最 終 報 告 書

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールの

ラットを用いる反復経口投与毒性・生殖発生毒性併合試験

（試験番号：07-112）

財団法人 畜産生物科学安全研究所

陳 述 書

試験の表題

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールのラットを用いる反復経口投与毒性・生殖発生毒性併合試験（試験番号：07-112）

本試験は、OECD 試験法ガイドライン[OECD GUIDELINE FOR TESTING OF CHEMICALS for Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test 422、(1996)]並びに化審法 GLP「新規化学物質等に係る試験を実施する試験施設に関する基準について」（平成 15 年 11 月 21 日付け薬食発第 1121003 号厚生労働省医薬食品局長、平成 15・11・17 製局第 3 号経済産業省製造産業局長、環保企発第 031121004 号環境省総合環境政策局長、連名通知）に定める基準に準拠して実施した。

試験責任者

安全性研究部　首席研究員

[redacted]

平成23 年　6月 23日

試験の表題

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールのラットを用いる反復経口投与毒性・生殖発生毒性併合試験（試験番号：07-112）

試験委託者

名　　称	厚生労働省 医薬食品局 審査管理課
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委託責任者	化学物質安全対策室

試験実施施設

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信頼性保証責任者	信頼性保証室　首席研究員 [redacted]

試験日程

試験開始	平成 21 年 2 月 3 日
動物搬入	平成 21 年 2 月 5 日
実験開始	平成 21 年 2 月 18 日
投与開始	平成 21 年 2 月 19 日
交配開始	平成 21 年 3 月 5 日
児動物解剖開始	平成 21 年 4 月 1 日
雌親解剖開始	平成 21 年 4 月 2 日
雄親解剖	平成 21 年 4 月 2 日
回復群解剖	平成 21 年 4 月 16 日
実験終了	平成 22 年 3 月 19 日
試験終了	平成 23 年 6 月 23 日

試験成績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からの逸脱

本試験に関し、予見することのできなかった試験成績の信頼性に影響を及ぼす疑いのある事態および試験計画書からの逸脱はなかった。

試資料の保管

次に示す本試験に関する一連の関係試資料は、試験終了後 10 年間、財団法人 畜産生物科学安全研究所において保管する。その後の処置については、試験委託者と協議して決定する。

1) 試験計画書
2) 被験物質に関する記録およびそのサンプル
3) 供試動物に関する記録
4) 試験結果に関する記録（親動物の一般状態、詳細な臨床観察、感覚反射機能検査、握力、自発運動量、体重、摂餌量、性周期、交配、分娩、哺育、尿検査、血液学検査、血液生化学検査、剖検、器官重量、病理組織学検査ならびに児動物の一般状態、成長、外表および内臓検査等に関する生データ）
5) 血液塗抹標本および病理標本（固定器官、包埋ブロック、組織標本）
6) 信頼性保証に関する記録
7) 最終報告書

試験責任者の署名および試験担当者の業務分担

試　験　責　任　者

財団法人　畜産生物科学安全研究所

安全性研究部　首席研究員

氏名 [redacted]　　平成23年 6月23日

試験担当者およびその業務分担

検疫責任者 : [redacted]

投与液の調製 : [redacted]

動物飼育・投与・臨床観察 : [redacted]

臨床検査 : [redacted]

病理検査 : [redacted]

信頼性保証証明書

試験表題 ： 2-(2*H*-ベンゾトリアゾール-2-イル)-4-(*tert*-ブチル)-6-(sec-ブチル)フェノールのラットを用いる反復経口投与毒性・生殖発生毒性併合試験

試験番号 ： 07-112

審査・査察実施日	試験責任者への報告日	運営管理者への報告日
1. 試験計画書審査		
平成21年02月03日	平成21年02月03日	平成21年02月03日
2. 試験計画書記載事項変更審査		
(変-1)		
平成22年07月16日	平成22年07月16日	平成22年07月16日
3. 試験実施状況査察		
動物導入		
平成21年02月05日	平成21年02月05日	平成21年02月05日
検　疫		
平成21年02月06日	平成21年02月06日	平成21年02月06日
被験物質調製		
平成21年02月16日	平成21年02月16日	平成21年02月16日
群分け・個体識別・詳細な臨床観察		
平成21年02月18日	平成21年02月18日	平成21年02月18日
体重測定・餌測定・投与・症状観察		
平成21年02月19日	平成21年02月19日	平成21年02月19日
交配開始		
平成21年03月05日	平成21年03月05日	平成21年03月05日
交尾確認		
平成21年03月06日	平成21年03月06日	平成21年03月06日
投与・症状観察・詳細な臨床観察		
平成21年03月17日	平成21年03月17日	平成21年03月17日
体重測定・餌測定		
平成21年03月18日	平成21年03月18日	平成21年03月18日
尿検査		
平成21年03月26日	平成21年03月26日	平成21年03月26日
尿検査		
平成21年03月27日	平成21年03月27日	平成21年03月27日
分娩の確認		
平成21年03月30日	平成21年03月30日	平成21年03月30日

審査・査察実施日	試験責任者への報告日	運営管理者への報告日
感覚反射機能検査・握力測定・自発運動量測定 平成21年04月01日	平成21年04月01日	平成21年04月01日
解剖(雄・雌・新生児)・病理組織標本作製（臓器・組織の固定）・血液学検査 平成21年04月02日	平成21年04月02日	平成21年04月02日
血液生化学検査 平成21年04月21日	平成21年04月21日	平成21年04月21日
病理組織標本作製(切り出し) 平成21年07月07日	平成21年07月07日	平成21年07月07日
病理組織標本作製(包埋) 平成21年07月14日	平成21年07月14日	平成21年07月14日
病理組織標本作製(薄切) 平成21年07月15日	平成21年07月15日	平成21年07月15日
病理組織標本作製(染色) 平成21年07月17日	平成21年07月17日	平成21年07月17日
4. 生データ査察 平成22年06月08日 ～ 同年06月09日	平成22年06月09日	平成22年06月09日
5. 報告書（草案）審査 平成22年06月09日 ～ 同年06月11日	平成22年06月11日	平成22年06月11日
6. 最終報告書審査 平成23年06月23日	平成23年06月23日	平成23年06月23日

上記の審査・査察により、本試験が「化審法 GLP」に従って実施され、本報告書には、当該試験で使用した方法・手順が忠実に記載され、試験成績には、当該試験の実施過程において得られた生データが正確に反映されていることを確認した。

平成 23 年 6 月 23 日
財団法人　畜産生物科学安全研究所

信頼性保証責任者 [redacted]

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要　約

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールの 0（被験物質の溶媒である局方オリブ油のみ投与)、0.8、4、20 および 100 mg/kg/day を、1 群雌雄各 12 匹の SD 系ラットに、交配開始 2 週間前から、雄は 42 日間、雌は分娩後哺育 4 日まで経口投与し、その反復投与毒性および生殖発生毒性を調べた。また、雄については対照群および 100 mg/kg 群の各 12 匹からそれぞれ 5 匹を選別し、雌についてはサテライト群として別に 1 群 5 匹の対照群および 500 mg/kg 群を設け、投与終了後 14 日間観察を継続し、毒性の回復性についても検討した。

1. 反復投与毒性

20 mg/kg 群で、雄に ALP および肝臓相対重量の高値並びに小葉中心性肝細胞肥大が認められた。100 mg/kg 群では、雄に血色素量の低値、ALP、コリンエステラーゼ、総タンパク、アルブミン、A/G 比、血糖および肝臓の絶対および相対重量の高値、雌に赤血球数、血色素量およびヘマトクリット値の低値並びに肝臓相対重量の高値、雌雄に小葉中心性肝細胞肥大が認められた。回復期間終了時屠殺動物では、肝臓および血液に対する影響は残るものの回復傾向にあり、毒性は可逆的であった。

2. 生殖発生毒性

いずれの被験物質投与群においても、親動物および児動物に対し、被験物質の投与に起因する変化は認められなかった。

以上の結果から、2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールの親動物への反復投与において、20 mg/kg 群で雄に肝臓に対する影響、100 mg/kg 群では雌雄に肝臓および血液に対する影響が認められ、無影響量（NOEL）および無毒性量(NOAEL)はいずれも、雄は 4 mg/kg/day、雌は 20 mg/kg/day と推定した。また、生殖発生毒性に関する NOEL および NOAEL は、いずれの被験物質投与群においても影響が認められなかったことから、いずれも 100 mg/kg/day と推定した。

目　的

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールをラットに反復経口投与し、本物質の反復投与毒性および生殖発生毒性を検討した。

材料および方法

1. 被験物質

被験物質である 2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノール(CAS No. 36437-37-3)は、水に不溶で、食物油に可溶な白色粉末である。試験には、CHANGZHOU HI-TECH CHEMICAL LIMITED (D-12/F, Midsouth Tower, 33W, Guanhe Rd, Changzhou, Jiangsu, P. R. China)より試薬(ロット番号 0808005 、純度 99.33%：2008 年 9 月 23 日分析）を購入し、冷暗所（2～6℃)、密栓下で保管して使用した。用いた被験物質は投与終了後に分析し、使用期間中安定であったことを確認した（Appendix 1)。本物質の特性は、Appendix 1 に示す。

投与液はオリブ油（局方、ロット番号 NL-3、小堺製薬株式会社）を溶媒とし、所定の投与用量となる濃度の溶液に調製した。調製した投与液は、1 日の使用量ごとに小分けし、使用時まで冷所（2～6℃)・遮光下で密栓して保管した。投与液中の被験物質は、冷所・遮光下で少なくとも 7 日間は安定であることが確認された（Appendix 2）ので、調製後 7 日以内に使用した。初回に調製された投与液について分析し、所定の濃度で調製されていることを確認した（Appendix 3)。

2. 動物および飼育条件

動物は、SD 系 [Crl : CD(SD)]ラットを用いた。ラットは、日本チャールス・リバー株式会社厚木飼育センター（神奈川県厚木市下古沢 795）から 8 週齢のものを搬入（雄 68 匹、雌 80 匹）し、14 日間試験環境に馴化させた。馴化期間中に検疫および雌については 10 日間の性周期観察も併せて行い、発育および一般健康状態が良好で、雌では性周期に異常の認められなかったものについて、投与開始前日に体重を測定し、無作為抽出法により雄は 60 匹、雌は 70 匹を選び、10 週齢で試験に用いた。1 群の動物数は雌雄各 12 匹とし、雌についてはさらに対照群と最高用量群の回復群として各 5 匹からなる 2 群のサテライト群を設け、無作為抽出法により群分けを行った。なお、雌の回復

群については交配を行わなかった。雄の回復群については、投与 42 日に対照群と最高用量群の中から体重による無作為抽出法によりそれぞれ 5 匹を選別し、回復群とした。投与開始時の平均体重(体重範囲)は、雄 385(354～422)g、雌 248(227～267)g であった。ラットは、温度 22±3℃、 湿度 55±10%、換気回数 10 回以上／時(オールフレッシュエアー方式)、照明 12 時間／日(午前 7 時点灯、午後 7 時消灯)に設定したバリアーシステム動物室(第 1 室)で、個体別にステンレス製金網ケージ〔260W×380D×180 H(mm)〕に収容し、これをステンレス製 5 段のラックに配置して飼育した。ただし、交尾の成立した雌は、妊娠 0 日に巣作り材料(ホワイトフレーク、日本チャールス・リバー株式会社)を入れたポリカーボネート製ケージ〔265W×426D×200H(mm)〕に収容し、分娩後は児動物と同居させた。飼料（固型飼料ラボ MR ストック、日本農産工業株式会社、ロット番号 20081266）および飲料水（孔径 1μm のカートリッジフィルターで濾過後紫外線照射した殺菌水道水）は、それぞれ給餌器および自動給水装置または給水瓶（ポリカーボネートケージの場合）により、自由に摂取させた。

動物の個体識別は、ラックおよびケージへの標識札の貼付、並びに耳パンチ法により行った。

飼育期間中、動物室の温度は 20.6～24.4℃、湿度は 46～58%の範囲で推移（Appendix 4）した。また、飼料および巣作り材料の汚染物質の分析結果（Appendices 5、6）は、「米国環境保護庁毒性物質規制法の飼料および媒体の汚染物質限度（1979）」等を参考にして当研究所が設定した許容範囲内にあり、飲料水は水道法に基づく水質基準に適合する（Appendix 7）ことが確認された。したがって、動物の飼育期間を通じて、試験成績の信頼性に影響を及ぼすと思われる環境要因の変化はなかったものと判断した。

本試験は、動物実験を科学的観点および倫理的な配慮の下に実施するために遵守すべき事項等を定めた、「財団法人 畜産生物科学安全研究所の動物実験実施規定」に従い、本施設の動物実験委員会の承認を得て行った。

3. 投与量の設定、試験群の構成および投与方法

本物質の 500、1000 および 2000 mg/kg/day を雌雄各 1 匹のラットに 3 日間反復経口投与した結果、いずれの用量にも変化は認められなかった。

そこで、1 群雌雄各 4 匹のラットに，本被験物質を 0（溶媒のみ）、30、100、300、

600 および 1000 mg/kg/day で 14 日間反復経口投与し、一般状態の観察、体重および摂餌量の測定、尿検査、血液学および血液生化学検査、剖検並びに器官重量の測定を行った。その結果、30 mg/kg 群で雄に肝臓相対重量の有意な高値が認められた。100 mg/kg 群では、雄の肝臓重量は絶対重量および相対重量とも有意な高値、雌の肝臓重量も同様の傾向を示したほか、雄に血清アルブミン濃度の高値傾向および A/G 比の有意な高値が認められた。300 mg/kg 群では、100 mg/kg 群で認められた変化に加えて、赤血球数、血色素濃度、ヘマトクリット値および MCHC の有意な低値が雄に、肝臓相対重量、アルブミン濃度および A/G 比の有意な高値並びに血色素濃度、MCHC およびプロトロンビン時間の有意な低値が雌に認められた。600 mg/kg 群ではさらに、雌雄に投与直後の流涎、雄に 2 匹の死亡、雌にヘマトクリット値および MCH の有意な低値並びに肝臓の絶対および相対重量と総コレステロール濃度の有意な高値が認められた。以上の変化に加えて、1000 mg/kg 群で雄の全例が死亡し、雌には体重増加量並びに胸腺の絶対および相対重量の有意な低値、血清 ALT 活性、総蛋白濃度、中性脂肪濃度および血糖値の有意な高値が認められた。

以上の成績から、本試験における投与量については、確実に反復投与毒性が発現すると予測される 100 mg/kg/day を最高用量とし、以下公比 5 で 20、4 および 0.8 mg/kg/day の計 4 用量を設定した。

試験群の構成は、①溶媒投与群（以下、対照群）、②被験物質の 0.8 mg/kg/day 投与群（0.8 mg/kg 群）、③同 4 mg/kg/day 投与群（4 mg/kg 群）、④同 20 mg/kg/day 投与群（20 mg/kg 群）および⑤同 100 mg/kg/day 投与群（100 mg/kg 群）の 5 群とした。

投与方法は、投与液量を体重 1kg 当たり 5 mL とし、テフロン製胃ゾンデを装着した注射筒を用いて投与液を胃内に投与した。対照群には、溶媒として用いた局方オリブ油を同様に投与した。各個体の投与液量は、至近日の測定体重を基に算出した。投与期間は、雌雄とも交配開始 14 日前から、雄は 42 日間、雌は交配および妊娠期間を経て分娩後の哺育 4 日まで、最短 42 日～最長 56 日間、1 日 1 回、午前中（9：03～11：59）に投与した。ただし、雌の回復群は、雄と同様に 42 日間投与した。

4. 観察および検査

1) 親動物に関する項目

親動物について、次の項目を観察あるいは検査した。なお、感覚機能検査、握力、自発運動量、尿検査、血液学検査、血液生化学検査、器官重量および病理組織学検査については、雄は投与35日に、雌は交配終了時に各群から無作為抽出法により雌雄各5匹を選び、検査の対象とした。

(1) 一般状態観察

投与期間中毎日、投与直後から投与後1時間に、動物の生死、外観、行動等について観察した。さらに、朝夕2回は、動物の生死や瀕死状態の有無について確認した。また、妊娠、出産、哺育の状態については、注意深く観察した。

(2) 詳細な臨床観察

投与開始前日およびその後は週1回、ケージサイドでの観察に加えて、動物をケージから取り出す時およびケージ外のアルミ製オープンフィールド（370W×560D×40Hmm）で、ケージからの出し易さ、ケージから出す時の扱い易さ、体躯緊張(弛緩～強直)、皮膚（色）、毛並み、立毛、眼分泌物、眼瞼閉鎖状態、眼球突出、流涙、口鼻分泌物（汚れ）、流涎、下腹部被毛の尿による汚れ、肛門周囲の便による汚れ、発声、呼吸、姿勢、痙攣、振戦、探索行動（覚醒度）、警戒性、自発運動（活動性）、歩行（よろめき）、異常行動（自咬、後ろ向き歩行等）、常同行動（過度の毛繕い、反復旋回運動等）、意識不全（混迷、カタレプシー、昏睡）、四肢筋緊張度、排尿および排糞について観察し、認められた変化を評点（Appendix 8）で記録した。動物には無作為化法で観察番号を付け、 観察者以外の者が群や動物番号を表示したケージの標識札を観察番号のみ表示した標識札に替え、観察者は観察番号順に観察を行うことにより、投与内容が不明な状態で観察した。

(3) 感覚機能検査

雄は最終投与日、雌は哺育期間中に1回、また回復群の雌雄は最終投与日および回復期間終了日に、聴覚反応（ピンセットで軽くケージを叩く音に対する驚愕反応）、視覚反応（顔面に棒を近づけた場合の接近反応）、触覚反応（腰部に触れた場合の反応）、痛覚反応（尾根部をピンセットで摘んだ場合の逃避、発声等の反応）、瞳孔反射（暗所から急に明るい場所に移した時の瞳孔の反射）および正向反射（面上で動物を背臥位にした場合の正常姿勢にもどる反射）を調べ、認められた反応を評点（Appendix 9）で記録した。

(4) 握力および自発運動量

雄は投与 41 日、雌は哺育 3 日、また、回復群の雌雄は投与 42 日（最終投与日）および回復 13 日に、雄は 30 および 60 分間、雌は 30 分間の自発運動量（自発運動量測定装置、SUPERMEX、室町機械株式会社、動物が発する遠赤外線をセンサーが感知し、測定装置内の区画間の間における移動回数を測定）並びに前肢および後肢の握力（ラット・マウス用握力測定装置、MK-380R/FR、室町機械株式会社）を測定した。回復群の雌の自発運動量は、30 および 60 分間測定した。

(5) 体重および摂餌量

体重は、雄については投与 1（投与開始日、投与直前）、7、14、21、28、35 および 42 日並びに回復 7（投与 49 日）および 14 日（投与 56 日）、雌は投与 1、7 および 14 日、妊娠 0、7、14 および 20 日並びに哺育 0 および 4 日に、また、サテライト群として設けた雌の回復群については交配を行わないため、雄と同じ日に測定した。さらに、雌雄とも屠殺日に測定した。摂餌量は、体重測定日に合わせて、ケージごとに翌日までの 24 時間飼料消費量を測定した。ただし、摂餌量の最終測定日は、雄では投与 41 日、雌では哺育 3 日、回復群では回復 13 日とした。交配期間中の投与 21 および 28 日には、交尾の成立していない雌雄の摂餌量は測定しなかった。

(6) 雌の性周期検査

雌について、馴化・検疫期間に引き続き、交配前の 2 週間を経て交配期間の交尾が確認されるまで、Giemsa 染色による膣垢塗抹標本を作製し、鏡検により性周期段階の判定を行った。また、投与開始日から交配開始日までの性周期段階の判定から性周期を算出した。1 性周期は、発情期（Ⅲ）像が認められた日から次のⅢ期像が認められた前日までとし、Ⅲ期像が連続した場合は、最初のⅢ期像が認められた日から起算した。

(7) 交配および分娩状態観察

交配前 2 週間の投与を終了（投与 15 日の午後）した雌雄を同一群内で 1 対 1 の組み合わせを作り、2 週間を限度として交尾が確認されるまで連続同居させた。交配期間中は毎朝一定時刻（9：30 頃）に交尾の確認を行い、交尾率（%）［（交尾動物数／同居動物数）×100］を算出した。交尾は、膣栓形成あるは膣垢中の精子の有無により確認し、確認された日を妊娠 0 日とした。分娩状態の観察も同じ時刻に行い、分娩の完了が確認された日を哺育 0 日とした。交配および分娩の観察結果から、各群について、受胎率（%）

[（受胎雌数／交尾成立雌数）×100]、妊娠期間（妊娠 0 日から分娩の完了が確認された日までの日数）および出産率（%）［（生児出産雌数／妊娠雌数）×100]を算出した。

(8) 雄の尿検査

雄について、投与 36 日および回復群については回復 8 日に、動物を約 3 時間代謝ケージに収容し、得られた尿について、外観の観察、試験紙法（マルティスティックス、バイエル・三共株式会社）による pH、潜血、タンパク、糖、ケトン体、ビリルビンおよびウロビリノーゲンの定性的検査並びに沈渣の検査（URI-CELL 液、ケンブリッジケミカルプロダクト社、で染色して鏡検）を行った。さらに、18 時間収容して得られた尿について、尿量、 比重（屈折計、エルマ光学株式会社）並びにナトリウムおよびカリウム（電解質自動分析装置、NAKL-132、東亜ディーケーケー株式会社）を測定した。

(9) 血液学検査

最終投与の翌日あるいは回復期間終了の翌日の解剖直前に、エーテル麻酔下で開腹して腹大動脈より採血した。動物は前日の午後 5 時より除餌し、水のみを給与した。採取した血液は 3 分割し、その一部は EDTA-2K で凝固阻止処理し、多項目自動血球計数装置（XT-2000iv、シスメックス株式会社）により、赤血球数（電気抵抗検出法）、血色素量（ラウリル硫酸ナトリウム-ヘモグロビン法）、ヘマトクリット値（赤血球パルス波高値検出法）、平均赤血球容積、平均赤血球血色素量、平均赤血球血色素濃度（以上、計算値）、白血球数、網状赤血球数、白血球百分率（以上、フローサイトメトリー法）および血小板数（電気抵抗検出法）を測定した。また、血液の一部を 3.8%クエン酸ナトリウム液で凝固阻止処理して血漿を得、血液凝固自動測定装置（KC-10A, 米アメルング社）により、プロトロンビン時間（Quick 一段法）および活性化部分トロンボプラスチン時間（エラヂン酸活性化法）を測定した。なお、必要に応じて検査できるように、血液塗抹標本を作製した。

(10) 血液生化学検査

採取した血液の一部から血清を分離し、生化学自動分析装置（JCA-BM8 型クリナライザー、日本電子株式会社）により、総タンパク(ビューレット法)、アルブミン(BCG 法)、A/G 比(計算値)、血糖(GluK[1] -G-6-PDH[2] 法)、総コレステロール(酵素法、CES[3] -COD[4] -POD[5] 系)、トリグリセライド(酵素法、LPL[6] -GK[7] -GPO[8] -POD[5] 系)、総ビ

リルビン(ジアゾ法)、尿素窒素(ウレアーゼ・UV 法)、クレアチニン (Jaffe 法)、AST、ALT、ALP(以上、JSCC[9] 法)、γ-GTP(SSCC 法 [10])、LDH(SFBC 法 [11])、ChE(BTC[12]-DTNB[13] 法)、カルシウム(OCPC 法)および無機リン(酵素法、PNP[14]-XOD[15]-POD[5] 系)を、また電解質自動分析装置(NAKL-132、東亜ディーケーケー株式会社)により、ナトリウム、カリウムおよび塩素(以上、イオン電極法)を測定した。

