006	4106	C	1	P
4007	4107	C	-a)	P
4008	4108	C	1	P
4009	4109	C	5	P
4010	4110	C	4	P
4011	4111	C	3	P
4012	NT249	C	4	NP

C: Copulated P: Pregnant
a): Overlooked on the day of copulation
NT249: Non-treatment animal, Tag No.249

Appendix 12-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 0

Dam number	Gestation length in days	No. of corpora lutea	No. of implan-tation sites	Implan-tation index % a)	Delivery index % b)	No. of stillborns (%)c)	No. of liveborns	External d) abnor-malities(%)e)
1101	22	15	15	100.0	100.0	1(6.7)	14	0(0.0)
1102	22	14	14	100.0	92.9	0(0.0)	13	0(0.0)
1103	22	17	17	100.0	94.1	0(0.0)	16	0(0.0)
1104	22	15	14	93.3	100.0	0(0.0)	14	0(0.0)
1105	22	14	14	100.0	100.0	1(7.1)	13	0(0.0)
1106	Non-pregnant							
1107	23	16	16	100.0	100.0	9(56.3)	7	0(0.0)
1108	22	15	13	86.7	84.6	0(0.0)	11	0(0.0)
1109	22	18	18	100.0	94.4	0(0.0)	17	0(0.0)
1110	22	16	14	87.5	92.9	0(0.0)	13	0(0.0)
1111	21	14	14	100.0	92.9	0(0.0)	13	0(0.0)
1112	22	17	17	100.0	100.0	0(0.0)	17	0(0.0)
Total		171	166			11	148	0
Mean	22.0	15.5	15.1	97.0	95.6	(6.4)	13.5	(0.0)
S.D.	0.4	1.4	1.6	5.3	4.9	(16.8)	2.8	(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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 50

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	17	17	100.0	100.0	2(11.8)	15	0(0.0)
2102	22	16	16	100.0	87.5	0(0.0)	14	0(0.0)
2103	22	17	17	100.0	100.0	0(0.0)	17	0(0.0)
2104	22	16	15	93.8	93.3	0(0.0)	14	0(0.0)
2105	22	14	14	100.0	92.9	0(0.0)	13	0(0.0)
2106	22	15	15	100.0	93.3	0(0.0)	14	0(0.0)
2107	22	18	15	83.3	100.0	0(0.0)	15	0(0.0)
2108	21	18	16	88.9	100.0	0(0.0)	16	0(0.0)
2109	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
2110	22	16	16	100.0	93.8	0(0.0)	15	0(0.0)
2111	21	17	17	100.0	88.2	0(0.0)	15	0(0.0)
2112	22	16	16	100.0	100.0	3(18.8)	13	0(0.0)
Total		196	189			5	176	0
Mean	21.8	16.3	15.8	96.7	95.8	(2.6)	14.7	(0.0)
S.D.	0.4	1.2	1.0	5.6	4.8	(6.1)	1.2	(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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 150

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	18	18	100.0	100.0	0(0.0)	18	0(0.0)
3102	22	17	17	100.0	100.0	0(0.0)	17	0(0.0)
3103	22	15	15	100.0	93.3	0(0.0)	14	0(0.0)
3104	22	17	17	100.0	94.1	1(6.3)	15	0(0.0)
3105	22	20	15	75.0	93.3	1(7.1)	13	0(0.0)
3106	21	16	16	100.0	100.0	0(0.0)	16	0(0.0)
3107	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
3108	22	16	15	93.8	100.0	0(0.0)	15	0(0.0)
3109	22	14	14	100.0	92.9	1(7.7)	12	0(0.0)
3110	21	16	16	100.0	100.0	0(0.0)	16	0(0.0)
3111	21	15	14	93.3	100.0	0(0.0)	14	0(0.0)
3112	22	14	14	100.0	100.0	0(0.0)	14	0(0.0)
Total		194	186			3	179	0
Mean	21.8	16.2	15.5	96.3	97.8	(1.8)	14.9	(0.0)
S.D.	0.5	1.7	1.3	7.3	3.3	(3.2)	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 12-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Delivery data on dams
Dose (mg/kg): 500