1) グルコキナーゼ、2) グルコース-6-リン酸脱水素酵素、3) コレステロールエステラーゼ、4) コレステロールオキシダーゼ、5) ペルオキシダーゼ、6) リポプロテインリパーゼ、7) グリセロールキナーゼ、8) L-α-グリセロリン酸オキシダーゼ、9) 日本臨床化学会、10) スカンジナビア臨床化学会、11) フランス臨床生物学会、12) ブチリルチオコリン、13) 5、5'-ジチオビス-2-ニトロ安息香酸、14) プリンヌクレオシドホスフォリラーゼ、15) キサンチンオキシダーゼ

(11) 剖検および器官重量

雄の計画屠殺動物は投与 42 日の翌日、雌は哺育 5 日、また、 回復群については回復 14 日の翌日に、それぞれエーテル麻酔下で放血屠殺し、体表、開口部粘膜および内部諸器官を肉眼的に観察した。また、各群雌雄各 5 匹の肝臓、腎臓、副腎、胸腺、脾臓、脳、心臓、下垂体、甲状腺および精嚢並びに全ての雄の精巣および精巣上体を秤量（絶対重量）し、屠殺日の体重に基づいて対体重比（相対重量）を算出した。なお、対器官は左右を一括して、下垂体および甲状腺は固定後に秤量した。雌については、卵巣の黄体数および子宮の着床数を調べ、着床率（%）［（着床数／黄体数）×100]を算出した。

(12) 病理組織学検査

全例について下記器官を採取し、10%中性リン酸緩衝ホルマリン液（精巣、精巣上体はブアン液で前固定）で固定し、保存した。

（脳、下垂体、甲状腺（上皮小体を含む）、胸腺、気管・肺（固定液を注入後浸漬）、胃、腸（パイヤー板を含む）、心臓、肝臓、脾臓、腎臓、副腎、膀胱、精巣、精巣上体、前立腺、精嚢、卵巣、子宮、脊髄（頸部、胸部、腰部）、坐骨神経、骨髄（大腿骨）、リンパ節（頸部リンパ節、腸間膜リンパ節）、乳腺）

病理組織学検査は、対照群および 100 mg/kg 群の雌雄各 5 匹の上記保存器官について実施した。精巣については、精子形成サイクル検査（ステージⅡ・Ⅲ、Ⅴ、ⅦおよびⅩⅡ）も行った。その結果、被験物質の投与による影響が雌雄の肝臓に認められたので、回復群を含むその他の群については、雌雄各 5 匹の肝臓について検査した。また、回復群の雄で、脾臓重量に変化が認められたため、回復群の雄については脾臓も検査した。

各群の肉眼的異常部位は全例について検査した。検査は、常法に従ってパラフィン切片を作製し、H-E 染色を施して鏡検した。また、精子形成サイクル検査のために精巣の PAS 染色標本も作製した。

2) 新生児に関する項目

(1) 産児数、性比および外表検査

分娩完了の確認後、各腹の産児数（生産児と死亡児の合計）を調べ、分娩率(%) [(総出産児数／着床数)×100]を、また肛門と生殖突起間の長短により性別を判定し、群ごとの性比を算出した。さらに、新生児について、口腔内を含む外表の異常を観察した。

(2) 一般状態観察

毎日、一般状態および生死を確認し、出生率（%）[（出産確認時生児数／総出産児数）×100]および哺育 4 日生存率（%）[（哺育 4 日の生児数／出産確認時生児数）×100]を算出した。

(3) 体重

新生児について、哺育 0 および 4 日に、雌雄別に腹ごとの体重を測定し、1 匹当たりの平均体重を算出した。

(4) 病理学検査

死亡例はその都度、生存例は哺育 4 日にエーテル麻酔下で放血死させ、胸部および腹部における主要器官について肉眼的に観察した。

5. 統計解析

得られた平均値あるいは頻度について、対照群との有意差(危険率 5%以下)を、次の方法で検定した。なお、出産児に関するデータは、1 腹の平均を 1 標本とした。

(1) パラメトリックデータ

多群間の比較については、Bartlett の分散検定を行った。分散が一様な場合は一元配置の分散分析を行い、その結果有意差を認めた場合、Dunnett 法により対照群に対する各群の比較検定を行った。分散が一様でない場合は、ノンパラメトリックデータに用いる検定法に従った（体重、体重増加量、摂餌量、握力、自発運動量、尿検査における定量的データ、血液学検査データ、血液生化学検査データ、器官重量、黄体数、着床数、

交尾成立期間、妊娠期間、産児数、生児数、死亡児数)。2 群間の比較については、F 検定を行い、その結果分散が一様な場合は Student の t 検定を、分散が一様でない場合は Aspin-Welch の t 検定を行った。

(2) ノンパラメトリックデータ

多群間の比較については、Kruskal-Wallis の順位検定を行い、その結果有意差を認めた場合、Dunnett 型の検定法により対照群と各群を比較した（白血球百分率、尿検査における定性的データ、精子形成サイクル検査、着床率、出生率、分娩率、性周期、新生児生存率)。2 群間の比較については、Mann-Whitney の U 検定を行った。

(3) カテゴリカルデータ

Fisher の直接確率法を用いた(詳細な臨床観察、感覚機能検査、一般状態の観察および病理学検査における異常例の発現率、交尾率、受胎率、出産率)。なお、病理組織学検査所見のうち、グレード分けしたデータについては Mann-Whitney の U 検定、児動物の性比については、χ^2 検定を用いた。

結　果

1. 反復投与毒性

1) 一般状態および死亡 (Tables 1～4、Appendices 10～13)

投与期間および回復期間とも、一般状態の変化および死亡は認められなかった。

2) 詳細な臨床観察 (Tables 5, 6、Appendices 14, 15)

投与期間中および回復期間中の観察において、各観察項目に有意な変化は認められなかった。

3) 感覚機能検査 (Tables 7, 8、Appendices 16, 17)

投与期間中および回復期間中の検査において、各検査項目に変化は認められなかった。

4) 握力および自発運動量 (Tables 9, 10、Appendices 18, 19)

投与期間中の検査において、20 mg/kg 群で雄に 30 分間および 60 分間の自発運動量、また、100 mg/kg 群で雄に 30 分間の自発運動量のいずれも有意な低値が認められた。しかしながら、投与期間中における回復群の雄の検査においては、自発運動量に有意な変化は認められなかった。一方、雌はサテライト群にのみ、後肢握力の有意な高値が認められた。回復期間中の検査においては、雄で 30 分間の自発運動量の有意な高値が認められた。

5) 体重 (Figures 1, 2、Tables 11, 12、Appendices 20, 21)

各測定時点の体重および体重増加量に変化は認められなかった。ただし、雌のサテライト群においては、投与 28 日および 35 日並びに回復 7 日および 14 日の体重に有意な高値が認められた。

6) 摂餌量 (Figures 3, 4、Tables 13, 14、Appendices 22, 23)

4 mg/kg 群の雄で偶発的と思われる一過性の低値が投与 28 日に認められた以外、摂餌量に変化は認められなかった。

7) 雄の尿検査 (Table 15、Appendix 24)

投与期間中および回復期間中の検査において、各検査項目に有意な変化は認められなかった。

8) 血液学検査 (Tables 16, 17、Appendices 25, 26、背景データ： Appendices 42, 43)

投与期間終了時屠殺動物において、20 および 100 mg/kg 群で雌に白血球百分率におけるリンパ球比の有意な低値が認められた。さらに、100 mg/kg 群では、雄に血色素量の有意な低値、雌に赤血球数、血色素量およびヘマトクリット値の有意な低値が認められた。回復期間終了時屠殺動物においては、雄に赤血球数、血色素量、ヘマトクリット値および平均赤血球血色素濃度の有意な低値並びに網状赤血球数の有意な高値、雌に平均赤血球容積および平均赤血球血色素量の有意な高値が認められた。

9) 血液生化学検査 (Tables 18, 19、Appendices 27, 28、背景データ： Appendices 42, 43)

投与期間終了時屠殺動物において、0.8 mg/kg 群で雄に尿素窒素の有意な低値が認められた。20 および 100 mg/kg 群では雄に ALP の有意な高値が認められた。さらに、100 mg/kg 群で雄にコリンエステラーゼ、総タンパク、アルブミン、A/G 比および血糖の有意な高値が認められた。回復期間終了時屠殺動物においては、雌雄にカリウム、雄で総タンパク、アルブミン、総コレステロール、中性脂肪および総ビリルビンのいずれも有意な高値が認められた。

10) 剖検 (Tables 20, 21、Appendices 29～30)

投与期間終了時屠殺動物において、100 mg/kg 群で雄の 2 匹に肝臓の大型化が認められた。回復期間終了時屠殺動物においては、変化は認められなかった。

11) 器官重量 (Tables 22, 23、Appendices 32～35)

投与期間終了時屠殺動物において、肝臓の 20 mg/kg 群の雄には相対重量、100 mg/kg 群の雄には絶対および相対重量、雌には相対重量の、いずれも有意な高値が認められた。また、20 mg/kg 群の雄にのみ、下垂体相対重量の有意な高値が認められ

た。回復期間終了時屠殺動物においては、雄に肝臓の絶対および相対重量並びに脾臓相対重量の有意な高値が認められた。

12) 病理組織学検査（Tables 24～26、Appendices 29～31、 Photos 1，2）

被験物質の投与に起因する変化として、投与期間終了時屠殺動物において、肝臓の小葉中心性肝細胞肥大が 20 mg/kg 群で雄の 3 匹、100 mg/kg 群で雄の 5 匹および雌の 2 匹に認められ、100 mg/kg 群の雄の変化は、20 mg/kg 群の雄や 100 mg/kg 群の雌の変化と比べて強かった。回復期間終了時屠殺動物においては、小葉中心性肝細胞肥大は雄の 2 匹にのみ認められ、変化の程度も投与期間終了時屠殺動物と比べて軽減していた。重量に変化の認められた雄の脾臓では、髄外造血の亢進が 2 匹に認められた。

なお、対照群にのみ、肺の出血（雄）および動脈壁鉱質沈着（雌）、腎臓の孤立性嚢胞（雄）並びに前立腺の間質リンパ球浸潤（雄）が認められた。また、対照群と被験物質投与群に共通して、肺の泡沫細胞集簇（雄）、心臓の心筋変性・線維化（雄）、肝臓の微小肉芽腫（雌雄）および巣状壊死（雄）、腺胃の胃底腺拡張（雄）、腎臓の近位尿細管上皮硝子滴（雄）、硝子円柱（雄）、好塩基性尿細管（雄）および遠位尿細管拡張（雌）並びに脾臓の髄外造血（雌雄）および褐色色素沈着（雌雄）が認められたが、被験物質投与群の変化は、発現率および変化の程度において対照群と差は認められなかった。さらに、肺の泡沫細胞集簇（雌）は被験物質投与群にのみ認められたが、この変化は、雄では対照群にも認められ、ラットの自然発生病変として知られている変化 [1] でもあることから、被験物質の投与とは関連性のない変化と判断された。また、精子形成サイクル検査において、各検査ステージに変化は認められなかった。

20 mg/kg 群で認められた妊娠不成立のペア（No. 037 と 542）について、雄では、下垂体、精巣、精巣上体、前立腺および精嚢等に、また、雌では下垂体、卵巣および子宮等に変化は認められず、妊娠不成立の原因となるような所見は認められなかった。また、100 mg/kg 群で哺育期間中に全児死亡が認められ雌親動物（No. 560）にも、下垂体、卵巣、子宮および乳腺に変化は認められなかった。

2. 生殖発生毒性

1) 親動物に及ぼす影響

(1) 性周期検査 (Table 27、Appendices 37, 38)

被験物質投与各群とも、対照群と比べて性周期に有意な変化は認められなかった。

(2) 交尾率および受胎率 (Table 27、Appendix 38)

交尾成立までに要する日数、交尾率および受胎率に有意な変化は認められなかった。いずれの投与群とも交尾不成立例は認められず、20 mg/kg 群で 1 例 (No. 037 と 542 のペア) の妊娠不成立例が認められた。また、4 および 20 mg/kg 群で交尾成立までに 14 日を要した例 (No. 032 と 537 および No. 042 と 547 のペア) の雌は、いずれも交配前は順調な性周期を示していたが、交配開始後 2 日 (No. 537) および 1 日 (No. 547) から発情休止期 (V) 像が続き、いずれも交配開始後 13 日に発情前期 (I) 像が認められ、翌日、発情期 (III) 像と共に精子および膣栓が認められ、交尾が確認されたことから、偽妊娠を起こしていたものと判断された。

(3) 黄体数、着床数および着床率 (Table 27、Appendix 38)

黄体数、着床数および着床率に有意な変化は認められなかった。

(4) 出産率および妊娠期間 (Table 27、Appendix 38)

出産率および妊娠期間に有意な変化は認められなかった。

(5) 分娩および哺育状態 (Table 27、Appendix 38)

100 mg/kg 群で 1 匹 (No. 560) が分娩後、哺育行動は示したものの、新生児の腹壁を透してみられるミルクスポットは認められず、哺育 2 日までに喰殺を含む全児の死亡が確認された。この例以外に、被験物質投与各群において分娩および哺育状態に変化は認められなかった。

2) 新生児に及ぼす影響

(1) 生存性および体重 (Table 28、Appendix 39)

一腹当たりの総出産児数、分娩率、哺育 4 日の新生児数、出生率、性比および新生児体重に有意な変化は認められず、新生児の一般状態にも異常は認められなかった。なお、0.8 mg/kg 群で哺育 0 日の雌の新生児数に有意な高値が認められたが、雄の新生児数および総生児数に変化はなく、また、高用量では認められない変化であることから、

偶発的なものと判断した。また、4 および 20 mg/kg 群で哺育 4 日の生存率がいずれも 100%であったため、統計学的有意差が認められた。

(2) 形態 (Table 29、30、Appendices 40、41)

外表検査では、いずれの投与群においても外表異常を有する児動物は認められなかった。内臓検査では、いずれの投与群においても内臓異常は認められず、内臓変異として、胸腺の頸部残留を呈する児動物が対照群で 1 匹（0.8%）および 100 mg/kg 群で 1 匹（0.6%）、腎盂拡張を呈する児動物が対照群で 1 匹（1.3%）および 100 mg/kg 群で 1 匹（0.6%）、左臍動脈遺残を呈する児動物が 0.8 mg/kg 群で 2 匹（1.2%）認められたが、これらは、いずれも 1 ないし 2 例の低い発現率であり、自然発生的範疇のものと判断した。

考　察

1. 反復投与毒性について

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールのラットへの反復投与により、肝臓および血液等に対する影響が認められた。

肝臓に対する影響について、肝臓重量が 20 mg/kg 群の雄では相対重量、100 mg/kg 群の雄では絶対および相対重量、雌では相対重量の、いずれも高値が認められ、病理組織学検査では、肝臓の小葉中心性肝細胞肥大が 20 mg/kg 群の雄および 100mg/kg 群の雌雄に認められた。雄の変化は雌に比べて強い傾向にあった。

血液生化学検査で雄に認められた 20 および 100 mg/kg 群の ALP の高値並びに 100 mg/kg 群のコリンエステラーゼ、総タンパク、アルブミンおよび A/G 比の高値は、肝臓に対する影響と関連した変化と考えられる。

血液に対する影響について、100 mg/kg 群で雄に血色素量、雌に赤血球数、血色素量およびヘマトクリット値のいずれも低値が認められた。

なお、20 および 100 mg/kg 群の雄で自発運動量の低値並びに雌のサテライト群で後肢握力の高値が認められたが、回復群の雄の投与期間中の検査や雌の投与期間終了時屠殺動物の検査では、自発運動量や握力には変化は認められず、また、関連する変化も認められなかった。さらに、1 例（20 mg/kg 群：No. 043）の自発運動量のみ基準値をやや下回った以外は、いずれの個体値も当研究所の背景データにおける基準値（雄の自発運動量：平均 7388, 4745～10032 Count/30 min.、平均 10648, 4319～16978 Count/60 min.、雌の後肢握力：平均 308, 73～543 g）内の値であった。

雌のサテライト群に認められた投与 28 日および 35 日並びに回復 7 日および 14 日の体重の高値について、摂餌量や投与期間中および回復期間中の体重増加量に有意な変化は認められなかった。

また、20 および 100 mg/kg 群の雌の白血球百分率におけるリンパ球比並びに 0.8 mg/kg 群の雄の尿素窒素の低値、20 mg/kg 群の雄の下垂体相対重量の高値については、用量相関性や関連する変化が認められなかった。さらに、100 mg/kg 群の雄の血糖の高値についても、背景データにおける基準値（Appendix 42 参照）内の変化であった。

したがって、これらの投与期間中あるいは投与期間終了時の検査で認められた自発運動量、握力、リンパ球比、尿素窒素、血糖および下垂体重量の変化は、いずれも被験物

質の投与とは無関係な偶発的変化と判断された。

回復期間終了時屠殺動物においては、投与期間終了時屠殺動物で認められた変化のうち、肝臓に対する影響に関して、雄では肝細胞の肥大および肝臓重量の高値並びに総タンパクおよびアルブミンの高値が認められた。投与期間終了時屠殺動物には認められなかった雄の総コレステロールの高値も、肝臓に対する影響と関連する変化と考えられる。しかしながら、投与期間終了時屠殺動物で認められた変化は明らかに軽減しており、また、雌では変化は認められず、回復傾向が明らかであった。

血液に対する影響に関して、雄では赤血球数、血色素量、ヘマトクリット値および平均赤血球血色素濃度の低値が認められ、貧血の回復傾向は明らかではなかった。また、貧血に対する反応性の変化と考えられる脾臓の髄外造血亢進および末梢血中網状赤血球数の高値も認められた。雄に認められた脾臓の相対重量高値は、脾臓の髄外造血亢進に伴う変化と考えられる。一方、雌では回復期間終了時屠殺動物において赤血球数、血色素量およびヘマトクリット値の変化は認められず、平均赤血球容積および平均赤血球血色素量の高値のみ認められ、回復傾向が明らかであった。

したがって、回復期間終了時屠殺動物においては、特に雄で投与による毒性変化が残存していたものの、本被験物質による毒性は可逆的であると判断された。

なお、回復期間中の検査で認められた雌雄のカリウムの高値並びに雄の自発運動量、中性脂肪および総ビリルビンの高値についても、その各個体値は、いずれも当研究所の背景データにおける基準値（雄の自発運動量：平均 7204, 4179～10228 Count/30 min.、その他は Appendix 42, 43 参照）内の値であった。したがって、これらは遅発的な毒性影響ではなく、偶発的変化と判断された。

2. 生殖発生毒性について

雌雄親動物の生殖能に対する影響について、観察した各指標とも対照群と比べて有意な変化は認められなかった。また、児動物に対しても、発生に関する各指標において被験物質の投与による影響は認められなかった。

以上の結果から、2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールの親動物への反復投与において、20mg/kg 群で雄に肝臓に対する影響、100

mg/kg 群では雌雄に肝臓および血液等に対する影響が認められ、無影響量（NOEL）および無毒性量(NOAEL)は、いずれも雄は 4 mg/kg/day、雌は 20 mg/kg/day と推定した。また、生殖発生毒性に関する NOEL および NOAEL は、いずれの被験物質投与群においても影響が認められなかったことから、いずれも 100 mg/kg/day と推定した。

文　献

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2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールの

ラットを用いる反復経口投与毒性・生殖発生毒性併合試験

(試験番号：07-112)

報告書　添付資料A

(図・群別平均値表)

財団法人　畜産生物科学安全研究所

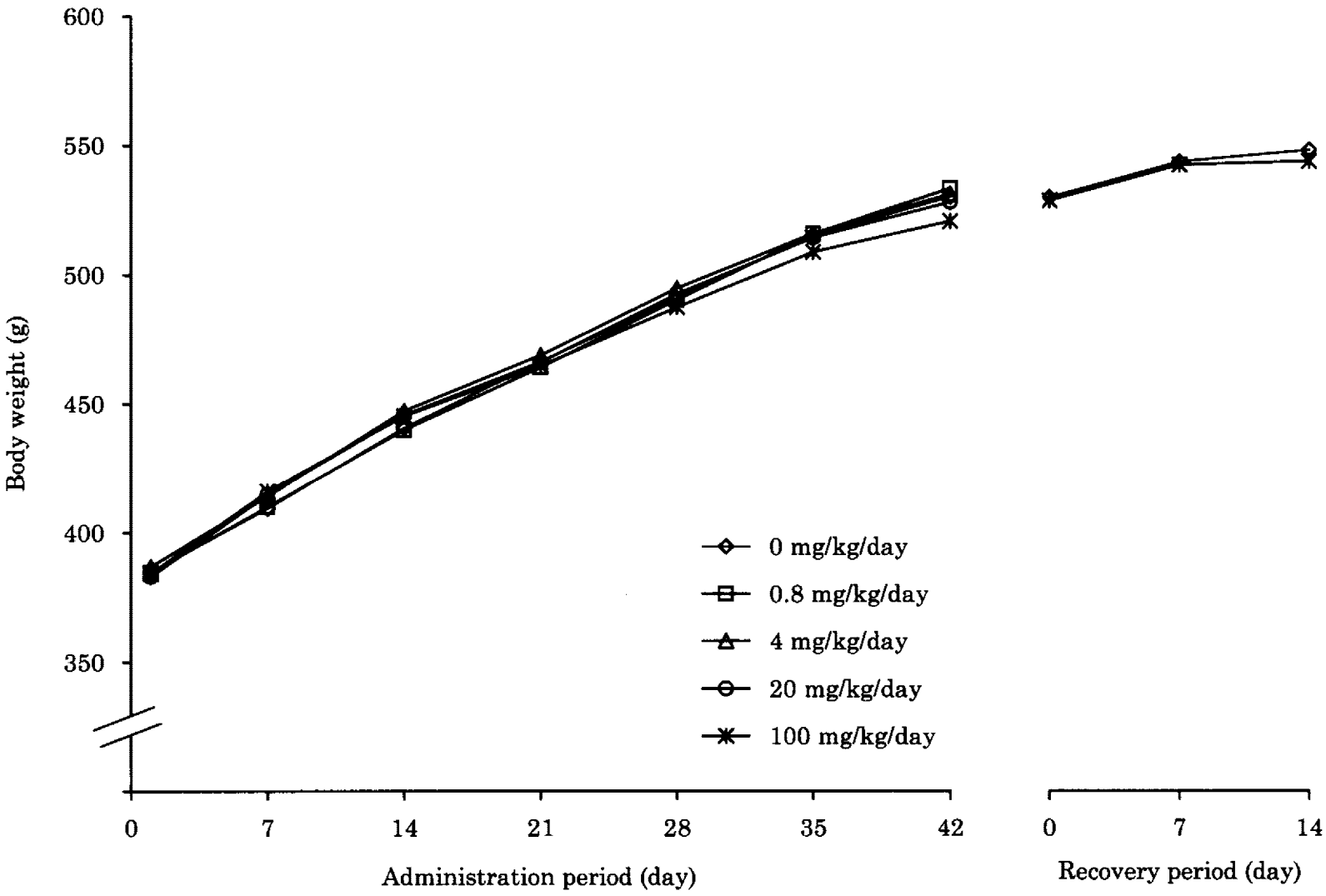


Fig.1 Body weight changes of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

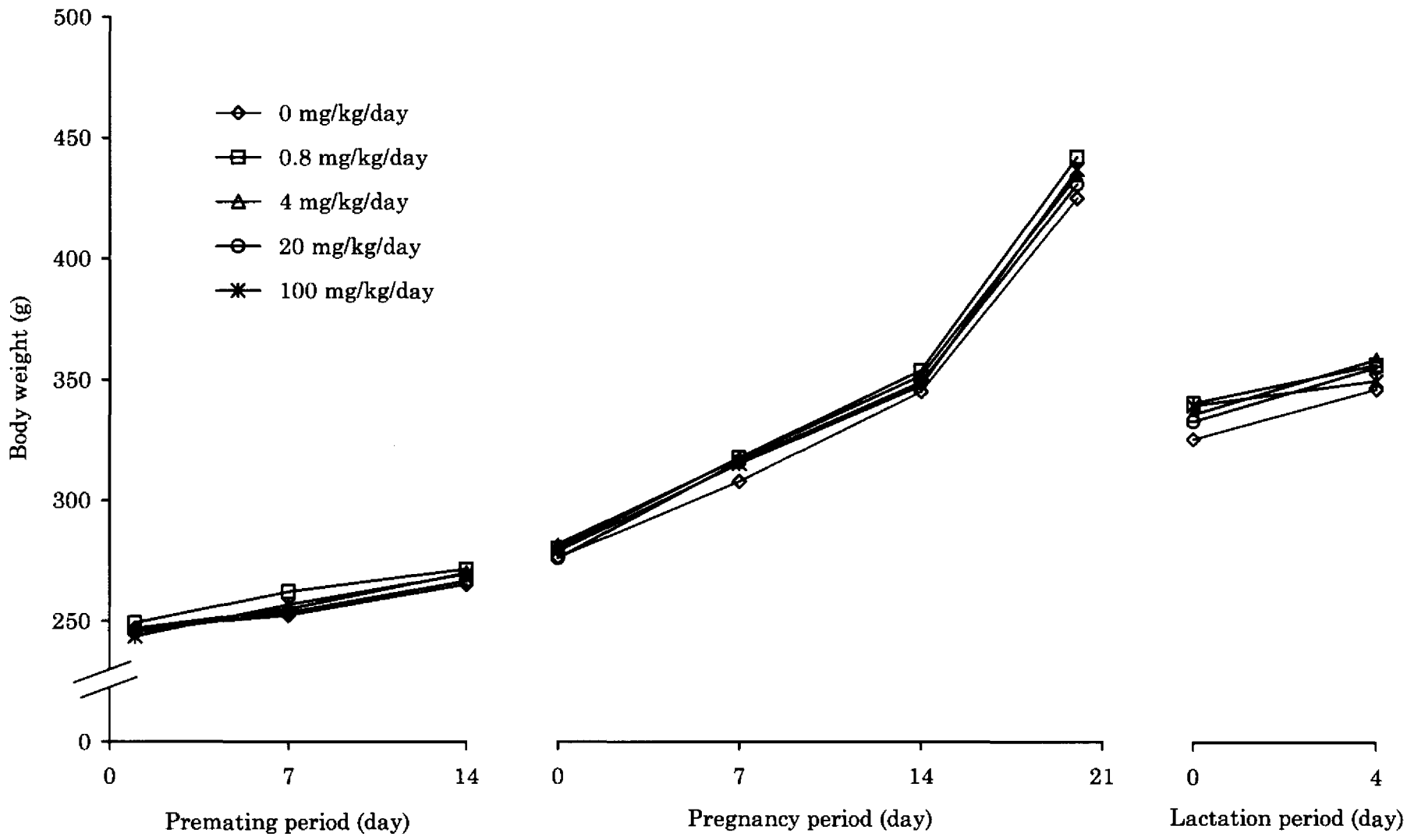


Fig.2-1 Body weight changes of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

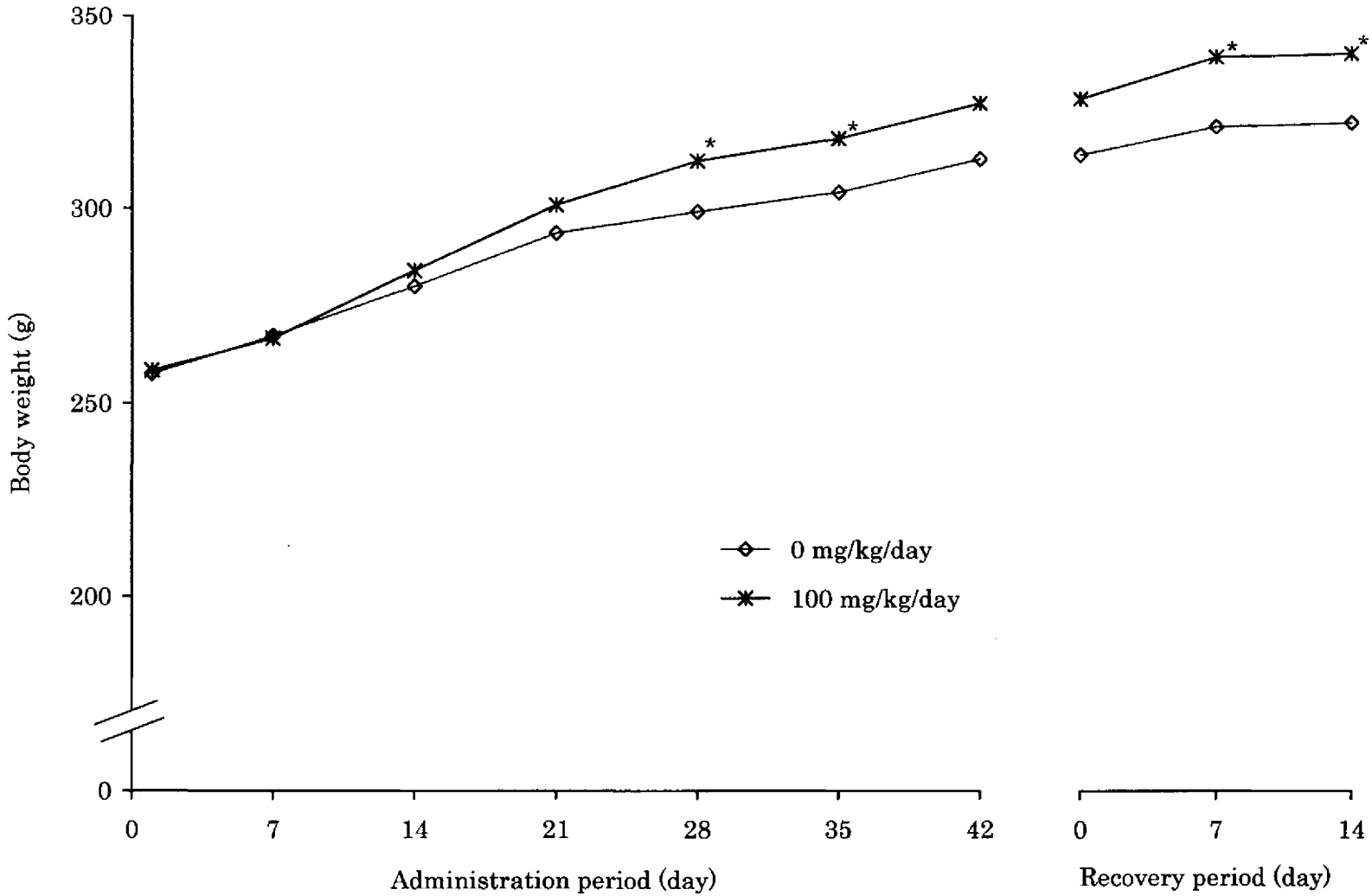


Fig.2-2 Body weight changes of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

* : Significantly different from control at 5% level of probability.

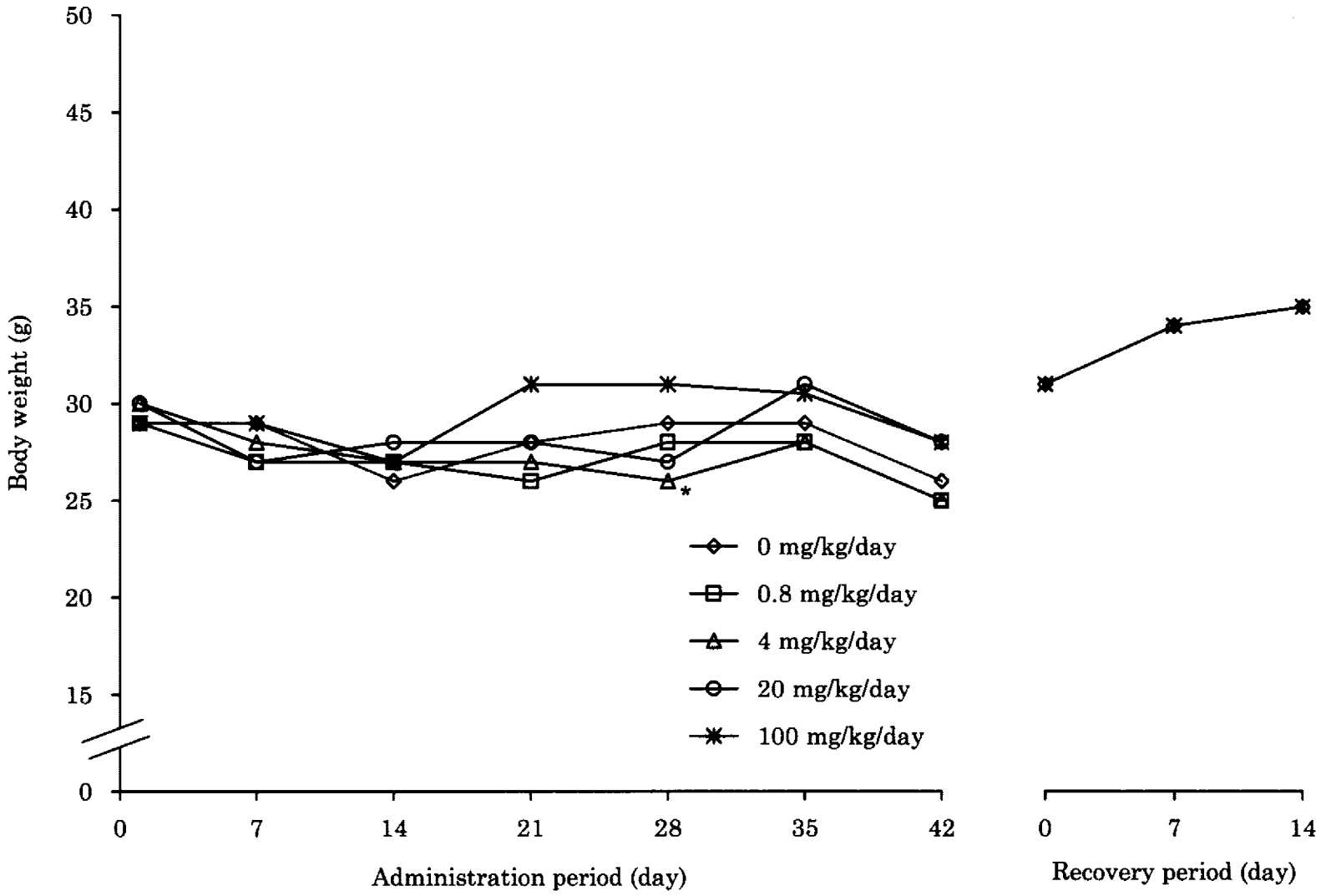


Fig.3 Food consumption of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

* : Significantly different from control at 5% level of probability.

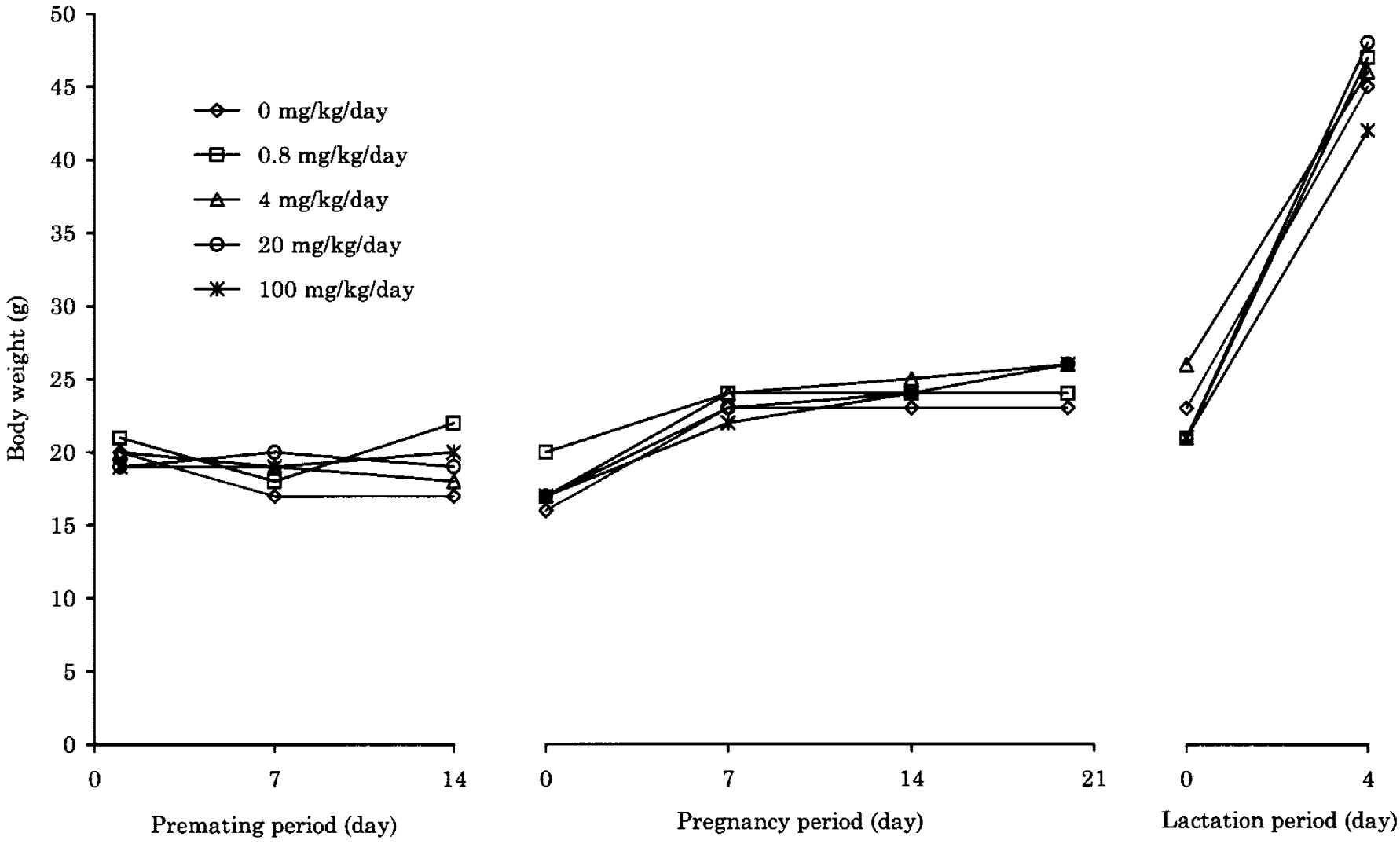


Fig.4-1 Food consumption of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

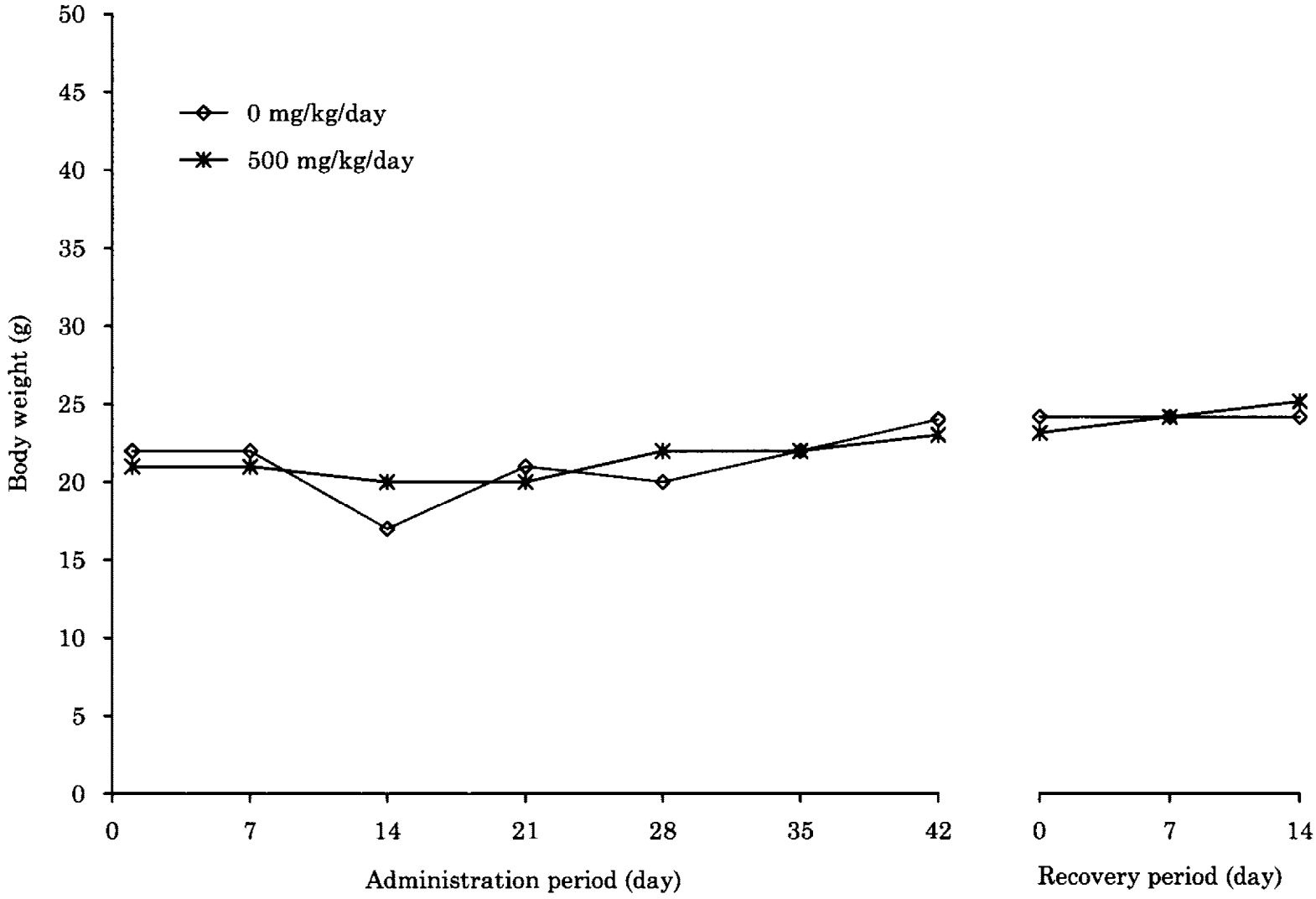


Fig.4-2 Food consumption of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Table 1 Mortality rate of male rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	0	0.8	4	20	100
No. of animals examined	12	12	12	12	12
No. of animals that died	0	0	0	0	0
Mortality (%)	0	0	0	0	0

Table 2 Mortality rate of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

						Satellite group	
Dose (mg/kg/day)	0	0.8	4	20	100	0	100
No. of animals examined	12	12	12	12	12	5	5
No. of animals that died	0	0	0	0	0	0	0
Mortality (%)	0	0	0	0	0	0	0

Table 3 Clinical signs of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

		Administration period					Recovery period	
General conditions	Dose (mg/kg/day)	0	0.8	4	20	100	0	100
	No. of animals	12	12	12	12	12	5	5
Abnormality		0	0	0	0	0	0	0

Table 4-1 Clinical signs of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

		Administration period				
General conditions	Dose (mg/kg/day)	0	0.8	4	20	100
	No. of animals	12	12	12	12	12
Abnormality		0	0	0	0	0

Table 4-2 Clinical signs of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

		Administration period		Recovery period	
General conditions	Dose (mg/kg/day)	0	100	0	100
	No. of animals	5	5	5	5
Abnormality		0	0	0	0

Table 5-1 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	9	7	11	11	12
	2 or more	3	5	1	1	0
	Color : Pale yellow	7/7	8/8	2/2	2/2	3/3
Defecation	Not detected or 1	9	10	10	10	10
	2 or more	3	2	2	2	2
	Appearance : Normal	4/4	4/4	2/2	2/2	3/3

Table 5-2 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg/day)	0	0.8	4	20	100
	No. of animals	12	12	12	12	12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	11	12	12
	Temporally in handling	0	0	1	0	0
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	9	9	12	11	10
	2 or more	3	3	0	1	2
	Color : Pale yellow	4/4	3/3	1/1	3/3	4/4
Defecation	Not detected or 1	12	11	11	12	11
	2 or more	0	1	1	0	1
	Appearance : Normal	-	1/1	2/2	-	2/2

Table 5-3 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	11	11	12	12	9
	2 or more	1	1	0	0	3
	Color : Pale yellow	1/1	1/1	-	2/2	5/5
Defecation	Not detected or 1	12	12	12	12	11
	2 or more	0	0	0	0	1
	Appearance : Normal	1/1	1/1	-	-	1/1

Table 5-4 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	11	10
	2 or more	0	0	0	1	2
	Color : Pale yellow	3/3	2/2	-	3/3	2/2
Defecation	Not detected or 1	11	12	12	12	12
	2 or more	1	0	0	0	0
	Appearance : Normal	1/1	1/1	-	-	-

Table 5-5 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	9	12	12	12	11
	2 or more	3	0	0	0	1
	Color : Pale yellow	4/4	1/1	-	2/2	6/6
Defecation	Not detected or 1	11	10	11	12	12
	2 or more	1	2	1	0	0
	Appearance : Normal	2/2	2/2	1/1	-	-

Table 5-6 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	11	12
	2 or more	0	0	0	1	0
	Color : Pale yellow	3/3	1/1	1/1	2/2	1/1
Defecation	Not detected or 1	10	12	12	12	12
	2 or more	2	0	0	0	0
	Appearance : Normal	3/3	1/1	-	-	-

Table 5-7 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	9	12	11	12	12
	2 or more	3	0	1	0	0
	Color : Pale yellow	4/4	1/1	2/2	1/1	1/1
Defecation	Not detected or 1	11	12	12	12	12
	2 or more	1	0	0	0	0
	Appearance : Normal	2/2	-	-	-	-

Table 5-8 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 1 of the recovery period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color: Pale yellow	3/3	-
Defecation	Not detected or 1	4	5
	2 or more	1	0
	Appearance:Normal	1/1	-

Table 5-9 Incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	3	5
	Temporally in handling	2	0
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color: Pale yellow	4/4	-
Defecation	Not detected or 1	3	5
	2 or more	2	0
	Appearance:Normal	2/2	-