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	17	17	100.0	100.0	0(0.0)	17	0(0.0)
4102	22	15	13	86.7	92.3	0(0.0)	12	0(0.0)
4103f)								
4104	21	14	14	100.0	100.0	0(0.0)	14	0(0.0)
4105	22	16	16	100.0	100.0	0(0.0)	16	0(0.0)
4106g)								
4107	22	13	13	100.0	92.3	0(0.0)	12	0(0.0)
4108	22	16	16	100.0	100.0	0(0.0)	16	0(0.0)
4109	21	16	16	100.0	100.0	2(12.5)	14	0(0.0)
4110	22	16	16	100.0	87.5	0(0.0)	14	0(0.0)
4111h)								
4112i)								
Total		123	121			2	115	0
Mean	21.8	15.4	15.1	98.3	96.5	(1.6)	14.4	(0.0)
S.D.	0.5	1.3	1.6	4.7	5.0	(4.4)	1.8	(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
f): Died on gestation day 13
g): Died on gestation day 17
h): Died on gestation day 12
i): Died on day 10 of administration

Appendix 13-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	14	15	93.3	14	14	100.0
1102	13	13	100.0	13	13	100.0
1103	16	16	100.0	16	16	100.0
1104	14	14	100.0	14	14	100.0
1105	13	14	92.9	13	13	100.0
1106	Non-pregnant					
1107c)	7	16	43.8	7	0	0.0
1108	11	11	100.0	11	11	100.0
1109	17	17	100.0	17	17	100.0
1110	13	13	100.0	13	13	100.0
1111	13	13	100.0	13	13	100.0
1112	17	17	100.0	17	16	94.1
Total	148	159		148	140	
Mean	13.5	14.5	93.6	13.5	12.7	90.4
S.D.	2.8	1.9	16.8	2.8	4.6	30.0

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100
c): All pups died by postnatal day 2.

Appendix 13-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 50

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	17	88.2	15	15	100.0
2102	14	14	100.0	14	14	100.0
2103	17	17	100.0	17	15	88.2
2104	14	14	100.0	14	14	100.0
2105	13	13	100.0	13	13	100.0
2106	14	14	100.0	14	14	100.0
2107	15	15	100.0	15	15	100.0
2108	16	16	100.0	16	16	100.0
2109	15	15	100.0	15	14	93.3
2110	15	15	100.0	15	15	100.0
2111	15	15	100.0	15	15	100.0
2112	13	16	81.3	13	13	100.0
Total	176	181		176	173	
Mean	14.7	15.1	97.5	14.7	14.4	98.5
S.D.	1.2	1.2	6.1	1.2	0.9	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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 150

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	18	18	100.0	18	18	100.0
3102	17	17	100.0	17	16	94.1
3103	14	14	100.0	14	14	100.0
3104	15	16	93.8	15	14	93.3
3105	13	14	92.9	13	13	100.0
3106	16	16	100.0	16	16	100.0
3107	15	15	100.0	15	15	100.0
3108	15	15	100.0	15	15	100.0
3109	12	13	92.3	12	12	100.0
3110	16	16	100.0	16	16	100.0
3111	14	14	100.0	14	14	100.0
3112	14	14	100.0	14	14	100.0
Total	179	182		179	177	
Mean	14.9	15.2	98.3	14.9	14.8	99.0
S.D.	1.7	1.5	3.2	1.7	1.6	2.5

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 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual viability index of pups
Dose (mg/kg): 500

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	17	17	100.0	17	16	94.1
4102	12	12	100.0	12	12	100.0
4103c)						
4104	14	14	100.0	14	12	85.7
4105	16	16	100.0	16	16	100.0
4106d)						
4107	12	12	100.0	12	12	100.0
4108	16	16	100.0	16	16	100.0
4109	14	16	87.5	14	14	100.0
4110	14	14	100.0	14	13	92.9
4111e)						
4112f)						
Total	115	117		115	111	
Mean	14.4	14.6	98.4	14.4	13.9	96.6
S.D.	1.8	1.9	4.4	1.8	1.9	5.3

a): (No. of liveborns / No. of delivered pups)×100
b): (No. of live pups on postnatal day 4 / No. of liveborns)×100
c): Died on gestation day 13
d): Died on gestation day 17
e): Died on gestation day 12
f): Died on day 10 of administration

Appendix 14-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	6	8	0	1	0.40	0.43	6	8	0.43
1102	4	9	0	0	0.31	0.31	4	9	0.31
1103	10	6	0	0	0.63	0.63	10	6	0.63
1104	9	5	0	0	0.64	0.64	9	5	0.64
1105	6	7	-e)	-e)	-e)	0.46	6	7	0.46
1106	Non-pregnant								
1107d)	3	4	6	3	0.56	0.43			
1108	7	4	0	0	0.64	0.64	7	4	0.64
1109	7	10	0	0	0.41	0.41	7	10	0.41
1110	9	4	0	0	0.69	0.69	9	4	0.69
1111	6	7	0	0	0.46	0.46	6	7	0.46
1112	6	11	0	0	0.35	0.35	5	11	0.31
Total	73	75	6	4			69	71	
Mean	6.6	6.8	0.6	0.4	0.51	0.50	6.9	7.1	0.50
S.D.	2.1	2.5	1.9	1.0	0.14	0.13	1.9	2.4	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.
e): One stillborn whose sex was unclear due to cannibalism.

Appendix 14-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 50

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)
2101	7	8	0	2	0.41	0.47	7	8	0.47
2102	3	11	0	0	0.21	0.21	3	11	0.21
2103	10	7	0	0	0.59	0.59	9	6	0.60
2104	6	8	0	0	0.43	0.43	6	8	0.43
2105	7	6	0	0	0.54	0.54	7	6	0.54
2106	11	3	0	0	0.79	0.79	11	3	0.79
2107	9	6	0	0	0.60	0.60	9	6	0.60
2108	6	10	0	0	0.38	0.38	6	10	0.38
2109	7	8	0	0	0.47	0.47	6	8	0.43
2110	8	7	0	0	0.53	0.53	8	7	0.53
2111	8	7	0	0	0.53	0.53	8	7	0.53
2112	5	8	2	1	0.44	0.38	5	8	0.38
Total	87	89	2	3			85	88	
Mean	7.3	7.4	0.2	0.3	0.49	0.49	7.1	7.3	0.49
S.D.	2.2	2.0	0.6	0.6	0.14	0.14	2.1	2.1	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

Appendix 14-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 150

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	5	13	0	0	0.28	0.28	5	13	0.28
3102	9	8	0	0	0.53	0.53	8	8	0.50
3103	7	7	0	0	0.50	0.50	7	7	0.50
3104	9	6	0	1	0.56	0.60	8	6	0.57
3105	7	6	-d)	-d)	-d)	0.54	7	6	0.54
3106	7	9	0	0	0.44	0.44	7	9	0.44
3107	8	7	0	0	0.53	0.53	8	7	0.53
3108	10	5	0	0	0.67	0.67	10	5	0.67
3109	4	8	1	0	0.38	0.33	4	8	0.33
3110	11	5	0	0	0.69	0.69	11	5	0.69
3111	10	4	0	0	0.71	0.71	10	4	0.71
3112	9	5	0	0	0.64	0.64	9	5	0.64
Total	96	83	1	1			94	83	
Mean	8.0	6.9	0.1	0.1	0.54	0.54	7.8	6.9	0.53
S.D.	2.1	2.4	0.3	0.3	0.14	0.14	2.0	2.4	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): One stillborn whose sex was unclear due to cannibalism.

Appendix 14-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual sex ratio of pups
Dose (mg/kg): 500

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	8	9	0	0	0.47	0.47	7	9	0.44
4102	4	8	0	0	0.33	0.33	4	8	0.33
4103d)									
4104	12	2	0	0	0.86	0.86	11	1	0.92
4105	9	7	0	0	0.56	0.56	9	7	0.56
4106e)									
4107	1	11	0	0	0.08	0.08	1	11	0.08
4108	10	6	0	0	0.63	0.63	10	6	0.63
4109	7	7	0	2	0.44	0.50	7	7	0.50
4110	6	8	0	0	0.43	0.43	6	7	0.46
4111f)									
4112g)									
Total	57	58	0	2			55	56	
Mean	7.1	7.3	0.0	0.3	0.48	0.48	6.9	7.0	0.49
S.D.	3.5	2.6	0.0	0.7	0.23	0.23	3.3	2.9	0.24