Table 6-1-1 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg/day) / No. of animals	0 / 12	0.8 / 12	4 / 12	20 / 12	100 / 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Color : Pale yellow	-	-	-	3/3	1/1
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-1-2 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	11	12	12
	Temporally in handling	0	0	1	0	0
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Colar : Pale yellow	1/1	-	-	1/1	4/4
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-1-3 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	11	12
	2 or more	0	0	0	1	0
	Colar : Pale yellow	1/1	-	2/2	1/1	-
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-1-4 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	11	12	12	12	12
	2 or more	1	0	0	0	0
	Colar : Pale yellow	3/3	-	-	-	-
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-1-5 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Colar : Pale yellow	-	1/1	-	-	-
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-1-6 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	11	12	12	12	12
	2 or more	1	0	0	0	0
	Colar : Pale yellow	2/2	-	1/1	1/1	1/1
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-1-7 Incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 12	0.8 12	4 12	20 12	100 12
Reactivity on removal from the cage	Normal	12	12	12	12	12
Reactivity on handling	Normal	12	12	12	12	12
Muscle tone	Normal	12	12	12	12	12
Skin	Normal	12	12	12	12	12
Fur	Normal	12	12	12	12	12
Piloerection	Not detected	12	12	12	12	12
Eye discharge	Not detected	12	12	12	12	12
Palpebral closure	Not detected	12	12	12	12	12
Exophthalmos	Not detected	12	12	12	12	12
Lacrimation	Not detected	12	12	12	12	12
Smudge around mouth-nose	Not detected	12	12	12	12	12
Salivation	Not detected	12	12	12	12	12
Blotted fur in the lower abdomen with urine	Not detected	12	12	12	12	12
Blotted fur around anus with feces	Not detected	12	12	12	12	12
Vocalization	Not detected	12	12	12	12	12
Breathing	Normal	12	12	12	12	12
Body position	Normal	12	12	12	12	12
Convulsion	Not detected	12	12	12	12	12
Tremor	Not detected	12	12	12	12	12
Exploration	Normal	12	12	12	12	12
Alertness	Normal	12	12	12	12	12
Locomotor activity	Normal	12	12	12	12	12
Walk	Normal	12	12	12	12	12
Abnormal behavior	Not detected	12	12	12	12	12
Stereotypy	Not detected	12	12	12	12	12
Failure of consciousness	Not detected	12	12	12	12	12
Limb tone	Normal	12	12	12	12	12
Urination	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Colar : Pale yellow	-	1/1	-	-	-
Defecation	Not detected or 1	12	12	12	12	12
	2 or more	0	0	0	0	0
	Appearance : Normal	-	-	-	-	-

Table 6-2-1 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color : Pale yellow	-	-
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-2 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color : Pale yellow	1/1	2/2
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-3 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color : Pale yellow	-	1/1
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-4 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	4
	2 or more	0	1
	Color : Pale yellow	-	3/3
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-5 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	4
	2 or more	0	1
	Color : Pale yellow	-	2/2
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-6 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	4
	2 or more	0	1
	Color : Pale yellow	1/1	1/1
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-7 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color : Pale yellow	-	1/1
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance : Normal	-	-

Table 6-2-8 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental rtoxicity screening test

〈 On week 1 of the recovery period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color: Pale yellow	2/2	4/4
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance:Normal	-	-

Table 6-2-9 Incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental rtoxicity screening test

〈 On week 2 of the recovery period 〉

Items	Dose(mg/kg/day) No. of animals	0 5	100 5
Reactivity on removal from the cage	Normal	5	5
Reactivity on handling	Normal	5	5
Muscle tone	Normal	5	5
Skin	Normal	5	5
Fur	Normal	5	5
Piloerection	Not detected	5	5
Eye discharge	Not detected	5	5
Palpebral closure	Not detected	5	5
Exophthalmos	Not detected	5	5
Lacrimation	Not detected	5	5
Smudge around mouth-nose	Not detected	5	5
Salivation	Not detected	5	5
Blotted fur in the lower abdomen with urine	Not detected	5	5
Blotted fur around anus with feces	Not detected	5	5
Vocalization	Not detected	5	5
Breathing	Normal	5	5
Body position	Normal	5	5
Convulsion	Not detected	5	5
Tremor	Not detected	5	5
Exploration	Normal	5	5
Alertness	Normal	5	5
Locomotor activity	Normal	5	5
Walk	Normal	5	5
Abnormal behavior	Not detected	5	5
Stereotypy	Not detected	5	5
Failure of consciousness	Not detected	5	5
Limb tone	Normal	5	5
Urination	Not detected or 1	5	5
	2 or more	0	0
	Color: Pale yellow	2/2	2/2
Defecation	Not detected or 1	5	5
	2 or more	0	0
	Appearance:Normal	-	-

Table 7-1 Incidence of responses in the sensory/reflex function test of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Items	Dose(mg/kg/day)	0	0.8	4	20	100
	No. of animals examined	5	5	5	5	5
Hearing reaction	Normal	5	5	5	5	5
Eye sight reaction	Normal	5	5	5	5	5
Sense of touch reaction	Normal	5	5	5	5	5
Pain reaction	Normal	5	5	5	5	5
Pupil reflex	Normal	5	5	5	5	5
Righting reflex	Normal	5	5	5	5	5

Table 7-2 Incidence of responses in the sensory/reflex function test of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Items	Dose(mg/kg/day)	0	100
	No. of animals examined	5	5
Hearing reaction	Normal	5	5
Eye sight reaction	Normal	5	5
Sense of touch reaction	Normal	5	5
Pain reaction	Normal	5	5
Pupil reflex	Normal	5	5
Righting reflex	Normal	5	5

Table 7-3 Incidence of responses in the sensory/reflex function test of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 2 of the recovery period >

Items	Dose(mg/kg/day) No. of animals examined	0 5	100 5
Hearing reaction	Normal	5	5
Eye sight reaction	Normal	5	5
Sense of touch reaction	Normal	5	5
Pain reaction	Normal	5	5
Pupil reflex	Normal	5	5
Righting reflex	Normal	5	5

Table 8-1 Incidence of responses in the sensory/reflex function test of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Items	Dose(mg/kg/day)	0	0.8	4	20	100
	No. of animals examined	5	5	5	5	5
Hearing reaction	Normal	5	5	5	5	5
Eye sight reaction	Normal	5	5	5	5	5
Sense of touch reaction	Normal	5	5	5	5	5
Pain reaction	Normal	5	5	5	5	5
Pupil reflex	Normal	5	5	5	5	5
Righting reflex	Normal	5	5	5	5	5

Table 8-2 Incidence of responses in the sensory/reflex function test of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈On week 6 of the administration period 〉

Items	Dose(mg/kg/day)	0	100
	No. of animals examined	5	5
Hearing reaction	Normal	5	5
Eye sight reaction	Normal	5	5
Sense of touch reaction	Normal	5	5
Pain reaction	Normal	5	5
Pupil reflex	Normal	5	5
Righting reflex	Normal	5	5

Table 8-3 Incidence of responses in the sensory/reflex function test of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 2 of the recovery period >

Items	Dose(mg/kg/day)	0	100
	No. of animals examined	5	5
Hearing reaction	Normal	5	5
Eye sight reaction	Normal	5	5
Sense of touch reaction	Normal	5	5
Pain reaction	Normal	5	5
Pupil reflex	Normal	5	5
Righting reflex	Normal	5	5

Table 9-1 Mean value of grip strength and motor activity of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	No. of animals	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	5	893 ± 54	474 ± 53	8442 ± 444	12209 ± 1252
0.8	5	946 ± 59	547 ± 57	7126 ± 1092	10789 ± 2664
4	5	1033 ± 93	457 ± 41	7370 ± 820	9284 ± 1685
20	5	859 ± 108	424 ± 76	5087 ** ± 1123	7290 ** ± 2924
100	5	871 ± 126	510 ± 100	6951 * ± 629	11308 ± 1711

Each value is exprssed as mean±S.D.

* : Significantly different from control at 5% level of probability.

** : Significantly different from control at 1% level of probability.

Table 9-2 Mean value of grip strength and motor activity of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	No. of animals	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	5	1087 ± 131	481 ± 75	8230 ± 1606	11902 ± 2887
100	5	828 ± 228	460 ± 128	8492 ± 263	14165 ± 1440

Each value is exprssed as mean±S.D.

Table 9-3 Mean value of grip strength and motor activity of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Dose (mg/kg/day)	No. of animals	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	5	706 ± 186	432 ± 92	6836 ± 552	8848 ± 1207
100	5	707 ± 95	452 ± 68	7863 * ± 825	14352 ± 1754

Each value is exprssed as mean±S.D.

* : Significantly different from control at 5% level of probability.

Table 10-1 Mean value of grip strength and motor activity of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	No. of animals	Grip strength (g)		Motor activity (counts)
		Forelimb	Hindlimb	$0\sim30_{min.}$
0	5	748 ± 72	477 ± 83	7333 ± 400
0.8	5	753 ± 127	393 ± 48	6648 ± 1132
4	5	661 ± 180	476 ± 84	6080 ± 1771
20	5	614 ± 61	425 ± 89	6313 ± 768
100	5	757 ± 108	536 ± 86	6423 ± 904

Each value is exprssed as mean±S.D.

Table 10-2 Mean value of grip strength and motor activity of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	No. of animals	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	5	750 ± 129	349 ± 15	8944 ± 504	12641 ± 2002
100	5	670 ± 127	428 * ± 44	8680 ± 1060	14406 ± 3401

Each value is exprssed as mean±S.D.

* : Significantly different from control at 5% level of probability.

Table 10-3 Mean value of grip strength and motor activity of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Dose (mg/kg/day)	No. of animals	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	5	610 ± 59	326 ± 54	7990 ± 1409	14132 ± 2802
100	5	550 ± 95	335 ± 47	7775 ± 1278	13462 ± 2187

Each value is exprssed as mean±S.D.

Table 11 Body weights of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Day	Administration period 1	7	14	21	28	35	42	Gain 1～42	Recovery period 42(0)	49(7)	56(14)	Gain 42～56
0		385 ± 17 (12)	410 ± 19 (12)	441 ± 24 (12)	467 ± 26 (12)	491 ± 30 (12)	515 ± 35 (12)	530 ± 37 (12)	145 ± 26 (12)	530 ± 40 (5)	544 ± 41 (5)	548 ± 39 (5)	18 ± 9 (5)
0.8		385 ± 18 (12)	410 ± 22 (12)	440 ± 30 (12)	464 ± 32 (12)	490 ± 34 (12)	516 ± 36 (12)	534 ± 40 (12)	149 ± 26 (12)				
4		387 ± 16 (12)	414 ± 18 (12)	447 ± 21 (12)	469 ± 18 (12)	495 ± 22 (12)	516 ± 26 (12)	531 ± 31 (12)	144 ± 24 (12)				
20		383 ± 15 (12)	415 ± 15 (12)	446 ± 19 (12)	466 ± 19 (12)	493 ± 17 (12)	514 ± 18 (12)	528 ± 20 (12)	145 ± 20 (12)				
100		384 ± 15 (12)	416 ± 15 (12)	445 ± 18 (12)	465 ± 18 (12)	488 ± 20 (12)	509 ± 23 (12)	521 ± 25 (12)	136 ± 22 (12)	529 ± 29 (5)	542 ± 40 (5)	544 ± 38 (5)	15 ± 9 (5)

Each value is expressed as mean±S.D.
(n) : No. of animals

Table 12-1 Body weights of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Day	Premating period 1	7	14	Gain 1~14	Premating period 0	7	14	20	Gain 0~20	Lactation period 0	4	Gain 0~4
0		247 ± 6 (12)	252 ± 6 (12)	265 ± 5 (12)	18 ± 5 (12)	276 ± 10 (12)	308 ± 7 (12)	345 ± 10 (12)	425 ± 22 (12)	149 ± 21 (12)	326 ± 15 (12)	347 ± 12 (10)	21 ± 11 (10)
0.8		249 ± 9 (12)	262 ± 10 (12)	272 ± 11 (12)	22 ± 9 (12)	280 ± 12 (12)	318 ± 15 (12)	354 ± 18 (12)	442 ± 18 (12)	162 ± 11 (12)	341 ± 26 (12)	357 ± 21 (12)	16 ± 12 (12)
4		247 ± 10 (12)	255 ± 10 (12)	270 ± 10 (12)	23 ± 6 (12)	282 ± 14 (12)	317 ± 12 (12)	352 ± 12 (12)	435 ± 16 (12)	153 ± 14 (12)	336 ± 19 (12)	359 ± 15 (12)	23 ± 9 (12)
20		245 ± 11 (12)	254 ± 11 (12)	267 ± 10 (12)	21 ± 10 (12)	284 ± 18 (11)	316 ± 17 (11)	349 ± 18 (11)	431 ± 25 (11)	147 ± 17 (11)	333 ± 17 (11)	356 ± 22 (11)	22 ± 15 (11)
100		244 ± 8 (12)	257 ± 8 (12)	270 ± 8 (12)	26 ± 6 (12)	279 ± 10 (12)	315 ± 9 (12)	348 ± 9 (12)	437 ± 15 (12)	158 ± 14 (12)	340 ± 13 (12)	350 ± 12 (10)	10 ± 12 (10)

Each value is expressed as mean±S.D.
(n) : No. of animals

Table 12-2 Body weights of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Day	Administration period 1	7	14	21	28	35	42	Gain 1~42	Recovery period 42(0)	49(7)	56(14)	Gain 42~56
0		258 ± 11 (5)	267 ± 9 (5)	280 ± 8 (5)	294 ± 8 (5)	299 ± 10 (5)	304 ± 6 (5)	313 ± 11 (5)	55 ± 5 (5)	313 ± 11 (5)	320 ± 10 (5)	321 ± 9 (5)	8 ± 7 (5)
100		258 ± 6 (5)	267 ± 6 (5)	284 ± 9 (5)	301 ± 4 (5)	312 * ± 8 (5)	318 * ± 11 (5)	327 ± 13 (5)	69 ± 15 (5)	327 ± 13 (5)	338 * ± 10 (5)	339 * ± 11 (5)	12 ± 7 (5)

Each value is expressed as mean±S.D.
(n) : No. of animals
* : Significantly different from control at 5% level of probability.

Table 13 Food consumption of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g/rat/day)

Dose		Administration period							Recovery period		
(mg/kg/day)	Day	1	7	14	21	28	35	41	42(0)	49(7)	55(13)
0		29 ± 3 (12)	29 ± 3 (12)	26 ± 3 (12)	28 ± 3 (12)	29 ± 3 (12)	29 ± 3 (12)	26 ± 3 (12)	31 ± 1 (5)	34 ± 2 (5)	35 ± 2 (5)
0.8		29 ± 2 (12)	27 ± 2 (12)	27 ± 3 (12)	26 ± 4 (12)	28 ± 2 (12)	28 ± 3 (12)	25 ± 3 (12)			
4		30 ± 4 (12)	28 ± 3 (12)	27 ± 3 (12)	27 ± 4 (11)	26 * ± 4 (11)	28 ± 3 (12)	25 ± 3 (12)			
20		30 ± 4 (12)	27 ± 2 (12)	28 ± 3 (12)	28 ± 2 (11)	27 ± 3 (11)	28 ± 2 (12)	25 ± 3 (12)			
100		29 ± 3 (12)	29 ± 3 (12)	27 ± 3 (12)	31 ± 3 (12)	31 ± 3 (12)	31 ± 2 (12)	28 ± 3 (12)	31 ± 2 (5)	34 ± 2 (5)	35 ± 1 (5)

Each value is expressed as mean±S.D.
(n) : No. of animals
* : Significantly different from control at 5% level of probability.

Table 14-1 Food consumption of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g/rat/day)

Dose (mg/kg/day)	Premating period			Pregnancy period				Lactation period	
Day	1	7	14	0	7	14	20	0	3
0	20 ± 2 (12)	17 ± 4 (12)	17 ± 3 (12)	16 ± 3 (12)	23 ± 3 (12)	23 ± 3 (12)	23 ± 4 (12)	23 ± 3 (12)	45 ± 4 (12)
0.8	21 ± 3 (12)	18 ± 3 (12)	22 ± 2 (12)	20 ± 6 (12)	24 ± 5 (12)	24 ± 3 (12)	24 ± 4 (12)	21 ± 4 (12)	47 ± 6 (12)
4	20 ± 2 (12)	19 ± 2 (12)	18 ± 3 (12)	17 ± 3 (12)	24 ± 2 (12)	25 ± 3 (12)	26 ± 3 (12)	26 ± 7 (12)	46 ± 7 (12)
20	19 ± 3 (12)	20 ± 1 (12)	19 ± 3 (12)	17 ± 4 (12)	23 ± 4 (12)	24 ± 3 (12)	26 ± 3 (12)	21 ± 7 (11)	48 ± 11 (11)
100	19 ± 4 (12)	19 ± 3 (12)	20 ± 2 (12)	17 ± 2 (12)	22 ± 4 (12)	24 ± 3 (12)	26 ± 4 (12)	21 ± 4 (10)	42 ± 7 (10)

Each value is expressed as mean±S.D.
(n) : No. of animals

Table 14-2 Food consumption of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g/rat/day)

Dose		Administration period							Recovery period		
(mg/kg/day)	Day	1	7	14	21	28	35	42	42(0)	49(7)	55(13)
0		22 ± 2 (5)	22 ± 2 (5)	17 ± 4 (5)	21 ± 1 (5)	20 ± 3 (5)	22 ± 1 (5)	24 ± 1 (5)	24 ± 1 (5)	24 ± 2 (5)	24 ± 2 (5)
100		21 ± 4 (5)	21 ± 3 (5)	20 ± 4 (5)	20 ± 4 (5)	22 ± 1 (5)	22 ± 1 (5)	23 ± 1 (5)	23 ± 1 (5)	24 ± 1 (5)	25 ± 3 (5)

Each value is expressed as mean±S.D.
(n) : No. of animals

Table 15 - 1 Urinary findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 6 of the administration period >

Dose (mg/kg/day)	No. of animals	Color		Cloudy		Volume[a)] (mL/18hr)	Specific[a)] gravity	Na[a)] (mEq/18hr)	K[a)] (mEq/18hr)	pH						Protein				
		PY	C	−	1+					6.0	6.5	7.0	7.5	8.0	8.5	−	±	1+	2+	3+
0	5	5		5		9.4 ± 3.5	1.063 ± 0.013	1.31 ± 0.54	4.21 ± 1.43				1		4		1	2	2	
0.8	5	5		5		9.7 ± 3.9	1.062 ± 0.013	1.52 ± 0.62	3.75 ± 1.35					3	2			3	2	
4	5	5		5		9.6 ± 2.9	1.059 ± 0.010	1.78 ± 0.57	3.92 ± 1.24						5		1	1	2	1
20	5	5		5		10.9 ± 5.4	1.063 ± 0.022	2.05 ± 1.03	4.77 ± 2.47				1		4			2	3	
100	5	5		5		7.7 ± 1.6	1.075 ± 0.011	1.37 ± 0.32	3.02 ± 0.59				1		4				4	1

Dose (mg/kg/day)	No. of animals	Glucose				Ketone body					Bilirubin				Occult blood					Urobilinogen		
		−	±	1+	2+	−	±	1+	2+	3+	−	1+	2+	3+	−	±	1+	2+	3+	0.1	1	2
0	5	5					3	2			5				5					5		
0.8	5	5					2	3			5				5					5		
4	5	5					3	2			5				5					5		
20	5	5					2	3			5				5					5		
100	5	5					1	4			5				5					5		

a) : Mean±S.D.
Color :PY(pale yellow), C(colorless).
Cloudy : −(negligible), 1+(cloudy).
Protein : −(negligible), ±(15～30mg/dL), 1+(30mg/dL), 2+(100mg/dL), 3+(300mg/dL).
Glucose : −(negligible), ±(0.1g/dL), 1+(0.25g/dL), 2+(0.5g/dL).
Ketone body : −(negligible), ±(5mg/dL), 1+(15mg/dL), 2+(40mg/dL),3+(80mg/dL).
Bilirubin : −(negligible), 1+(slight), 2+(moderate), 3+(marked).
Occult blood : −(negligible), ±(trace), 1+(slight), 2+(moderate), 3+(marked).
Urobilinogen : Ehrlich unit/dL.

Table 15 - 2 Urinary findings of male rats treated with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 6 of the administration period >

Dose (mg/kg/day)	No. of animals	Erythrocytes				Leukocytes				Crystals									
										Mg				Ca			Ams		
		−	1+	2+	3+	−	1+	2+	3+	−	1+	2+	3+	−	1+	2+	−	1+	2+
0	5	5				5				3	2			5			5		
0.8	5	5				5				4	1			5			5		
4	5	5				5				3	2			5			5		
20	5	5				5				3	2			5			5		
100	5	5				5				3	2			5			5		

Dose (mg/kg/day)	No. of animals	Epithelial cells										Casts						Fat globules		
		Sq				R			S			G		H		W				
		−	1+	2+	3+	−	1+	2+	−	1+	2+	−	1+	−	1+	−	1+	−	1+	2+
0	5	4	1			5			5			5		5		5		5		
0.8	5	4	1			5			5			5		5		5		5		
4	5	5				5			5			5		5		5		5		
20	5	4	1			5			5			5		5		5		5		
100	5	4	1			5			5			5		5		5		5		

− : Not observed, 1+ : A few in some fields, 2+ : A few in all fields, 3+ : Many in all fields.
Crystals : Mg (ammonium magnesium phosphate), Ca (calcium carbonate), Ams (amorphous).
Epithelial cells : Sq (squamous), R (round), S (spindle).
Casts : G (granule), H (hyaline), W (waxy).

Table 15 - 3 Urinary findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 2 of the recovery period >

Dose (mg/kg/day)	No. of animals	Color		Cloudy		Volume[a)] (mL/18hr)	Specific[a)] gravity	Na[a)] (mEq/18hr)	K[a)] (mEq/18hr)	pH						Protein				
		PY	C	−	1+					6.0	6.5	7.0	7.5	8.0	8.5	−	±	1+	2+	3+
0	5	5		5		10.5 ± 2.1	1.066 ± 0.005	1.65 ± 0.79	4.55 ± 1.18					1	4		1	3	1	
100	5	5		5		9.1 ± 3.0	1.072 ± 0.005	1.66 ± 0.56	3.74 ± 0.99						5			1	4	

Dose (mg/kg/day)	No. of animals	Glucose				Ketone body					Bilirubin				Occult blood					Urobilinogen		
		−	±	1+	2+	−	±	1+	2+	3+	−	1+	2+	3+	−	±	1+	2+	3+	0.1	1	2
0	5	5				2	1	2			5				5					5		
100	5	5					1	4			5				5					5		

a) : Mean±S.D.
Color :PY(pale yellow), C(colorless).
Cloudy : −(negligible), 1+(cloudy).
Protein : −(negligible), ±(15~30mg/dL), 1+(30mg/dL), 2+(100mg/dL), 3+(300mg/dL).
Glucose : −(negligible), ±(0.1g/dL), 1+(0.25g/dL), 2+(0.5g/dL).
Ketone body : −(negligible), ±(5mg/dL), 1+(15mg/dL), 2+(40mg/dL),3+(80mg/dL).
Bilirubin : −(negligible), 1+(slight), 2+(moderate), 3+(marked).
Occult blood : −(negligible), ±(trace), 1+(slight), 2+(moderate), 3+(marked).
Urobilinogen : Ehrlich unit/dL.

Table 15 - 4 Urinary findings of male rats treated with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 2 of the recovery period >

Dose (mg/kg/day)	No. of animals	Erythrocytes				Leukocytes				Crystals									
										Mg				Ca			Ams		
		−	1+	2+	3+	−	1+	2+	3+	−	1+	2+	3+	−	1+	2+	−	1+	2+
0	5	5				5				4	1			5			5		
100	5	5				5				4	1			5			5		

Dose (mg/kg/day)	No. of animals	Epithelial cells										Casts						Fat globules		
		Sq				R			S			G		H		W				
		−	1+	2+	3+	−	1+	2+	−	1+	2+	−	1+	−	1+	−	1+	−	1+	2+
0	5	5				5			5			5		5		5		5		
100	5	5				5			5			5		5		5		5		

− : Not observed, 1+ : A few in some fields, 2+ : A few in all fields, 3+ : Many in all fields.
Crystals : Mg (ammonium magnesium phosphate), Ca (calcium carbonate), Ams (amorphous).
Epithelial cells : Sq (squamous), R (round), S (spindle).
Casts : G (granule), H (hyaline), W (waxy).