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): Died on gestation day 13
e): Died on gestation day 17
f): Died on gestation day 12
g): Died on day 10 of administration

Appendix 15-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	7.2	9.6	2.4	6.7	9.3	2.6
1102	6.7	11.0	4.3	6.4	10.4	4.0
1103	6.6	10.3	3.7	6.1	9.4	3.3
1104	6.2	9.1	2.9	5.8	8.7	2.9
1105	6.5	10.4	3.9	6.1	9.7	3.6
1106	Non-pregnant					
1107	6.2	b)		6.1	b)	
1108	6.8	11.6	4.8	6.7	11.5	4.8
1109	6.0	8.5	2.5	5.5	7.9	2.4
1110	7.1	10.1	3.0	6.6	10.0	3.4
1111	6.2	9.7	3.5	5.8	9.2	3.4
1112	6.4	10.1	3.7	5.9	9.5	3.6
Mean	6.5	10.0	3.5	6.2	9.6	3.4
S.D.	0.4	0.9	0.8	0.4	1.0	0.7

Unit: g
a): Postnatal day
b): All pups died by postnatal day 2.

Appendix 15-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 50

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
2101	6.3	9.4	3.1	6.1	9.4	3.3
2102	6.7	10.0	3.3	6.4	9.6	3.2
2103	6.1	9.0	2.9	5.9	8.6	2.7
2104	6.7	10.5	3.8	6.3	10.3	4.0
2105	6.5	10.1	3.6	6.3	9.6	3.3
2106	6.7	10.5	3.8	6.5	10.1	3.6
2107	6.3	9.9	3.6	6.0	9.5	3.5
2108	5.8	8.6	2.8	5.5	8.2	2.7
2109	6.0	8.7	2.7	5.9	8.6	2.7
2110	6.6	10.1	3.5	6.2	9.6	3.4
2111	6.3	8.9	2.6	6.0	9.1	3.1
2112	5.9	8.8	2.9	5.8	9.3	3.5
Mean	6.3	9.5	3.2	6.1	9.3	3.3
S.D.	0.3	0.7	0.4	0.3	0.6	0.4

Unit: g
a): Postnatal day

Appendix 15-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 150

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
3101	6.2	8.1	1.9	5.7	7.8	2.1
3102	5.9	9.6	3.7	5.7	8.9	3.2
3103	6.6	10.4	3.8	6.2	10.4	4.2
3104	7.1	10.8	3.7	6.5	9.9	3.4
3105	6.2	11.3	5.1	5.9	10.5	4.6
3106	5.9	8.1	2.2	5.5	7.8	2.3
3107	6.6	9.8	3.2	6.3	9.7	3.4
3108	6.4	10.3	3.9	6.1	9.7	3.6
3109	6.3	6.8	0.5	6.1	6.4	0.3
3110	5.7	8.7	3.0	5.5	8.7	3.2
3111	6.3	9.5	3.2	6.0	8.8	2.8
3112	6.4	11.1	4.7	6.0	10.4	4.4
Mean	6.3	9.5	3.2	6.0	9.1	3.1
S.D.	0.4	1.4	1.3	0.3	1.3	1.2

Unit: g
a): Postnatal day

Appendix 15-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual body weight of pups
Dose (mg/kg): 500

Dam number	Male 0	Male 4a)	Male Gain	Female 0	Female 4a)	Female Gain
4101	6.3	8.3	2.0	5.9	8.2	2.3
4102	6.1	9.1	3.0	5.8	9.1	3.3
4103b)						
4104	5.6	7.3	1.7	5.2	6.2	1.0
4105	6.5	9.9	3.4	6.1	9.2	3.1
4106c)						
4107	7.0	10.5	3.5	6.3	9.3	3.0
4108	5.6	9.0	3.4	5.3	8.4	3.1
4109	5.9	9.0	3.1	5.5	8.4	2.9
4110	6.8	10.2	3.4	6.4	9.5	3.1
4111d)						
4112e)						
Mean	6.2	9.2	2.9	5.8	8.5	2.7
S.D.	0.5	1.0	0.7	0.4	1.1	0.8