Table 16 - 1 Hematological findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	No. of animals	RBC (10^4/μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	5	865 ± 37	15.4 ± 0.6	48.2 ± 2.3	56 ± 1	17.9 ± 0.2	32.0 ± 0.3	27.5 ± 4.0	15.4 ± 1.3
0.8	5	899 ± 61	15.7 ± 0.4	48.5 ± 1.4	54 ± 3	17.5 ± 0.9	32.3 ± 0.5	26.7 ± 9.6	15.4 ± 0.4
4	5	900 ± 46	15.9 ± 0.7	49.3 ± 2.8	55 ± 2	17.7 ± 0.5	32.3 ± 0.6	20.9 ± 6.5	15.5 ± 0.5
20	5	846 ± 41	15.4 ± 0.5	48.6 ± 1.7	58 ± 2	18.3 ± 0.6	31.7 ± 0.3	20.0 ± 5.4	14.8 ± 0.7
100	5	844 ± 36	14.4 * ± 0.5	45.9 ± 1.6	54 ± 1	17.0 ± 0.2	31.3 ± 0.6	27.6 ± 3.4	14.7 ± 0.3

Dose (mg/kg/day)	No. of animals	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	5	18.7 ± 1.2	127 ± 14	80 ± 15	0.0 ± 0.0	1.3 ± 0.3	22.0 ± 6.2	71.4 ± 6.1	5.3 ± 1.0
0.8	5	18.0 ± 1.3	124 ± 16	93 ± 35	0.0 ± 0.0	1.0 ± 0.4	18.5 ± 7.8	75.5 ± 7.6	5.0 ± 1.3
4	5	18.7 ± 1.8	140 ± 22	84 ± 33	0.0 ± 0.0	1.0 ± 0.5	18.0 ± 4.6	76.3 ± 5.3	4.6 ± 1.1
20	5	17.2 ± 2.0	139 ± 10	88 ± 18	0.0 ± 0.0	1.2 ± 0.4	14.2 ± 5.0	80.4 ± 4.6	4.3 ± 1.2
100	5	18.7 ± 1.4	142 ± 8	96 ± 15	0.0 ± 0.0	0.8 ± 0.2	18.9 ± 3.2	75.4 ± 3.5	5.0 ± 0.3

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability.

Table 16 - 2 Hematological findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	No. of animals	RBC (10^4/μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	5	893 ± 38	15.4 ± 0.5	47.9 ± 1.2	54 ± 2	17.3 ± 0.6	32.2 ± 0.6	23.8 ± 7.9	15.7 ± 0.9
100	5	800 ** ± 37	13.9 ** ± 0.1	44.0 ** ± 0.3	55 ± 3	17.3 ± 0.8	31.5 * ± 0.2	49.6 ** ± 10.4	14.8 ± 1.0

Dose (mg/kg/day)	No. of animals	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	5	19.1 ± 1.1	122 ± 26	97 ± 21	0.0 ± 0.0	1.1 ± 0.3	19.4 ± 4.9	74.3 ± 6.1	5.4 ± 1.6
100	5	18.1 ± 1.3	144 ± 25	91 ± 14	0.0 ± 0.0	3.7 ± 6.2	19.4 ± 6.5	72.4 ± 10.8	4.6 ± 0.4

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability.
** : Significantly different from control at 1% level of probability.

Table 17 - 1 Hematological findings of female rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	No. of animals	RBC (10^4/μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	5	713 ± 21	13.5 ± 0.2	43.3 ± 0.5	61 ± 1	18.9 ± 0.5	31.1 ± 0.4	81.5 ± 16.1	17.1 ± 0.6
0.8	5	691 ± 26	13.4 ± 0.6	42.2 ± 1.8	61 ± 3	19.4 ± 0.6	31.8 ± 0.7	86.6 ± 18.5	17.8 ± 1.2
4	5	692 ± 14	13.3 ± 0.2	42.3 ± 0.8	61 ± 2	19.3 ± 0.4	31.5 ± 0.5	78.9 ± 6.4	17.9 ± 0.8
20	5	661 ± 60	12.7 ± 0.7	41.3 ± 2.0	63 ± 3	19.3 ± 0.9	30.8 ± 0.4	96.7 ± 37.1	17.6 ± 0.7
100	5	629 ** ± 33	12.2 ** ± 0.5	40.2 ** ± 1.6	64 ± 3	19.4 ± 0.8	30.3 ± 0.2	101.8 ± 22.0	18.0 ± 0.3

Dose (mg/kg/day)	No. of animals	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	5	16.7 ± 1.0	168 ± 22	76 ± 25	0.0 ± 0.0	0.7 ± 0.4	24.4 ± 6.4	71.2 ± 5.7	3.6 ± 1.7
0.8	5	16.9 ± 0.8	145 ± 17	68 ± 10	0.0 ± 0.0	0.9 ± 0.4	27.5 ± 1.7	64.9 ± 2.5	6.7 ± 2.4
4	5	16.4 ± 0.6	144 ± 9	81 ± 13	0.0 ± 0.0	0.6 ± 0.4	29.6 ± 5.9	66.2 ± 6.3	3.5 ± 1.1
20	5	15.9 ± 1.1	147 ± 15	78 ± 21	0.0 ± 0.0	0.6 ± 0.3	36.8 ± 8.7	58.3 ** ± 7.9	4.3 ± 2.5
100	5	16.2 ± 0.2	136 ± 16	88 ± 23	0.0 ± 0.0	0.9 ± 0.5	34.9 ± 5.4	60.9 * ± 6.3	3.3 ± 1.2

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability.
** : Significantly different from control at 1% level of probability.

Table 17 - 2 Hematological findings of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	No. of animals	RBC (10^4/μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	5	805 ± 51	14.4 ± 0.7	43.6 ± 2.1	54 ± 2	17.9 ± 0.5	32.9 ± 0.4	28.7 ± 5.6	15.7 ± 0.6
100	5	797 ± 35	15.0 ± 0.6	46.3 ± 1.9	58 ** ± 1	18.8 ** ± 0.3	32.4 ± 0.4	32.0 ± 13.0	16.2 ± 0.8

Dose (mg/kg/day)	No. of animals	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	5	16.7 ± 1.1	128 ± 7	38 ± 4	0.0 ± 0.0	1.8 ± 0.4	25.4 ± 4.4	70.5 ± 4.0	2.0 ± 0.5
100	5	16.8 ± 0.6	116 ± 15	39 ± 11	0.0 ± 0.0	1.8 ± 0.7	22.0 ± 4.2	73.0 ± 5.4	3.2 ± 1.6

Each value is expressed as mean±S.D.
** : Significantly different from control at 1% level of probability.

Table 18 - 1 Blood biochemical findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	No. of animals	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	5	286 ± 44	67 ± 8	33 ± 3	348 ± 79	0.79 ± 0.18	31 ± 11	5.73 ± 0.39	2.74 ± 0.42	0.92 ± 0.16	70 ± 8
0.8	5	418 ± 159	73 ± 14	36 ± 9	437 ± 132	1.31 ± 0.41	36 ± 15	5.74 ± 0.22	2.72 ± 0.23	0.90 ± 0.10	59 ± 10
4	5	321 ± 37	67 ± 8	28 ± 3	419 ± 46	1.19 ± 0.49	37 ± 10	5.69 ± 0.26	2.80 ± 0.12	0.97 ± 0.07	59 ± 10
20	5	412 ± 137	72 ± 15	35 ± 12	773 ** ± 206	1.25 ± 0.41	90 ± 38	5.59 ± 0.17	2.85 ± 0.22	1.05 ± 0.13	59 ± 13
100	5	403 ± 78	88 ± 10	53 ± 15	976 ** ± 87	1.14 ± 0.23	162 ** ± 61	6.28 * ± 0.44	3.65 ** ± 0.32	1.39 ** ± 0.08	70 ± 18

Dose (mg/kg/day)	No. of animals	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	5	59 ± 21	147 ± 11	12.6 ± 0.8	0.35 ± 0.06	0.25 ± 0.02	10.0 ± 0.5	7.5 ± 0.8	147 ± 2	5.00 ± 0.88	106 ± 2
0.8	5	45 ± 17	160 ± 18	10.3 * ± 1.2	0.34 ± 0.04	0.27 ± 0.03	10.0 ± 0.7	7.7 ± 1.0	147 ± 2	4.84 ± 0.73	105 ± 2
4	5	29 ± 7	145 ± 8	11.6 ± 1.2	0.32 ± 0.05	0.26 ± 0.02	9.9 ± 0.4	7.4 ± 0.7	147 ± 2	4.91 ± 0.93	105 ± 1
20	5	34 ± 9	161 ± 6	13.0 ± 2.0	0.32 ± 0.04	0.26 ± 0.03	10.2 ± 0.4	8.1 ± 0.7	147 ± 2	5.06 ± 0.50	105 ± 1
100	5	56 ± 39	166 * ± 8	12.8 ± 0.9	0.30 ± 0.03	0.25 ± 0.02	10.3 ± 0.8	8.4 ± 0.6	147 ± 1	5.34 ± 0.37	103 ± 2

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability.
** : Significantly different from control at 1% level of probability.

Table 18 - 2 Blood biochemical findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	No. of animals	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	5	319 ± 75	86 ± 12	47 ± 8	322 ± 71	1.02 ± 0.33	30 ± 13	5.42 ± 0.28	2.54 ± 0.08	0.89 ± 0.10	54 ± 16
100	5	424 ± 125	126 ± 73	111 ± 94	409 ± 71	0.92 ± 0.51	50 ± 26	6.15 ** ± 0.19	3.20 ** ± 0.26	1.09 ± 0.17	123 ** ± 13

Dose (mg/kg/day)	No. of animals	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	5	32 ± 15	141 ± 8	14.0 ± 3.5	0.35 ± 0.02	0.23 ± 0.02	9.6 ± 0.5	6.5 ± 0.9	148 ± 1	4.28 ± 0.17	108 ± 2
100	5	61 * ± 15	155 ± 14	16.7 ± 2.7	0.32 ± 0.05	0.27 * ± 0.02	10.1 ± 0.3	7.0 ± 0.3	147 ± 1	4.99 ** ± 0.31	107 ± 1

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability.
** : Significantly different from control at 1% level of probability.

Table 19 - 1 Blood biochemical findings of female rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-*tert*-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	No. of animals	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	5	408 ± 120	109 ± 62	71 ± 10	450 ± 140	0.97 ± 0.23	290 ± 92	5.98 ± 0.40	3.09 ± 0.29	1.07 ± 0.10	71 ± 15
0.8	5	376 ± 70	87 ± 14	58 ± 17	323 ± 135	0.81 ± 0.18	313 ± 166	5.88 ± 0.48	3.07 ± 0.41	1.10 ± 0.14	65 ± 13
4	5	402 ± 129	99 ± 19	77 ± 24	367 ± 96	1.01 ± 0.24	320 ± 100	5.63 ± 0.32	2.65 ± 0.15	0.89 ± 0.06	73 ± 13
20	5	367 ± 94	98 ± 34	69 ± 16	450 ± 97	0.89 ± 0.34	229 ± 56	5.66 ± 0.16	2.85 ± 0.14	1.01 ± 0.08	69 ± 6
100	5	366 ± 114	90 ± 15	64 ± 12	343 ± 44	0.73 ± 0.28	227 ± 79	5.54 ± 0.22	2.83 ± 0.27	1.05 ± 0.15	67 ± 13

Dose (mg/kg/day)	No. of animals	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	5	104 ± 43	146 ± 15	20.6 ± 3.3	0.46 ± 0.05	0.28 ± 0.05	10.7 ± 0.5	8.6 ± 0.5	148 ± 3	4.48 ± 0.18	106 ± 3
0.8	5	106 ± 41	151 ± 9	20.0 ± 5.2	0.45 ± 0.04	0.25 ± 0.04	10.8 ± 0.6	9.3 ± 2.0	147 ± 1	4.20 ± 0.23	107 ± 3
4	5	81 ± 15	143 ± 12	16.5 ± 1.5	0.41 ± 0.03	0.27 ± 0.02	10.4 ± 0.5	8.5 ± 1.0	148 ± 2	4.73 ± 0.95	109 ± 2
20	5	94 ± 41	150 ± 8	24.0 ± 3.8	0.51 ± 0.05	0.27 ± 0.04	11.0 ± 0.6	9.2 ± 1.4	148 ± 2	4.29 ± 0.43	109 ± 2
100	5	78 ± 26	148 ± 8	19.8 ± 2.2	0.42 ± 0.04	0.26 ± 0.05	10.4 ± 0.2	8.8 ± 0.9	146 ± 2	4.21 ± 0.67	108 ± 1

Each value is expressed as mean±S.D.

Table 19 - 2 Blood biochemical findings of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	No. of animals	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	5	344 ± 16	82 ± 15	39 ± 14	155 ± 76	1.30 ± 0.57	758 ± 344	6.46 ± 0.27	3.42 ± 0.21	1.13 ± 0.09	87 ± 7
100	5	348 ± 39	71 ± 17	35 ± 9	178 ± 55	1.59 ± 0.75	400 ± 148	6.09 ± 0.46	3.17 ± 0.44	1.09 ± 0.18	89 ± 19

Dose (mg/kg/day)	No. of animals	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	5	21 ± 6	149 ± 9	16.8 ± 2.5	0.38 ± 0.05	0.27 ± 0.01	10.2 ± 0.3	5.7 ± 0.5	147 ± 1	4.61 ± 0.06	105 ± 2
100	5	28 ± 16	151 ± 8	19.1 ± 1.2	0.40 ± 0.03	0.26 ± 0.04	10.0 ± 0.4	5.8 ± 0.8	147 ± 1	4.90 * ± 0.21	104 ± 2

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability.

Table 20 Incidence of necropsy findings of male rats treated orally with carbazole in the combined repeated dose toxicity study with reproduction/developmental toxicity screening test

Organ	: Findings	Grade		At the end of administration period					At the end of recovery period	
			Dose(mg/kg/day)	0	0.8	4	20	100	0	100
			No. of animals	7	12	12	12	7	5	5
Liver	: Large	+		0	0	0	0	2	0	0

Grade, + : Slight.

Table 21 Incidence of necropsy findings of female rats treated orally with carbazole in the combined repeated dose toxicity study with reproduction/developmental toxicity screening test

Organ : Findings	Grade		At the end of administration period					At the end of recovery period[a]	
		Dose(mg/kg/day)	0	0.8	4	20	100	0	100
		No. of animals	12	12	12	12	12	5	5
Abnormality			0	0	0	0	0	0	0

a : Satellite group.

Table 22-1 Absolute and relative organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

	Dose (mg/kg/day)	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Seminal vesicle (g)	Testis (g)	Epididymis (g)	Pituitary (mg)	Thyroid (mg)
Absolute	0	506 ±35 (7)	2.07 ±0.02 (5)	0.33 ±0.05 (5)	1.38 ±0.12 (5)	12.94 ±0.45 (5)	3.03 ±0.18 (5)	62.7 ±8.6 (5)	0.86 ±0.15 (5)	2.45 ±0.41 (5)	3.41 ±0.21 (7)	1.34 ±0.09 (7)	13.6 ±1.6 (5)	32.0 ±5.7 (5)
	0.8	509 ±36 (12)	2.06 ±0.07 (5)	0.56 ±0.42 (5)	1.37 ±0.11 (5)	13.13 ±1.77 (5)	2.86 ±0.39 (5)	62.3 ±6.9 (5)	0.85 ±0.21 (5)	2.29 ±0.19 (5)	3.48 ±0.32 (12)	1.44 ±0.11 (12)	13.5 ±1.6 (5)	30.0 ±4.2 (5)
	4	510 ±30 (12)	2.13 ±0.05 (5)	0.32 ±0.06 (5)	1.44 ±0.10 (5)	13.93 ±1.61 (5)	3.34 ±0.19 (5)	63.8 ±9.7 (5)	0.75 ±0.09 (5)	2.66 ±0.42 (5)	3.51 ±0.29 (12)	1.36 ±0.12 (12)	14.3 ±1.9 (5)	35.6 ±1.7 (5)
	20	506 ±19 (12)	2.06 ±0.15 (5)	0.33 ±0.03 (5)	1.45 ±0.10 (5)	18.91 ±3.12 (5)	3.25 ±0.22 (5)	61.8 ±7.3 (5)	0.78 ±0.11 (5)	2.27 ±0.26 (5)	3.47 ±0.26 (12)	1.33 ±0.14 (12)	15.6 ±0.6 (5)	33.2 ±4.1 (5)
	100	491 ±23 (7)	2.04 ±0.06 (5)	0.30 ±0.03 (5)	1.44 ±0.08 (5)	26.67 ** ±2.45 (5)	3.26 ±0.15 (5)	62.7 ±3.7 (5)	0.84 ±0.07 (5)	2.24 ±0.40 (5)	3.71 ±0.38 (7)	1.35 ±0.11 (7)	14.1 ±0.9 (5)	36.3 ±4.4 (5)
Relative @	0	506 ±35 (7)	0.41 ±0.03 (5)	0.07 ±0.01 (5)	0.27 ±0.03 (5)	2.55 ±0.14 (5)	0.60 ±0.05 (5)	12.3 ±1.6 (5)	0.17 ±0.03 (5)	0.49 ±0.11 (5)	0.68 ±0.07 (7)	0.27 ±0.03 (7)	2.7 ±0.2 (5)	6.3 ±1.0 (5)
	0.8	509 ±36 (12)	0.42 ±0.04 (5)	0.12 ±0.09 (5)	0.28 ±0.03 (5)	2.63 ±0.21 (5)	0.57 ±0.08 (5)	12.5 ±1.5 (5)	0.17 ±0.05 (5)	0.47 ±0.07 (5)	0.69 ±0.07 (12)	0.28 ±0.03 (12)	2.7 ±0.2 (5)	6.0 ±0.7 (5)
	4	510 ±30 (12)	0.43 ±0.03 (5)	0.06 ±0.01 (5)	0.29 ±0.01 (5)	2.79 ±0.13 (5)	0.67 ±0.06 (5)	12.8 ±1.5 (5)	0.15 ±0.02 (5)	0.54 ±0.11 (5)	0.69 ±0.06 (12)	0.27 ±0.03 (12)	2.9 ±0.2 (5)	7.2 ±0.6 (5)
	20	506 ±19 (12)	0.42 ±0.03 (5)	0.07 ±0.01 (5)	0.29 ±0.01 (5)	3.81 * ±0.58 (5)	0.66 ±0.06 (5)	12.5 ±1.5 (5)	0.16 ±0.02 (5)	0.46 ±0.06 (5)	0.69 ±0.06 (12)	0.26 ±0.03 (12)	3.1 ** ±0.2 (5)	6.7 ±0.9 (5)
	100	491 ±23 (7)	0.42 ±0.02 (5)	0.06 ±0.01 (5)	0.30 ±0.02 (5)	5.46 ** ±0.51 (5)	0.67 ±0.04 (5)	12.8 ±0.6 (5)	0.17 ±0.01 (5)	0.46 ±0.07 (5)	0.76 ±0.09 (7)	0.28 ±0.02 (7)	2.9 ±0.3 (5)	7.4 ±1.1 (5)

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight.
(n) : Number of animals.

* : Significantly different from control at 5% level of probability.
* * : Significantly different from control at 1% level of probability.

Table 22-2 Absolute and relative organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

	Dose (mg/kg/day)	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Seminal vesicle (g)	Testis (g)	Epididy-mis (g)	Pituitary (mg)	Thyroid (mg)
Absolute	0	509 ±35 (5)	2.14 ±0.03 (5)	0.31 ±0.08 (5)	1.50 ±0.08 (5)	12.23 ±1.02 (5)	3.38 ±0.22 (5)	77.3 ±13.8 (5)	0.87 ±0.09 (5)	2.78 ±0.32 (5)	3.41 ±0.24 (5)	1.45 ±0.14 (5)	15.5 ±2.2 (5)	37.6 ±6.7 (5)
	100	505 ±33 (5)	2.07 ±0.10 (5)	0.33 ±0.10 (5)	1.44 ±0.16 (5)	16.58 ** ±1.54 (5)	3.44 ±0.40 (5)	66.5 ±3.7 (5)	0.97 ±0.12 (5)	2.75 ±0.23 (5)	3.46 ±0.29 (5)	1.47 ±0.13 (5)	15.0 ±1.4 (5)	36.3 ±6.6 (5)
Relative @	0	509 ±35 (5)	0.42 ±0.04 (5)	0.06 ±0.02 (5)	0.29 ±0.02 (5)	2.41 ±0.23 (5)	0.66 ±0.05 (5)	15.1 ±1.9 (5)	0.17 ±0.01 (5)	0.55 ±0.04 (5)	0.67 ±0.02 (5)	0.29 ±0.02 (5)	3.0 ±0.2 (5)	7.4 ±1.3 (5)
	100	505 ±33 (5)	0.41 ±0.04 (5)	0.06 ±0.02 (5)	0.29 ±0.02 (5)	3.28 ** ±0.17 (5)	0.68 ±0.05 (5)	13.2 ±1.1 (5)	0.19 * ±0.02 (5)	0.55 ±0.05 (5)	0.69 ±0.04 (5)	0.29 ±0.03 (5)	3.0 ±0.2 (5)	7.2 ±1.3 (5)

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight.
(n) : Number of animals.
* : Significantly different from control at 5% level of probability.
* * : Significantly different from control at 1% level of probability.

Table 23-1 Absolute and relative organ weights of female rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

	Dose (mg/kg/day)	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Pituitary (mg)	Thyroid (mg)
Absolute	0	324 ±13 (5)	1.86 ±0.07 (5)	0.30 ±0.08 (5)	1.01 ±0.07 (5)	10.84 ±0.71 (5)	1.87 ±0.25 (5)	71.9 ±13.2 (5)	0.69 ±0.18 (5)	18.8 ±1.5 (5)	22.1 ±4.0 (5)
	0.8	329 ±20 (5)	1.86 ±0.06 (5)	0.30 ±0.10 (5)	0.91 ±0.05 (5)	10.57 ±0.36 (5)	1.84 ±0.06 (5)	79.0 ±9.5 (5)	0.70 ±0.09 (5)	18.7 ±2.4 (5)	24.1 ±3.6 (5)
	4	331 ±17 (5)	1.87 ±0.04 (5)	0.27 ±0.06 (5)	0.93 ±0.03 (5)	10.86 ±0.75 (5)	2.01 ±0.29 (5)	75.9 ±9.6 (5)	0.77 ±0.05 (5)	18.3 ±3.8 (5)	22.7 ±2.9 (5)
	20	321 ±26 (5)	1.95 ±0.09 (5)	0.23 ±0.07 (5)	0.96 ±0.06 (5)	11.10 ±1.29 (5)	1.88 ±0.13 (5)	72.1 ±5.6 (5)	0.68 ±0.09 (5)	16.7 ±1.5 (5)	24.0 ±2.1 (5)
	100	329 ±13 (5)	1.87 ±0.03 (5)	0.31 ±0.05 (5)	0.96 ±0.06 (5)	11.95 ±0.64 (5)	1.98 ±0.09 (5)	73.8 ±10.4 (5)	0.74 ±0.07 (5)	18.5 ±2.5 (5)	25.4 ±1.6 (5)
Relative @	0	324 ±13 (5)	0.58 ±0.02 (5)	0.09 ±0.03 (5)	0.31 ±0.02 (5)	3.35 ±0.12 (5)	0.58 ±0.08 (5)	22.2 ±4.1 (5)	0.21 ±0.06 (5)	5.8 ±0.5 (5)	6.8 ±1.2 (5)
	0.8	329 ±20 (5)	0.57 ±0.03 (5)	0.09 ±0.03 (5)	0.28 ±0.02 (5)	3.22 ±0.10 (5)	0.56 ±0.02 (5)	24.0 ±2.2 (5)	0.21 ±0.04 (5)	5.7 ±0.7 (5)	7.3 ±0.9 (5)
	4	331 ±17 (5)	0.57 ±0.03 (5)	0.08 ±0.01 (5)	0.28 ±0.01 (5)	3.28 ±0.08 (5)	0.61 ±0.08 (5)	23.0 ±3.5 (5)	0.23 ±0.02 (5)	5.5 ±1.1 (5)	6.8 ±0.8 (5)
	20	321 ±26 (5)	0.61 ±0.06 (5)	0.07 ±0.02 (5)	0.30 ±0.02 (5)	3.45 ±0.12 (5)	0.59 ±0.04 (5)	22.5 ±1.7 (5)	0.21 ±0.02 (5)	5.3 ±0.7 (5)	7.5 ±1.2 (5)
	100	329 ±13 (5)	0.57 ±0.03 (5)	0.10 ±0.01 (5)	0.29 ±0.02 (5)	3.63 * ±0.21 (5)	0.60 ±0.01 (5)	22.5 ±3.7 (5)	0.22 ±0.02 (5)	5.6 ±0.8 (5)	7.7 ±0.6 (5)

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight.
(n) : Number of animals.
* : Significantly different from control at 5% level of probability.

Table 23-2 Absolute and relative organ weights of female rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

	Dose (mg/kg/day)	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Pituitary (mg)	Thyroid (mg)
Absolute	0	301 ±9 (5)	1.93 ±0.10 (5)	0.32 ±0.08 (5)	0.99 ±0.10 (5)	7.75 ±0.40 (5)	1.91 ±0.16 (5)	73.8 ±9.5 (5)	0.57 ±0.06 (5)	19.3 ±3.6 (5)	23.8 ±4.7 (5)
	100	312 ±12 (5)	1.95 ±0.07 (5)	0.37 ±0.06 (5)	1.01 ±0.06 (5)	7.97 ±0.61 (5)	1.96 ±0.06 (5)	72.7 ±12.4 (5)	0.65 ±0.13 (5)	17.4 ±1.9 (5)	28.0 ±3.4 (5)
Relative @	0	301 ±9 (5)	0.64 ±0.04 (5)	0.10 ±0.03 (5)	0.33 ±0.04 (5)	2.58 ±0.12 (5)	0.64 ±0.06 (5)	24.5 ±3.1 (5)	0.19 ±0.02 (5)	6.4 ±1.2 (5)	7.9 ±1.5 (5)
	100	312 ±12 (5)	0.63 ±0.03 (5)	0.12 ±0.02 (5)	0.33 ±0.02 (5)	2.55 ±0.15 (5)	0.63 ±0.02 (5)	23.4 ±4.3 (5)	0.21 ±0.04 (5)	5.6 ±0.7 (5)	8.9 ±1.0 (5)

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight.
(n) : Number of animals.

Table 24-1 Incidence of histopathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with reproduction/developmental toxicity screening test

Organs	: Findings	Grade	At the end of administration period						At the end of recovery period	
		Dose(mg/kg/day)	0	0.8	4	20	100		0	100
		No. of animals	5	5	5	5	5		5	5
Lung	: Hemorrhage	-	4	#	#	#	5		#	#
		+	1	#	#	#	0		#	#
	Accumulation, foam cell	-	4	#	#	#	3		#	#
		+	1	#	#	#	2		#	#
Heart	: Myocardial degeneration/fibrosis	-	3	#	#	#	3		#	#
		+	2	#	#	#	2		#	#
Liver	: Hypertrophy, hepatocyte, centrilobular	-	5	5	5	2	0		5	3
		+	0	0	0	3	0		0	2
		++	0	0	0	0	5	**	0	0
	Microgranuloma	-	4	5	4	5	5		5	4
		+	1	0	1	0	0		0	1
	Necrosis, focal	-	5	4	4	5	3		4	5
		+	0	1	1	0	2		1	0
Glandular stomach	: Dilatation, fundic gland	-	4	#	#	#	4		#	#
		+	1	#	#	#	1		#	#
Kidney	: Hyaline droplet, proximal tubular epithelium	-	1	#	#	#	3		#	#
		+	4	#	#	#	2		#	#

Grade, - : Negative; + : Slight; ++ : Moderate; # : Not examined.

No abnormalities were detected in the the brain, pituitary, thyroid, parathyroid, thymus, trachea, small intestine, large intestine, adrenal, urinary bladder, testis, epididymis, seminal vesicle, spinal cord, sciatic nerve, bone marrow and lymph nodes from animals of control and 100 mg/kg groups.

** : Significantly different from control at 1% level of probability.

Table 24-2 Incidence of histopathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with reproduction/developmental toxicity screening test

Organs	Findings	Grade	At the end of administration period					At the end of recovery period	
		Dose(mg/kg/day)	0	0.8	4	20	100	0	100
		No. of animals	5	5	5	5	5	5	5
Kidney (Continued)	Cast, hyaline, unilateral	-	4	#	#	#	4	#	#
		+	1	#	#	#	1	#	#
	Basophilic tubule	-	4	#	#	#	4	#	#
		+	1	#	#	#	1	#	#
	Cyst, solitary, unilateral	-	4	#	#	#	5	#	#
		+	1	#	#	#	0	#	#
Spleen	Hematopoiesis, extramedullary	-	0	#	#	#	0	0	0
		+	5	#	#	#	5	5	3
		++	0	#	#	#	0	0	2
	Deposit, pigment, brown	-	0	#	#	#	0	0	0
		+	5	#	#	#	5	5	5
Prostate	Cellular infiltration, lymphocyte, interstitium	-	4	#	#	#	5	#	#
		+	1	#	#	#	0	#	#

b : Examined the animal with a macroscopic abnormality.
Grade, - : Negative; + : Slight; ++ : Moderate; # : Not examined.
No abnormalities were detected in the the brain, pituitary, thyroid, parathyroid, thymus, trachea, small intestine, large intestine, adrenal, urinary bladder, testis, epididymis, seminal vesicle, spinal cord, sciatic nerve, bone marrow and lymph nodes from animals of control and 100 mg/kg groups.

Table 25 Incidence of histopathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with reproduction/developmental toxicity screening test

Organs	: Findings	Grade	At the end of administration period					At the end of recovery period[a]	
		Dose(mg/kg/day)	0	0.8	4	20	100	0	100
		No. of animals	5	5	5	5	5	5	5
Lung	: Accumulation, foam cell	-	5	#	#	#	3	#	#
		+	0	#	#	#	2	#	#
	Mineralization, artery	-	4	#	#	#	5	#	#
		+	1	#	#	#	0	#	#
Liver	: Hypertrophy, hepatocyte, centrilobular	-	5	5	5	5	3	5	5
		+	0	0	0	0	2	0	0
	Microgranuloma	-	5	4	5	4	5	4	5
		+	0	1	0	1	0	1	0
Kidney	: Dilatation, distal tubular, unilateral	-	4	#	#	#	4	#	#
		+	1	#	#	#	1	#	#
Spleen	: Hematopoiesis, extramedullary	-	0	#	#	#	0	#	#
		+	4	#	#	#	4	#	#
		++	1	#	#	#	1	#	#
	Deposit, pigment, brown	-	0	#	#	#	0	#	#
		+	3	#	#	#	3	#	#
		++	2	#	#	#	2	#	#

a : Satellite group. b : Examined the animal with a macroscopic abnormality.
Grade, - : Negative; + : Slight; ++ : Moderate; # : Not examined.
No abnormalities were detected in the brain, pituitary, thyroid, parathyroid, thymus, trachea, heat, stomach, small intestine, large intestine, adrenal, urinary bladder, ovary, uterus, mammary gland, testis, spinal cord, sciatic nerve, bone marrow and lymph nodes from animals of control and 100 mg/kg groups.

Table 26 The number of cells in seminiferous epithelia assessed by the individual examination in male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	No. of animals		Stage II-III			Stage V			Stage VII			Stage XII	
			G	P	T	G	P	T	G	R/P	T	G	Z/P
0	5	Mean	0.47	1.86	5.76	0.58	1.91	6.06	0.06	3.14	6.05	0.06	4.66
		S.D.	0.04	0.11	0.36	0.04	0.12	0.31	0.01	0.07	0.36	0.01	0.11
100	5	Mean	0.49	1.92	6.05	0.58	1.89	6.17	0.05	3.34	6.11	0.06	4.51
		S.D.	0.01	0.10	0.20	0.04	0.07	0.23	0.004	0.19	0.29	0.01	0.26

G : spermatogonia.
P : pachytene spermatocyte.
R : preleptotene spermatocyte.
Z : zygotene spermatocyte.
T : round spermatid.

Table 27 Reproduction results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	0	0.8	4	20	100
Estrous cycle (days, Mean ± S.D.)	4.1 ± 0.2	4.2 ± 0.4	4.1 ± 0.2	4.1 ± 0.2	4.3 ± 0.6
No. of pairs mated	12	12	12	12	12
No. of pairs with successful copulation	12	12	12	12	12
Copulation index (%)	100	100	100	100	100
Pairing days until copulation (days, Mean ± S.D.)	2.6 ± 1.5	1.6 ± 0.8	3.4 ± 3.6	4.0 ± 3.2	2.1 ± 1.2
No. of pregnant females	12	12	12	11	12
Fertility index (%)	100	100	100	91.7	100
No. of corpora lutea (Mean ± S.D.)	15.8 ± 1.5	16.7 ± 0.9	15.8 ± 1.4	15.1 ± 1.6	16.1 ± 1.6
No. of implantation sites (Mean ± S.D.)	15.2 ± 2.2	16.0 ± 1.0	14.8 ± 1.6	14.8 ± 2.2	15.0 ± 3.0
Implantation index (%, Mean ± S.D.)	95.5 ± 7.9	96.0 ± 4.0	94.3 ± 7.0	97.9 ± 7.0	92.7 ± 13.8
No. of pregnant females with parturition	12	12	12	11	12
Gestation length (days, Mean ± S.D.)	22.4 ± 0.5	22.3 ± 0.5	22.5 ± 0.5	22.6 ± 0.5	22.5 ± 0.5
No. of pregnant females with live pups	12	12	12	11	12
Gestation index (%)	100	100	100	100	100
No. of pregnant females with live pups on day 4	12	12	12	11	11

Copulation index = (No. of pairs with successful copulation/No. of pairs mated) ×100.
Fertility index = (No. of pregnant females/No. of pairs with successful copulation) ×100.
Gestation index = (No. of females with live pups/No. of pregnant females) ×100.

Table 28 Litter results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose(mg/kg/day)	0	0.8	4	20	100
No. of pregnant females with live pups	12	12	12	11	12
No. of pups born	14.2 ± 1.7	14.8 ± 1.9	13.8 ± 1.8	13.6 ± 2.2	13.8 ± 3.2
Delivery index (%)	93.9 ± 6.6	92.9 ± 11.2	92.6 ± 5.3	92.0 ± 5.3	91.3 ± 7.6
No. of pups alive on day 0 of lactation					
Total	14.1 ± 1.7	14.8 ± 1.9	13.8 ± 1.8	13.3 ± 2.1	13.6 ± 3.1
Male	7.8 ± 2.2	6.7 ± 1.5	6.8 ± 2.3	7.9 ± 1.9	6.5 ± 1.5
Female	6.3 ± 1.5	8.2 ± 1.6 *	7.0 ± 1.5	5.4 ± 1.6	7.1 ± 2.7
Live birth index (%)	99.5 ± 1.8	100.0 ± 0.0	100.0 ± 0.0	97.4 ± 6.0	98.5 ± 3.8
Sex ratio(Male/Female)	1.27	0.82	0.96	1.50	0.91
No. of pups alive on day 4 of lactation					
Total	13.6 ± 1.7	14.7 ± 1.9	13.8 ± 1.8	13.3 ± 2.1	12.0 ± 4.8
Male	7.5 ± 2.2	6.7 ± 1.5	6.8 ± 2.3	7.9 ± 1.9	5.8 ± 2.4
Female	6.1 ± 1.6	8.0 ± 1.8	7.0 ± 1.5	5.4 ± 1.6	6.2 ± 3.2
Viability index (%)	96.5 ± 4.7	98.8 ± 2.7	100.0 ± 0.0 *	100.0 ± 0.0 *	89.4 ± 28.3
Body weight of live pups (g)					
on day 0					
Male	7.1 ± 0.6	7.2 ± 0.8	7.3 ± 0.7	7.2 ± 0.4	7.3 ± 0.6
Female	6.7 ± 0.5	6.7 ± 0.6	6.9 ± 0.7	6.9 ± 0.5	6.8 ± 0.7
on day 4					
Male	11.7 ± 1.1	11.6 ± 1.7	11.9 ± 1.1	11.7 ± 1.0	11.8 ± 1.7
Female	11.1 ± 1.0	11.0 ± 1.5	11.6 ± 1.2	11.4 ± 0.9	11.2 ± 1.9

Delivery index = (No. of pups born/No. of implantation sites)×100.
Live birth index = (No. of live pups on day 0/No. of pups born)×100.
Viability index = (No. of live pups on day 4/No. of live pups on day 0)×100.
Sex ratio = Total number of male pups/Total number of female pups.
Each value is expressed as Mean±S.D.,except sex retio.
* : Significantly different from control at 5% level of probability.

Table 29 External findings of pups from pregnant rats treated orally 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

Dose(mg/kg/day)	0	0.8	4	20	100
No. of pups examined	170	178	165	150	166
No. of pups with external malformations#	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

: No. of pups (Mean±S.D. of individual litter percentages).

Table 30 Visceral findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose(mg/kg/day)	0	0.8	4	20	100
No. of pups examined	169	177	165	148	163
No. of pups with visceral malformations#	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
No. of pups with visceral variations#	2 (2.0±3.7)	2 (1.2±2.8)	0 (0)	0 (0)	2 (1.1±2.6)
Visceral variations#					
Thymic remnant in neck	1 (0.8±2.6)	0 (0)	0 (0)	0 (0)	1 (0.6±1.9)
Dilatation of renal pelvis	1 (1.3±2.9)	0 (0)	0 (0)	0 (0)	1 (0.6±1.9)
Persistent left umbilical artery	0 (0)	2 (1.2±2.8)	0 (0)	0 (0)	0 (0)

: No. of pups (Mean±S.D. of individual litter percentages).

2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールの

ラットを用いる反復経口投与毒性・生殖発生毒性併合試験

(試験番号：07-112)

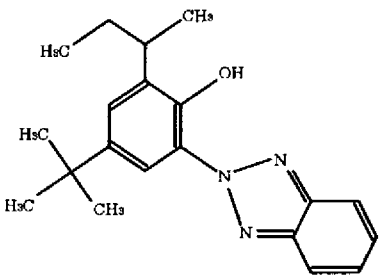
報告書　添付資料B

(個体別表等)

財団法人　畜産生物科学安全研究所

Appendix 1 Test item characterization

被験物質の特性

名　　称	2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノール [英名：2-(2H-Benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol]
CAS 番号	36437-37-3
ロット番号	0808005
純　　度	99.33%（2008 年 9 月 23 日分析）
入 手 先	CHANGZHOU HI-TECH CHEMICAL LIMITED（D-12/F, Midsouth Tower, 33W, Guanhe Rd, Changzhou, Jiangsu, P. R. China）より、試薬を購入
入手日・量	平成 20 年 10 月 21 日・1000g
構 造 式	

物 性 等：

化学名	2-(2*H*-ベンゾトリアゾール-2-イル)-4-(*tert*-ブチル)-6-(sec-ブチル)フェノール
性状(常温)	白色粉末
分子式	$C_{20}H_{25}N_3O$
分子量	323.44
溶 解 性	水に不溶
安 定 性	安定〔実験終了後、残余被験物質を分析（液体クロマトグラフ法により実施、2009 年 9 月 15 日）した結果、実験開始前の分析値の比率 99.9%であり、実験期間中被験物質は安定であったことを確認した。〕
保管条件	日光、高温多湿を避けて冷蔵で保管

Appendix 2 Stability of the test article in the dosing solutions

被験物質の投与形態での安定性

「2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールのラットを用いる反復経口投与毒性・生殖発生毒性併合試験（試験番号：07-112)」を実施するに当たり、被験物質の投与形態での安定性を調べるため、溶媒としてオリブ油（ロット番号 NL-3、小堺製薬株式会社）を用いて 2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノール（ロット番号：0808005）の 0.02%、0.2 および 20% 濃度の溶解液を調製し、調製直後および調製後冷所（2～6℃)、遮光下で 3 日および 7 日保存後、それぞれ室温・遮光下で 1 日保存したものについて上、中および下層よりサンプリングし、濃度を分析した。得られた結果は、次表に示す。

調製濃度 (%)	分析時点	分析値（%）			
		上層	中層	下層	平均値
0.02	調製直後	0.020	0.020	0.020	0.020
	4 日後	0.020	0.020	0.020	0.020
	8 日後	0.021	0.021	0.021	0.021
0.2	調製直後	0.20	0.19	0.20	0.20
	4 日後	0.22	0.21	0.22	0.22
	8 日後	0.22	0.21	0.21	0.21
20	調製直後	22.8	22.8	22.9	22.8
	4 日後	19.7	19.7	19.7	19.7
	8 日後	21.4	21.3	21.5	21.4

以上の結果から、オリブ油に溶解した 2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールは、冷所（2～6℃）で 7 日保存後、室温・遮光下で 1 日保存した場合において、均一、かつ安定であることが確認された。

Appendix 3 Analysis of concentrations of the test article in the dosing solutions

投与液中の被験物質濃度の確認

「2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールのラットを用いる反復経口投与毒性・生殖発生毒性併合試験（試験番号：07-112)」のための被験物質投与液について、所定の濃度で調製されていることを確認するため、初回及び最終回に調製された 2-(2H-ベンゾトリアゾール-2-イル)-4-(tert-ブチル)-6-(sec-ブチル)フェノールのオリブ油による溶液（0.8 mg/kg 群用：0.16 mg/mL、4 mg/kg 群用：0.8 mg/mL、20 mg/kg 群用：4 mg/mL および 100 mg/kg 群用：20 mg/mL）について、それぞれ 3 反復分析した。得られた結果は、次表に示す。

調製濃度	分析値（mg/mL）			
(mg/mL)	上層	中層	下層	平均値
0.16	0.168	0.165	0.166	0.166
0.8	0.83	0.82	0.82	0.82
4	4.1	4.2	4.1	4.1
20	20.0	20.1	20.0	20.0

以上の結果から、被験物質投与液は、所定の濃度で調製されていることが確認された。

Appendix 4-1 Environmental conditions of animal room

Result of temperature and relative humidity at animal room No.1

Permissible level : Temperature ; 22±3℃, Humidity ; 55±10%

Date	Temperature(℃)	Humidity(%)	Note
2009/2/5	21.3 - 22.2	50 - 52	Arrival of animals
2009/2/6	21.6 - 22.2	53 - 54	
2009/2/7	21.4 - 22.2	53 - 57	
2009/2/8	21.5 - 22.3	52 - 58	
2009/2/9	21.8 - 22.6	51 - 56	Start of estrous cycle
2009/2/10	22.1 - 22.7	51 - 54	
2009/2/11	22.0 - 23.1	51 - 56	
2009/2/12	22.4 - 22.9	53 - 55	
2009/2/13	22.0 - 22.6	51 - 58	
2009/2/14	23.0 - 23.8	48 - 52	
2009/2/15	22.8 - 23.6	52 - 56	
2009/2/16	22.7 - 23.2	50 - 54	
2009/2/17	21.5 - 22.1	53 - 55	
2009/2/18	22.1 - 23.0	54 - 56	Grouping
2009/2/19	22.1 - 22.9	53 - 55	Start of administration
2009/2/20	22.3 - 22.6	51 - 55	
2009/2/21	22.2 - 23.2	50 - 53	
2009/2/22	22.1 - 23.2	51 - 55	
2009/2/23	22.6 - 23.0	50 - 54	
2009/2/24	22.3 - 22.6	52 - 54	
2009/2/25	22.2 - 23.3	51 - 54	
2009/2/26	22.0 - 23.4	52 - 55	
2009/2/27	21.5 - 22.5	52 - 57	
2009/2/28	22.5 - 23.1	51 - 53	
2009/3/1	22.8 - 23.2	52 - 55	
2009/3/2	22.7 - 23.1	50 - 54	
2009/3/3	22.7 - 22.9	52	
2009/3/4	22.5 - 23.0	53 - 55	
2009/3/5	22.7 - 23.4	51 - 54	Start of mating
2009/3/6	23.0	50 - 51	
2009/3/7	23.2 - 23.5	49 - 52	
2009/3/8	23.3 - 23.4	51	
2009/3/9	23.2 - 23.4	49 - 54	
2009/3/10	23.1 - 23.6	51	
2009/3/11	22.8 - 23.3	52 - 53	

Appendix 4-2 Environmental conditions of animal room

Result of temperature and relative humidity at animal room No.1

Permissible level : Temperature ; 22±3℃, Humidity ; 55±10%

Date	Temperature(℃)	Humidity(%)	Note
2009/3/12	21.8 - 23.4	51 - 57	
2009/3/13	23.0 - 23.2	49 - 52	
2009/3/14	23.4	49 - 51	
2009/3/15	23.0 - 23.5	50 - 53	
2009/3/16	23.0 - 23.6	47 - 57	
2009/3/17	22.9 - 23.6	48 - 50	
2009/3/18	23.4 - 24.0	49 - 50	
2009/3/19	23.6 - 24.4	46 - 51	End of mating
2009/3/20	23.8 - 23.9	48 - 50	
2009/3/21	22.6 - 23.3	51 - 56	
2009/3/22	22.7 - 23.1	53 - 55	
2009/3/23	22.7 - 23.1	49 - 55	
2009/3/24	21.7 - 23.2	51 - 55	
2009/3/25	22.7 - 23.2	51 - 54	
2009/3/26	22.9 - 23.4	53 - 54	
2009/3/27	22.7 - 23.3	50 - 54	
2009/3/28	22.9 - 23.2	50 - 53	
2009/3/29	22.8 - 23.4	51 - 54	
2009/3/30	23.0 - 24.0	47 - 53	
2009/3/31	23.3 - 23.6	49 - 51	
2009/4/1	23.3 - 23.5	52 - 53	
2009/4/2	23.0 - 23.4	48 - 53	Necropsy of male[a]
2009/4/3	21.6 - 22.6	51 - 58	
2009/4/4	21.6 - 22.5	51 - 53	
2009/4/5	21.7 - 22.4	52 - 53	
2009/4/6	21.3 - 23.3	47 - 56	
2009/4/7	21.7 - 22.7	49 - 52	
2009/4/8	21.4 - 22.5	51 - 53	
2009/4/9	21.4 - 22.2	52 - 56	
2009/4/10	20.6 - 21.9	52 - 57	
2009/4/11	22.2 - 22.9	47 - 50	
2009/4/12	21.0 - 21.8	54 - 57	
2009/4/13	21.8 - 23.4	47 - 53	
2009/4/14	21.4 - 23.0	48 - 54	
2009/4/15	20.7 - 21.9	54 - 58	
2009/4/16	21.6 - 22.3	51 - 53	Necropsy[b]

a:At the end of administration period b:At the end of recovery period

TOKYO KENBIKYO-IN FOUNDATION

Institute for Food and Environment Sciences
IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103-0015, JAPAN
TEL: 03(3663)9681 FAX: 03(3663)9685

Date : January 28, 2009

CERTIFICATE

Applicant	: NIHON NOSAN KOGYO K.K
Samples	: LABO MR-STOCK, Lot No.20081266
Date of Application	: January 6 , 2009
Date of Examination	: January 6 , 2009 ~ January 28 , 2009
Examination No.	: 260901-0001

As a result of tests carried out on the sample submitted under the above mentioned name on January 6, 2009, we herewith report as follows :

RESULTS

Aflatoxin B_1	not detected	(detection limit 5 ppb)
Aflatoxin B_2	not detected	(detection limit 5 ppb)
Aflatoxin G_1	not detected	(detection limit 5 ppb)
Aflatoxin G_2	not detected	(detection limit 5 ppb)
Arsenic(As)	0.15 ppm	(detection limit 0.01 ppm)
Lead(Pb)	0.2 ppm	(detection limit 0.1 ppm)
Cadmium(Cd)	0.10 ppm	(detection limit 0.01 ppm)
Chromium(Cr)	1.3 ppm	(detection limit 0.1 ppm)
Mercury(Hg)	not detected	(detection limit 0.01 ppm)
Polychlorinatedbiphenyl(PCBs)	not detected	(detection limit 0.01 ppm)
Total BHC*[1]	not detected	(detection limit 0.05 ppm)
Parathion	not detected	(detection limit 0.05 ppm)
Malathion	not detected	(detection limit 0.05 ppm)
Total DDT*[2]	not detected	(detection limit 0.05 ppm)

*[1] Expressed as total amounts of α-BHC, β-BHC, γ-BHC and δ-BHC

*[2] Expressed as total amounts of op'-DDT , pp'-DDT ,op'-DDD , pp-DDD , op'-DDE and pp'-DDE

continued.