Unit: g
a): Postnatal day
b): Died on gestation day 13
c): Died on gestation day 17
d): Died on gestation day 12
e): Died on day 10 of administration

Appendix 16-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	0	
1103	0	
1104	0	
1105	0	
1106	Non-pregnant	
1107	3 (3 + 0)	NAF
1108	0	
1109	0	
1110	0	
1111	0	
1112	0	

NAF: No abnormal findings

Appendix 16-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 50

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	0	
2102	0	
2103	2 (1 + 1)	NAF
2104	0	
2105	0	
2106	0	
2107	0	
2108	0	
2109	1 (1 + 0)	NAF
2110	0	
2111	0	
2112	0	

NAF: No abnormal findings

Appendix 16-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 150

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	0	
3112	0	

NAF: No abnormal findings

Appendix 16-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in dead pups
Dose (mg/kg): 500

Dam number	No. of pups examined Total (Male + Female)	Findings
4101	1 (1 + 0)	NAF
4102	0	
4103a)		
4104	2 (1 + 1)	NAF
4105	0	
4106b)		
4107	0	
4108	0	
4109	0	
4110	1 (0 + 1)	NAF
4111c)		
4112d)		

NAF: No abnormal findings
a): Died on gestation day 13
b): Died on gestation day 17
c): Died on gestation day 12
d): Died on day 10 of administration

Appendix 17-1 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-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	14 (6 + 8)	NAF
1102	13 (4 + 9)	NAF
1103	16 (10 + 6)	NAF
1104	14 (9 + 5)	NAF
1105	13 (6 + 7)	NAF
1106	Non-pregnant	
1107a)		
1108	11 (7 + 4)	NAF
1109	17 (7 + 10)	NAF
1110	13 (9 + 4)	NAF
1111	13 (6 + 7)	NAF
1112	16 (5 + 11)	NAF

NAF: No abnormal findings
a): All pups died by postnatal day 2.

Appendix 17-2 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 50

Dam number	No. of pups examined Total (Male + Female)	Findings
2101	15 (7 + 8)	NAF
2102	14 (3 + 11)	NAF
2103	15 (9 + 6)	NAF
2104	14 (6 + 8)	NAF
2105	13 (7 + 6)	NAF
2106	14 (11 + 3)	NAF
2107	15 (9 + 6)	NAF
2108	16 (6 + 10)	NAF
2109	14 (6 + 8)	NAF
2110	15 (8 + 7)	NAF
2111	15 (8 + 7)	NAF
2112	13 (5 + 8)	NAF

NAF: No abnormal findings

Appendix 17-3 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 150

Dam number	No. of pups examined Total (Male + Female)	Findings
3101	18 (5 + 13)	NAF
3102	16 (8 + 8)	NAF
3103	14 (7 + 7)	NAF
3104	14 (8 + 6)	NAF
3105	13 (7 + 6)	NAF
3106	16 (7 + 9)	NAF
3107	15 (8 + 7)	NAF
3108	15 (10 + 5)	NAF
3109	12 (4 + 8)	NAF
3110	16 (11 + 5)	NAF
3111	14 (10 + 4)	NAF
3112	14 (9 + 5)	NAF

NAF: No abnormal findings

Appendix 17-4 Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of 2-tert-Butylcyclohexan-1-yl acetate by oral administration in rats
Individual externally for gross abnormalities in pups on postnatal day 4
Dose (mg/kg): 500

Dam number	No. of pups examined Total (Male + Female)	Findings
4101	16 (7 + 9)	NAF
4102	12 (4 + 8)	NAF
4103a)		
4104	12 (11 + 1)	NAF
4105	16 (9 + 7)	NAF
4106b)		
4107	12 (1 + 11)	NAF
4108	16 (10 + 6)	NAF
4109	14 (7 + 7)	NAF
4110	13 (6 + 7)	NAF
4111c)		
4112d)		

NAF: No abnormal findings
a): Died on gestation day 13
b): Died on gestation day 17
c): Died on gestation day 12
d): Died on day 10 of administration