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Date : January 28, 2009

CERTIFICATE

Applicant	: NIHON NOSAN KOGYO K.K
Samples	: LABO MR-STOCK, Lot No.20081266
Date of Application	: January 6 , 2009
Date of Examination	: January 6 , 2009 ～ January 28 , 2009
Examination No.	: 260901-0002

As a result of tests carried out on the sample submitted under the above mentioned name on January 6, 2009, we herewith report as follows :

RESULT

Selenium(Se) ····· 0.6 ppm (detection limit 0.1 ppm)

,D.V.M.,Ph.D.
Director
Institute for Food and Environment Sciences
TOKYO KENBIKYO-IN FOUNDATION

TOKYO KENBIKYO-IN FOUNDATION

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Heptachlor ·····	not detected	(detection limit 0.01 ppm)
Dieldrin ·····	not detected	(detection limit 0.01 ppm)
Aldrin ·····	not detected	(detection limit 0.01 ppm)
N-Nitrosodiethylamine ·····	not detected	(detection limit 10 ppb)
N-Nitrosodimethylamine ·····	not detected	(detection limit 10 ppb)

,D.V.M.,Ph.D.
Director
Institute for Food and Environment Sciences
TOKYO KENBIKYO-IN FOUNDATION

NOSAN

DATE Jan 8. 2009

MICROBIOLOGICAL INSPECTION

Customer
RESEARCH INSTITUTE FOR ANIMAL SCIENCE
IN BIOCHEMISTORY AND TOXICOLOGY
Sample Designation
LABO MR STOCK
Lot No.20081266

S.P.C.	6.8×10^{3} CFU/g
Coliform Group	Negative
Salmonella	Negative
Molds	<20 CFU/g

NOSAN CORPORATION
R & D Center
Veternery & Hygene Service Group
5246 TAKURA, TSUKUBASHI, 300-2615 JAPAN

, Director

eurofins

Analytical report code AR-09-JP-000436-02

0 5 5 0 0 2 9 0 0 0 0 0 0 0 2 5 4 1

Eurofins order code: EUJPTO-00000299
Report date: 25.02.2009

Charles River Laboratories Japan Co., Ltd.

Received on: 03.02.2009

ANALYTICAL REPORT

Sample code: : 257-2009-02000034
Client code: : ホワイトフレーク

Analysed between: 03.02.2009 – 25.02.2009

Analysis:	*Result:*	*Unit:*	*LOQ:*
J1003 Arsenic			
Arsenic (As)	**<0.10**	ppm	0.10
J1005 Cadmium			
Cadmium (Cd)	**0.05**	ppm	0.01
J1013 Lead			
Lead (Pb)	**0.15**	ppm	0.05
J1018 Mercury			
Mercury (Hg)	**<0.005**	ppm	0.005
JJ006 Aflatoxins B1 B2 G1 G2			
Aflatoxin B1	**<0.1**	ppb	0.1
Aflatoxin B2	**<0.1**	ppb	0.1
Aflatoxin G1	**<0.1**	ppb	0.1
Aflatoxin G2	**<0.1**	ppb	0.1
J7211 Moulds (LMBG, Agar,Food, 30℃)			
Moulds	**4000**	cfu/g	<10
JJB01 Total plate count, aerob, mesophil			
Aerobic count (30℃)	**41 000**	cfu/g	<10
J9122 Salmonella (food, from 1g)			
Salmonella	**Absence**	/25 g	
JJB35 E.coli (food, ECD-Agar)			
Escherichia coli	**Absence**	cfu/g	
J3246 Water content (Feed, VDLUFA)			
Moisture	**10.3**	%	0.1

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Analytical report code AR-09-JP-000436-02

Eurofins order code: EUJPTO-00000299

SP001 Organochlorine Pesticides incl. Pyrethroids			
gamma-HCH (Lindane)	**<0.001**	ppm	0.001
DDT (total)	**<0.01**	ppm	
p,p'-DDT	**<0.001**	ppm	0.001
o,p'-DDT	**<0.001**	ppm	0.001
p,p'-DDE	**<0.002**	ppm	0.002
o,p'-DDE	**<0.002**	ppm	0.002
p,p'-DDD	**<0.002**	ppm	0.002
o,p'-DDD	**<0.002**	ppm	0.002
Endrin	**<0.002**	ppm	0.002
Dieldrin	**<0.001**	ppm	0.001
Aldrin	**<0.001**	ppm	0.001
Heptachlor	**<0.001**	ppm	0.001
SP004 Organophosphorus Pesticides			
Parathion-ethyl	**<0.01**	ppm	0.01
Diazinon	**<0.01**	ppm	0.01
Malathion	**<0.01**	ppm	0.01
Parathion-methyl	**<0.01**	ppm	0.01
SP103 Polychlorobiphenyl (indicator PCBs)			
7 PCB (sum)	**<0.07**	ppm	
PCB IUPAC 28	**<0.01**	ppm	0.01
PCB IUPAC 52	**<0.01**	ppm	0.01
PCB IUPAC 101	**<0.01**	ppm	0.01
PCB IUPAC 118	**<0.01**	ppm	0.01
PCB IUPAC 138	**<0.01**	ppm	0.01
PCB IUPAC 153	**<0.01**	ppm	0.01
PCB IUPAC 180	**<0.01**	ppm	0.01

Chemistry Customer Services Manager

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Eurofins Analytics K.K 1-29-10 Maeno-cho 174-0063 Itabashi-ku, Tokyo - JAPAN Page 2/2

Analytical Certificate of Tap water

Issue No. D-080856
Date: 2. Mar. 2009

Messrs. RESEARCH INSTITUTE FOR ANIMAL SCIENCE IN BIOCHEMISTRY & TOXICOLOGY

TOKYO TECHNICAL SERVICE Co.,Ltd
8-Chome-20-20 Nishikasai Edogawa-ku Tokyo
Tel: 03(3688)3284 Faxi 03(3877)5388
Registerd No.170 Article20.3 of the waterworks law
Registerd No. Tokyo-bowater-327
(Analyst of Drinking water in buil. facilities)
Director of analysis : Fujii. Y
Sampling by : Received sample

Sample: Tap water
Sampling spot: Clean room
Date of sampling: 17. Feb. 2009
Purpose of analysis: Suitability inspection according to the Criteria of the Waterworks Law (10Items)

No.	Items	Unit	Results	*Criteria*
1	Bacteria	count/ml	0	*less than 100*
2	Coliform count	--	Non-detected	*Non-detected*
3	Nitrogen(as nitrite&nitrate)	mg/l	1.5	*less than 10*
4	Chloride ion	mg/l	9.2	*less than 200*
5	Organic substance (Total Organic Carbon)	mg/l	0.7	*less than 5*
6	p H	--	7.5	*5.8~8.6*
7	Taste	--	normal	*Not abnormal*
8	Odor	--	normal	*Not abnormal*
9	Degree of Color	degree	Below 1	*less than 5*
10	Tubidity	degree	Below 1	*less than 2*

Methods of analysis are based on The Ministry of Health and Welfare Order No.101(30.May.2003)
The result of above-mentioned items of tap water suits the criteria of the Waterworks Law

Appendix 8 Scoring lists for clinical signs in detailed observation of rats

Reactivity on removal from the cage	1: Normal (easy); 2: Slightly difficult; 3: Difficult; 4: Almost impossible; 5: Impossible for aggression
Reactivity on handling	1: Normal(easy for handling); 2: Slightly hard as resistance; 3: Hard as resistance; 4: Fairly hard as escape; 5: Impossible for handling
Muscle tone	1: Atonic; 2: Slightly atonic; 3: Normal; 4: Slightly rigid; 5: Rigid
Skin	1: Normal; 2: Slightly flush; 3: Flush; 4: Discoloration; 5: Pale
Fur	1: Normal; 2: Poor(slight); 3: Poor(moderate); 4: Poor(severe)
Piloerection	1: Not detected; 2: Around head; 3: Around head and back; 4: Almost whole body; 5: Whole body
Eye discharge	1: Not detected; 2: Slight; 3: Moderate; 4: Severe; 5: Almost closing eye
Palpebral closure	1: Not detected; 2: 1/4; 3: 1/2; 4: 3/4; 4: Closure
Exophthalmos	1: Not detected; 2: Very slight; 3: Slight; 4: Moderate; 5: Severe
Lacrimation	1: Not detected; 2: Slightly moisture around eye; 3: Moisture; 4: Fairly moisture; 5: Lacrimation
Smudge around mouth-nose	1: Not detected; 2: Slight; 3: Moderate; 4: Severe
Salivation	1: Not detected; 2: Slightly moisture around mouth; 3: Moisture; 4: Fairly moisture; 5: Salivation
Blotted fur in the lower abdomen with urine	1: Not detected; 2: Slight; 3: Moderate; 4: Severe
Blotted fur around anus with feces	1: Not detected; 2: Slight; 3: Moderate; 4: Severe
Vocalization	1: Not detected; 2: Temporal in handling; 3: Slightly continuous; 4: Almost continuous; 5: Absolutely continuous
Breathing	1: Normal; 2: Slight panting; 3: Moderate panting; 4: Severe panting with opened mouth; 5: Endeavor breathing
Body position	1: Normal; 2: Reluctance; 3: Lateral position; 4: Prone position; 5: Supine position
Convulsion	1: Not detected; 2: Intermittent; 3: Slightly continuous; 4: Almost continuous; 5: Absolutely continuous
Tremor	1: Not detected; 2: Intermittent; 3: Slightly continuous; 4: Almost continuous; 5: Absolutely continuous
Exploration	1: Not detected; 2: Slight; 3: Normal; 4: Moderate; 5: Frequent
Alertness	1: No alertness to falling from edge; 2: Slight alertness as nearly as falling; 3: Normal; 4: Slightly hypersensitive; 5: Hypersensitive on the edge
Locomotor activity	1: Decreased; 2: Slightly decreased; 3: Normal; 4: Slightly increased; 5:Increased
Walk	1: Normal; 2: Slightly reeling gait; 3: Reeling gait ataxic gait?
Abnormal behavior	1: Not detected; 2: Slightly repeated; 3: Repeated; 4: Fairly repeated; 5: Frequently repeated
Stereotypy	1: Not detected; 2: Rarely; 3: Sometimes; 4: Frequently
Failure of consciousness	1: Not detected; 2: Stupor; 3: Catalepsy; 4: Coma
Limb tone	1: Normal tone; 2: Weak tone; 3: Lacking tone; 4: No response for slackness
Urination	Frequency, type and color
Defecation	Frequency, type and color

Appendix 9 Scoring lists for sensory/reflex function tests of rats

---

Hearing reaction

1: Normal; 2: Slight insensitivity; 3: Insensitivity; 4: No reaction

Eye sight reaction

1: Normal; 2: Slightly late reaction for avoidance;
3: Late reaction for avoidance; 4: No reaction for avoidance

Sense of touch reaction

1: No reaction; 2: Slight reaction; 3: Normal; 4: Slight hypersensitivity;
5: Hypersensitivity

Pain reaction

1: Normal (immediate reaction for avoidance); 2: Slightly late reaction for avoidance;
3: Late reaction for avoidance; 4: No reaction

Pupil reflex (Reaction to light)

1: Normal (immedeate miosis); 2: No reflex

Righting reflex

1: Normal (immedeate reflex); 2: Slightly late reflex; 3: Late reflex; 4: No reflex

---

Appendix 10-1 Individual fate and mortality rate in time course of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0 mg/kg/day)

Animal number	Days of admnistration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
001																			
002																			
003																			
004																			
005																			
006																			
007																			
008																			
009																			
010																			
011																			
012																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
001																			
002																			
003																			
004																			
005																			
006																			
007																			
008																			
009																			
010																			
011																			
012																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 39	40	41	42	(1) 43	(2) 44	(3) 45	(4) 46	(5) 47	(6) 48	(7) 49	(8) 50	(9) 51	(10) 52	(11) 53	(12) 54	(13) 55	(14) 56	57
001																			KR
002																			KR
003					TK														
004					TK														
005																			KR
006					TK														
007					TK														
008																			KR
009					TK														
010					TK														
011																			KR
012					TK														
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

( ) : Days of recovery

TK : Terminal killing. KR : Killed by design at the end of 14-day recovery period.

A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 10-2 Individual fate and mortality rate in time course of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0.8 mg/kg/day)

Animal number	Days of admnistration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
013																			
014																			
015																			
016																			
017																			
018																			
019																			
020																			
021																			
022																			
023																			
024																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
013																			
014																			
015																			
016																			
017																			
018																			
019																			
020																			
021																			
022																			
023																			
024																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 39	40	41	42	43
013					TK
014					TK
015					TK
016					TK
017					TK
018					TK
019					TK
020					TK
021					TK
022					TK
023					TK
024					TK
A	0	0	0	0	
B	0	0	0	0	

TK : Terminal killing.

A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 10-3 Individual fate and mortality rate in time course of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(4 mg/kg/day)

Animal number	Days of admnistration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
025																			
026																			
027																			
028																			
029																			
030																			
031																			
032																			
033																			
034																			
035																			
036																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
025																			
026																			
027																			
028																			
029																			
030																			
031																			
032																			
033																			
034																			
035																			
036																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 39	40	41	42	43
025					TK
026					TK
027					TK
028					TK
029					TK
030					TK
031					TK
032					TK
033					TK
034					TK
035					TK
036					TK
A	0	0	0	0	
B	0	0	0	0	

TK : Terminal killing.

A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 10-4 Individual fate and mortality rate in time course of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(20 mg/kg/day)

Animal number	Days of admnistration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
037																			
038																			
039																			
040																			
041																			
042																			
043																			
044																			
045																			
046																			
047																			
048																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
037																			
038																			
039																			
040																			
041																			
042																			
043																			
044																			
045																			
046																			
047																			
048																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 39	40	41	42	43
037					TK
038					TK
039					TK
040					TK
041					TK
042					TK
043					TK
044					TK
045					TK
046					TK
047					TK
048					TK
A	0	0	0	0	
B	0	0	0	0	

TK : Terminal killing.

A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 10-5 Individual fate and mortality rate in time course of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(100 mg/kg/day)

Animal number	Days of admnistration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
049																			
050																			
051																			
052																			
053																			
054																			
055																			
056																			
057																			
058																			
059																			
060																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
049																			
050																			
051																			
052																			
053																			
054																			
055																			
056																			
057																			
058																			
059																			
060																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 39	40	41	42	(1) 43	(2) 44	(3) 45	(4) 46	(5) 47	(6) 48	(7) 49	(8) 50	(9) 51	(10) 52	(11) 53	(12) 54	(13) 55	(14) 56	57
049					TK														
050					TK														
051					TK														
052																			KR
053																			KR
054					TK														
055					TK														
056																			KR
057					TK														
058					TK														
059																			KR
060																			KR
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

( ) : Days of recovery

TK : Terminal killing. KR : Killed by design at the end of 14-day recovery period.

A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-1 Individual fate and mortality rate in time course of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
501																			
502																			
503																			
504																			
505																			
506																			
507																			
508																			
509																			
510																			
511																			
512																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
501																			
502																			
503																			
504																			
505																			
506																			
507																			
508																			
509																			
510																			
511																			
512																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 39	40	41	42	43	44	45	46	47
501					TK				
502						TK			
503					TK				
504								TK	
505					TK				
506						TK			
507									TK
508								TK	
509								TK	
510								TK	
511									TK
512							TK		
A	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	

TK : Terminal killing on day 5 after parturition.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-2 Individual fate and mortality rate in time course of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
513																			
514																			
515																			
516																			
517																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
513																			
514																			
515																			
516																			
517																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of admnistration 39	40	41	42	(1) 43	(2) 44	(3) 45	(4) 46	(5) 47	(6) 48	(7) 49	(8) 50	(9) 51	(10) 52	(11) 53	(12) 54	(13) 55	(14) 56	57
513																			KR
514																			KR
515																			KR
516																			KR
517																			KR
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

( ) : Days of recovery
KR : Killed by design at the end of 14-day recovery period.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-3 Individual fate and mortality rate in time course of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0.8 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
518																			
519																			
520																			
521																			
522																			
523																			
524																			
525																			
526																			
527																			
528																			
529																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
518																			
519																			
520																			
521																			
522																			
523																			
524																			
525																			
526																			
527																			
528																			
529																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 39	40	41	42	43	44	45
518					TK		
519						TK	
520						TK	
521						TK	
522					TK		
523					TK		
524							TK
525					TK		
526							TK
527							TK
528					TK		
529						TK	
A	0	0	0	0	0	0	
B	0	0	0	0	0	0	

TK : Terminal killing on day 5 after parturition.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-4 Individual fate and mortality rate in time course of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(4 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
530																			
531																			
532																			
533																			
534																			
535																			
536																			
537																			
538																			
539																			
540																			
541																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
530																			
531																			
532																			
533																			
534																			
535																			
536																			
537																			
538																			
539																			
540																			
541																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56
530								TK										
531						TK												
532							TK											
533						TK												
534						TK												
535					TK													
536								TK										
537																		TK
538								TK										
539									TK									
540						TK												
541								TK										
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

TK : Terminal killing on day 5 after parturition.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-5 Individual fate and mortality rate in time course of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(20 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
542	NP																		
543																			
544																			
545																			
546																			
547																			
548																			
549																			
550																			
551																			
552																			
553																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
542																			
543																			
544																			
545																			
546																			
547																			
548																			
549																			
550																			
551																			
552																			
553																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57
542					TK														
543						TK													
544								TK											
545									TK										
546									TK										
547																			TK
548									TK										
549									TK										
550						TK													
551								TK											
552							TK												
553							TK												
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

NP : Non-pregnant.
TK : Terminal killing on day 5 after parturition.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-6 Individual fate and mortality rate in time course of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(100 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
554																			
555																			
556																			
557																			
558																			
559																			
560																			
561																			
562																			
563																			
564																			
565																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
554																			
555																			
556																			
557																			
558																			
559																			
560																			
561																			
562																			
563																			
564																			
565																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 39	40	41	42	43	44	45	46	47
554							TK		
555					TK				
556					TK				
557						TK			
558								TK	
559						TK			
560					KL				
561						TK			
562							TK		
563									TK
564								TK	
565					TK				
A	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	

KL : Killed because all pups died after delivery.
TK : Terminal killing on day 5 after parturition.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 11-7 Individual fate and mortality rate in time course of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(100 mg/kg/day)

Animal number	Days of administration 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
566																			
567																			
568																			
569																			
570																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
566																			
567																			
568																			
569																			
570																			
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Animal number	Days of administration 39	40	41	42	(1) 43	(2) 44	(3) 45	(4) 46	(5) 47	(6) 48	(7) 49	(8) 50	(9) 51	(10) 52	(11) 53	(12) 54	(13) 55	(14) 56	57
566																			KR
567																			KR
568																			KR
569																			KR
570																			KR
A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

( ) : Days of recovery
KR : Killed by design at the end of 14-day recovery period.
A : Cumulative number of dead animals. B : Mortality rate (%).

Appendix 12-1 Individual general conditions of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Fate	Days of death	General conditions
0	001	KR	57	NAD
	002	KR	57	NAD
	003	TK	43	NAD
	004	TK	43	NAD
	005	KR	57	NAD
	006	TK	43	NAD
	007	TK	43	NAD
	008	KR	57	NAD
	009	TK	43	NAD
	010	TK	43	NAD
	011	KR	57	NAD
	012	TK	43	NAD
0.8	013	TK	43	NAD
	014	TK	43	NAD
	015	TK	43	NAD
	016	TK	43	NAD
	017	TK	43	NAD
	018	TK	43	NAD
	019	TK	43	NAD
	020	TK	43	NAD
	021	TK	43	NAD
	022	TK	43	NAD
	023	TK	43	NAD
	024	TK	43	NAD
4	025	TK	43	NAD
	026	TK	43	NAD
	027	TK	43	NAD
	028	TK	43	NAD
	029	TK	43	NAD
	030	TK	43	NAD
	031	TK	43	NAD
	032	TK	43	NAD
	033	TK	43	NAD
	034	TK	43	NAD
	035	TK	43	NAD
	036	TK	43	NAD

TK : Terminal killing.
KR : Killed by design at the end of 14-day recovery period.
NAD : No abnormalities were detected.

Appendix 12-2 Individual general conditions of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Fate	Days of death	General conditions
20	037	TK	43	NAD
	038	TK	43	NAD
	039	TK	43	NAD
	040	TK	43	NAD
	041	TK	43	NAD
	042	TK	43	NAD
	043	TK	43	NAD
	044	TK	43	NAD
	045	TK	43	NAD
	046	TK	43	NAD
	047	TK	43	NAD
	048	TK	43	NAD
100	049	TK	43	NAD
	050	TK	43	NAD
	051	TK	43	NAD
	052	KR	57	NAD
	053	KR	57	NAD
	054	TK	43	NAD
	055	TK	43	NAD
	056	KR	57	NAD
	057	TK	43	NAD
	058	TK	43	NAD
	059	KR	57	NAD
	060	KR	57	NAD

TK : Terminal killing.
KR : Killed by design at the end of 14-day recovery period.
NAD : No abnormalities were detected.

Appendix 13-1 Individual general conditions of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Fate	Days of death	General conditions
0	501	TK	43	NAD
	502	TK	44	NAD
	503	TK	43	NAD
	504	TK	46	NAD
	505	TK	43	NAD
	506	TK	44	NAD
	507	TK	47	NAD
	508	TK	46	NAD
	509	TK	46	NAD
	510	TK	46	NAD
	511	TK	47	NAD
	512	TK	45	NAD
	513 [a]	KR	57	NAD
	514 [a]	KR	57	NAD
	515 [a]	KR	57	NAD
	516 [a]	KR	57	NAD
	517 [a]	KR	57	NAD
0.8	518	TK	43	NAD
	519	TK	44	NAD
	520	TK	44	NAD
	521	TK	44	NAD
	522	TK	43	NAD
	523	TK	43	NAD
	524	TK	45	NAD
	525	TK	43	NAD
	526	TK	45	NAD
	527	TK	45	NAD
	528	TK	43	NAD
	529	TK	44	NAD

a : Animals of the satellite group, which were not mated.
TK : Terminal killing on day 5 after parturition.
KR : Killed by design at the end of 14-day recovery period.
NAD : No abnormalities were detected.

Appendix 13-2 Individual general conditions of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Fate	Days of death	General conditions
4	530	TK	46	NAD
	531	TK	44	NAD
	532	TK	45	NAD
	533	TK	44	NAD
	534	TK	44	NAD
	535	TK	43	NAD
	536	TK	46	NAD
	537	TK	56	NAD
	538	TK	46	NAD
	539	TK	47	NAD
	540	TK	44	NAD
	541	TK	46	NAD
20	542 NP	TK	43	NAD
	543	TK	44	NAD
	544	TK	46	NAD
	545	TK	47	NAD
	546	TK	47	NAD
	547	TK	57	NAD
	548	TK	47	NAD
	549	TK	47	NAD
	550	TK	44	NAD
	551	TK	46	NAD
	552	TK	45	NAD
	553	TK	45	NAD

TK : Terminal killing on day 5 after parturition.
NP : Non-pregnant.
NAD : No abnormalities were detected.

Appendix 13-3 Individual general conditions of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Fate	Days of death	General conditions
100	554	TK	45	NAD
	555	TK	43	NAD
	556	TK	43	NAD
	557	TK	44	NAD
	558	TK	46	NAD
	559	TK	44	NAD
	560 KL	TK	43	NAD
	561	TK	44	NAD
	562	TK	45	NAD
	563	TK	47	NAD
	564	TK	46	NAD
	565	TK	43	NAD
	566 [a]	KR	57	NAD
	567 [a]	KR	57	NAD
	568 [a]	KR	57	NAD
	569 [a]	KR	57	NAD
	570 [a]	KR	57	NAD

KL : Killed because all pups died after delivery.
a : Animals of the satellite group, which were not mated.
TK : Terminal killing on day 5 after parturition.
KR : Killed by design at the end of 14-day recovery period.
NAD : No abnormalities were detected.

Appendix 14-1-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	1	0	2	0	0	1	1	2	0	2	0
	: tone of color	PY	PY	-	PY	-	-	PY	PY	PY	-	PY	-
Defecation	: count	2	0	0	2	0	0	0	0	4	0	1	0
	: appearance	N	-	-	N	-	-	-	-	N	-	N	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-1-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	1	4	1	0	0	5	3	2	1	2
	: tone of color	-	-	PY	PY	PY	-	-	PY	PY	PY	PY	PY
Defecation	: count	0	0	3	1	0	0	0	1	2	0	0	0
	: appearance	-	-	N	N	-	-	-	N	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-1-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	0	3	0	0	0	0	0	0
	: tone of color	PY	-	-	-	-	PY	-	-	-	-	-	-
Defecation	: count	0	2	0	2	0	0	0	0	0	0	0	0
	: appearance	-	N	-	N	-	-	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-1-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	037	038	039	040	041	042	043	044	045	046	047	048
		20											
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	3	0	0	0	0	1
	: tone of color	-	-	-	-	-	-	PY	-	-	-	-	PY
Defecation	: count	0	0	0	0	0	0	2	0	0	0	0	4
	: appearance	-	-	-	-	-	-	N	-	-	-	-	N

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-1-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	1	0	0	0	0	0	1	1	0
	: tone of color	-	-	-	PY	-	-	-	-	-	PY	PY	-
Defecation	: count	0	1	0	2	0	0	0	0	3	0	0	0
	: appearance	-	N	-	N	-	-	-	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-2-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	2	0	0	0	0	0	0	1	2	0	2	0
	: tone of color	PY	-	-	-	-	-	-	PY	PY	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-2-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	2	0	0	0	3	2	0	0	0
	: tone of color	-	-	-	PY	-	-	-	PY	PY	-	-	-
Defecation	: count	0	0	5	0	0	0	0	0	0	0	0	0
	: appearance	-	-	N	-	-	-	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-2-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	2
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	1	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	PY	-	-	-	-	-	-	-	-
Defecation	: count	2	0	0	0	0	0	0	0	0	1	0	0
	: appearance	N	-	-	-	-	-	-	-	-	N	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-2-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		037	038	039	040	041	042	043	044	045	046	047	048
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	0	0	3	0	0	1	0	0
	: tone of color	PY	-	-	-	-	-	PY	-	-	PY	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-2-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	1	0	0	0	0	2	0	2	0
	: tone of color	PY	-	-	PY	-	-	-	-	PY	-	PY	-
Defecation	: count	5	0	0	0	0	0	0	0	1	0	0	0
	: appearance	N	-	-	-	-	-	-	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-3-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg)	0											
	Animal number	001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	2	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	1	0	0	0
	: appearance	-	-	-	-	-	-	-	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-3-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	2	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	PY	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	1	0	0	0	0	0	0	0	0	0	0
	: appearance	-	N	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-3-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg)	4											
	Animal number	025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 14-3-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	037	038	039	040	041	042	043	044	045	046	047	048
		20											
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	1	1	0	0	0	0
	: tone of color	-	-	-	-	-	-	PY	PY	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-3-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	2	0	0	0	0	0	1	0	3	0	2	1
	: tone of color	PY	-	-	-	-	-	PY	-	PY	-	PY	PY
Defecation	: count	0	0	0	0	0	0	0	0	5	0	0	0
	: appearance	-	-	-	-	-	-	-	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-4-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	0	0	0	0	1	0	1	0
	: tone of color	PY	-	-	-	-	-	-	-	PY	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	2	0	0	0
	: appearance	-	-	-	-	-	-	-	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-4-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	1	0	0	0	0	1	0	0	0	0
	: tone of color	-	-	PY	-	-	-	-	PY	-	-	-	-
Defecation	: count	0	0	0	1	0	0	0	0	0	0	0	0
	: appearance	-	-	-	N	-	-	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-4-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 14-4-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		037	038	039	040	041	042	043	044	045	046	047	048
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	4	0	0	0	0	0	1	0	0	0	0	1
	: tone of color	PY	-	-	-	-	-	PY	-	-	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-4-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	2	0	0	2
	: tone of color	-	-	-	-	-	-	-	-	PY	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-5-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	4	0	0	0	0	0	2	2	1	0	0	0
	: tone of color	PY	-	-	-	-	-	PY	PY	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	1	0	3	0	0	0
	: appearance	-	-	-	-	-	-	N	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-5-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg)	0.8											
	Animal number	013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	1	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	PY	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	2	2	0	0	0	0	0	0	0	0
	: appearance	-	-	N	N	-	-	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-5-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	2	0	0	0	0	0	0
	: appearance	-	-	-	-	-	N	-	-	-	-	-	-

N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-5-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg)	20											
	Animal number	037	038	039	040	041	042	043	044	045	046	047	048
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	0	0	1	0	0	0	0	0
	: tone of color	PY	-	-	-	-	-	PY	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-5-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	1	0	2	1	0	1	0	0	1
	: tone of color	PY	-	-	PY	-	PY	PY	-	PY	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-6-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	1	0	0	0	0	1	0	0	0	1	0
	: tone of color	-	PY	-	-	-	-	PY	-	-	-	PY	-
Defecation	: count	0	0	0	0	0	0	1	0	2	0	2	0
	: appearance	-	-	-	-	-	-	N	-	N	-	N	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-6-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	1	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	PY	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	1	0	0	0	0	0	0	0	0	0
	: appearance	-	-	N	-	-	-	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-6-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	1	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-6-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	037	038	039	040	041	042	043	044	045	046	047	048
		20											
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	1	0	2	0	0	0	0	0
	: tone of color	-	-	-	-	PY	-	PY	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-6-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	1	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	PY	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-7-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		001	002	003	004	005	006	007	008	009	010	011	012
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	2	0	0	0	0	0	1	2	2	0	0	0
	: tone of color	PY	-	-	-	-	-	PY	PY	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	1	0	6	0	0	0
	: appearance	-	-	-	-	-	-	N	-	N	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-7-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		013	014	015	016	017	018	019	020	021	022	023	024
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	1
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-7-3 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		025	026	027	028	029	030	031	032	033	034	035	036
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	2	0	1	0	0
	: tone of color	-	-	-	-	-	-	-	PY	-	PY	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-7-4 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	037	038	039	040	041	042	043	044	045	046	047	048
		20											
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	1	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	PY	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-7-5 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		049	050	051	052	053	054	055	056	057	058	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	1
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 14-8-1 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the recovery period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	001	002	005	008	011	052	053	056	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	1	1	0	0	0	0	0	0
	: tone of color	PY	-	PY	PY	-	-	-	-	-	-
Defecation	: count	0	0	0	2	0	0	0	0	0	0
	: appearance	-	-	-	N	-	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 14-8-2 Individual incidence of clinical signs in detailed observation of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	001	002	005	008	011	052	053	056	059	060
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	2	1	2	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	1	1	1	0	0	0	0	0
	: tone of color	PY	-	PY	PY	PY	-	-	-	-	-
Defecation	: count	0	0	2	0	3	0	0	0	0	0
	: appearance	-	-	N	-	N	-	-	-	-	-

PY : Pale yellow; N : Normal.
Criterions for scoring are shown in appendix 8.

Appendix 15-1-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-1-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-1-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		530	531	532	533	534	535	536	537	538	539	540	541
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-1-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	1	0	1	0	0	0	1	0
	: tone of color	-	-	-	-	PY	-	PY	-	-	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-1-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	1	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-2-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	1	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	PY	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-2-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-2-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		530	531	532	533	534	535	536	537	538	539	540	541
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	2	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-2-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	1	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	PY	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-2-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	1	0	0	0	0	0	0	1	1	1	0
	: tone of color	-	PY	-	-	-	-	-	-	PY	PY	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-3-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	1
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-3-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg)	0.8											
	Animal number	518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-3-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		530	531	532	533	534	535	536	537	538	539	540	541
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	1	0	0	0	0	1	0
	: tone of color	-	-	-	-	-	PY	-	-	-	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-3-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	2	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-3-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-4-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg)	0											
	Animal number	501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	2	0	1	0	0	0	0	0	0	1
	: tone of color	-	-	PY	-	PY	-	-	-	-	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-4-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) Animal number	0.8											
		518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-4-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		530	531	532	533	534	535	536	537	538	539	540	541
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-4-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg)	20											
	Animal number	542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-4-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-5-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg)	0											
	Animal number	501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-5-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg)	0.8											
	Animal number	518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	1	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	PY	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-5-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg) Animal number	4											
		530	531	532	533	534	535	536	537	538	539	540	541
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-5-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg)	20											
	Animal number	542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-5-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-6-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	1	0	0	2
	: tone of color	-	-	-	-	-	-	-	-	PY	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-6-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0.8											
		518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-6-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		530	531	532	533	534	535	536	537	538	539	540	541
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	1	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	PY	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-6-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	1	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-6-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	1	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	PY	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-7-1 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	0											
		501	502	503	504	505	506	507	508	509	510	511	512
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-7-2 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg)	0.8											
	Animal number	518	519	520	521	522	523	524	525	526	527	528	529
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	1	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	PY	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-7-3 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	4											
		030	031	032	033	034	035	036	037	038	039	040	041
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-7-4 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	20											
		542	543	544	545	546	547	548	549	550	551	552	553
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-7-5 Individual incidence of clinical signs in detailed observation of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg) / Animal number	100											
		554	555	556	557	558	559	560	561	562	563	564	565
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-8 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 Before administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	0	0	0	0
	: tone of color	-	-	-	-	-	-	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-9 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 1 of the administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	0	1	1	0	0	0
	: tone of color	PY	-	-	-	-	PY	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-10 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	1	0	0	0	0
	: tone of color	-	-	-	-	-	PY	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-11 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 3 of the administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	1	2	0	1	0
	: tone of color	-	-	-	-	-	PY	PY	-	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-12 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 4 of the administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	0	2	0	0	1
	: tone of color	-	-	-	-	-	-	PY	-	-	PY
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-13 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 5 of the administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	0	2	0	0	0	0
	: tone of color	PY	-	-	-	-	PY	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-14 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	0	0	0	0	0	1	0	0	0	0
	: tone of color	-	-	-	-	-	PY	-	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

Criterions for scoring are shown in appendix 8.

Appendix 15-15 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 1 of the recovery period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	1	1	1	1	1	0
	: tone of color	PY	-	-	-	PY	PY	PY	PY	PY	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 15-16 Individual incidence of clinical signs in detailed observation of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Items	Dose(mg/kg)	0					100				
	Animal number	513	514	515	516	517	566	567	568	569	570
Reactivity on removal from the cage		1	1	1	1	1	1	1	1	1	1
Reactivity on handling		1	1	1	1	1	1	1	1	1	1
Muscle tone		3	3	3	3	3	3	3	3	3	3
Skin		1	1	1	1	1	1	1	1	1	1
Fur		1	1	1	1	1	1	1	1	1	1
Piloerection		1	1	1	1	1	1	1	1	1	1
Eye discharge		1	1	1	1	1	1	1	1	1	1
Palpebral closure		1	1	1	1	1	1	1	1	1	1
Exophthalmos		1	1	1	1	1	1	1	1	1	1
Lacrimation		1	1	1	1	1	1	1	1	1	1
Smudge around mouth-nose		1	1	1	1	1	1	1	1	1	1
Salivation		1	1	1	1	1	1	1	1	1	1
Blotted fur in the lower abdomen with urine		1	1	1	1	1	1	1	1	1	1
Blotted fur around anus with feces		1	1	1	1	1	1	1	1	1	1
Vocalization		1	1	1	1	1	1	1	1	1	1
Breathing		1	1	1	1	1	1	1	1	1	1
Body position		1	1	1	1	1	1	1	1	1	1
Convulsion		1	1	1	1	1	1	1	1	1	1
Tremor		1	1	1	1	1	1	1	1	1	1
Exploration		3	3	3	3	3	3	3	3	3	3
Alertness		3	3	3	3	3	3	3	3	3	3
Locomotor activity		3	3	3	3	3	3	3	3	3	3
Walk		1	1	1	1	1	1	1	1	1	1
Abnormal behavior		1	1	1	1	1	1	1	1	1	1
Stereotypy		1	1	1	1	1	1	1	1	1	1
Failure of consciousness		1	1	1	1	1	1	1	1	1	1
Limb tone		1	1	1	1	1	1	1	1	1	1
Urination	: count	1	0	0	0	1	1	1	0	0	0
	: tone of color	PY	-	-	-	PY	PY	PY	-	-	-
Defecation	: count	0	0	0	0	0	0	0	0	0	0
	: appearance	-	-	-	-	-	-	-	-	-	-

PY : Pale yellow.
Criterions for scoring are shown in appendix 8.

Appendix 16-1 Individual sensory/reflex function data of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Dose (mg/kg/day)	Animal No.	Hearing reaction	Eye sight reaction	Sense of touch reaction	Pain reaction	Pupil reflex	Righting reflex
0	003	1	1	3	1	1	1
	004	1	1	3	1	1	1
	007	1	1	3	1	1	1
	010	1	1	3	1	1	1
	012	1	1	3	1	1	1
0.8	013	1	1	3	1	1	1
	015	1	1	3	1	1	1
	016	1	1	3	1	1	1
	021	1	1	3	1	1	1
	024	1	1	3	1	1	1
4	025	1	1	3	1	1	1
	029	1	1	3	1	1	1
	032	1	1	3	1	1	1
	034	1	1	3	1	1	1
	035	1	1	3	1	1	1
20	040	1	1	3	1	1	1
	041	1	1	3	1	1	1
	043	1	1	3	1	1	1
	044	1	1	3	1	1	1
	047	1	1	3	1	1	1
100	051	1	1	3	1	1	1
	054	1	1	3	1	1	1
	055	1	1	3	1	1	1
	057	1	1	3	1	1	1
	058	1	1	3	1	1	1

Appendix 16-2 Individual sensory/reflex function data of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Dose (mg/kg/day)	Animal No.	Hearing reaction	Eye sight reaction	Sense of touch reaction	Pain reaction	Pupil reflex	Righting reflex
0	001	1	1	3	1	1	1
	002	1	1	3	1	1	1
	005	1	1	3	1	1	1
	008	1	1	3	1	1	1
	011	1	1	3	1	1	1
100	052	1	1	3	1	1	1
	053	1	1	3	1	1	1
	056	1	1	3	1	1	1
	059	1	1	3	1	1	1
	060	1	1	3	1	1	1

Appendix 16-3 Individual sensory/reflex function data of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined dose toxicity study with the reproduction/developmental toxicity screening test

〈On week 2 of the recovery period 〉

Dose (mg/kg/day)	Animal No.	Hearing reaction	Eye sight reaction	Sense of touch reaction	Pain reaction	Pupil reflex	Righting reflex
0	001	1	1	3	1	1	1
	002	1	1	3	1	1	1
	005	1	1	3	1	1	1
	008	1	1	3	1	1	1
	011	1	1	3	1	1	1
100	052	1	1	3	1	1	1
	053	1	1	3	1	1	1
	056	1	1	3	1	1	1
	059	1	1	3	1	1	1
	060	1	1	3	1	1	1

Appendix 17-1 Individual sensory/reflex function data of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Dose (mg/kg/day)	Animal No.	Hearing reaction	Eye sight reaction	Sense of touch reaction	Pain reaction	Pupil reflex	Righting reflex
0	504	1	1	3	1	1	1
	505	1	1	3	1	1	1
	507	1	1	3	1	1	1
	508	1	1	3	1	1	1
	511	1	1	3	1	1	1
0.8	519	1	1	3	1	1	1
	520	1	1	3	1	1	1
	523	1	1	3	1	1	1
	525	1	1	3	1	1	1
	528	1	1	3	1	1	1
4	532	1	1	3	1	1	1
	534	1	1	3	1	1	1
	535	1	1	3	1	1	1
	536	1	1	3	1	1	1
	538	1	1	3	1	1	1
20	544	1	1	3	1	1	1
	545	1	1	3	1	1	1
	546	1	1	3	1	1	1
	548	1	1	3	1	1	1
	551	1	1	3	1	1	1
100	554	1	1	3	1	1	1
	557	1	1	3	1	1	1
	558	1	1	3	1	1	1
	561	1	1	3	1	1	1
	564	1	1	3	1	1	1

Appendix 17-2 Individual sensory/reflex function data of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

<On week 6 of the administration period >

Dose (mg/kg/day)	Animal No.	Hearing reaction	Eye sight reaction	Sense of touch reaction	Pain reaction	Pupil reflex	Righting reflex
0	513	1	1	3	1	1	1
	514	1	1	3	1	1	1
	515	1	1	3	1	1	1
	516	1	1	3	1	1	1
	517	1	1	3	1	1	1
100	566	1	1	3	1	1	1
	567	1	1	3	1	1	1
	568	1	1	3	1	1	1
	569	1	1	3	1	1	1
	570	1	1	3	1	1	1

Appendix 17-3 Individual sensory/reflex function data of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈On week 2 of the recovery period 〉

Dose (mg/kg/day)	Animal No.	Hearing reaction	Eye sight reaction	Sense of touch reaction	Pain reaction	Pupil reflex	Righting reflex
0	513	1	1	3	1	1	1
	514	1	1	3	1	1	1
	515	1	1	3	1	1	1
	516	1	1	3	1	1	1
	517	1	1	3	1	1	1
100	566	1	1	3	1	1	1
	567	1	1	3	1	1	1
	568	1	1	3	1	1	1
	569	1	1	3	1	1	1
	570	1	1	3	1	1	1

Appendix 18-1 Individual grip strength and motor activity data of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenoln in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	Animal number	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	0～30min.	0～60min.
0	003	808	509	7996	11318
	004	951	460	8670	11593
	007	880	536	8377	11671
	010	923	467	9079	12068
	012	901	397	8086	14397
	Mean	893	474	8442	12209
0.8	013	902	576	8209	12436
	015	878	608	7831	11331
	016	1028	551	6485	11148
	021	961	455	7561	12831
	024	963	543	5544	6197
	Mean	946	547	7126	10789
4	025	1125	462	6465	9810
	029	985	451	7982	9236
	032	1088	518	6509	6525
	034	1073	450	8156	11081
	035	894	404	7740	9767
	Mean	1033	457	7370	9284
20	040	927	467	5993	9426
	041	952	416	4771	4897
	043	858	341	3505	3839
	044	882	530	4829	7542
	047	678	368	6335	10746
	Mean	859	424	5087	7290
100	051	942	359	6684	10479
	054	720	525	7492	12599
	055	764	469	5981	8701
	057	906	599	7162	12018
	058	1021	598	7435	12743
	Mean	871	510	6951	11308

Appendix 18-2 Individual grip strength and motor activity data of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	Animal number	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	001	854	405	9386	16621
	002	1136	487	8810	12681
	005	1168	603	8775	10388
	008	1131	468	8784	9567
	011	1144	441	5395	10254
	Mean	1087	481	8230	11902
100	052	1151	622	8526	12833
	053	606	331	8855	12415
	056	899	478	8123	15027
	059	874	539	8417	14915
	060	609	332	8541	15633
	Mean	828	460	8492	14165

Appendix 18-3 Individual grip strength and motor activity data of male rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Dose (mg/kg/day)	Animal number	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	001	934	499	6968	9221
	002	582	426	6999	10022
	005	787	346	6322	9263
	008	767	548	7612	8917
	011	459	341	6280	6816
	Mean	706	432	6836	8848
100	052	871	553	8490	15323
	053	709	474	8690	16506
	056	638	449	6589	11809
	059	670	403	7717	13857
	060	649	380	7828	14266
	Mean	707	452	7863	14352

Appendix 19-1 Individual grip strength and motor activity data of female rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	Animal number	Grip strength (g)		Motor activity (counts)
		Forelimb	Hindlimb	$0\sim30_{min.}$
0	504	756	418	7377
	505	804	622	6658
	507	796	441	7482
	508	760	434	7724
	511	625	472	7424
	Mean	748	477	7333
0.8	519	698	375	6305
	520	570	431	5039
	523	800	340	7419
	525	912	365	6488
	528	784	455	7990
	Mean	753	393	6648
4	532	541	366	9102
	534	458	440	4607
	535	619	463	5067
	536	895	520	6007
	538	791	590	5616
	Mean	661	476	6080
20	544	712	502	6293
	545	577	344	6331
	546	571	335	6821
	548	637	413	5066
	551	573	530	7052
	Mean	614	425	6313
100	554	720	659	7432
	557	845	451	6013
	558	648	568	7207
	561	677	545	6241
	564	896	457	5224
	Mean	757	536	6423

Appendix 19-2 Individual grip strength and motor activity data of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 6 of the administration period 〉

Dose (mg/kg/day)	Animal number	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	513	699	342	8520	13159
	514	613	331	9243	12038
	515	958	372	9659	13983
	516	774	351	8821	9481
	517	707	348	8475	14544
	Mean	750	349	8944	12641
100	566	580	392	8767	10186
	567	662	440	7395	12650
	568	741	375	8229	14615
	569	523	454	8704	15200
	570	843	481	10303	19377
	Mean	670	428	8680	14406

Appendix 19-3 Individual grip strength and motor activity data of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

〈 On week 2 of the recovery period 〉

Dose (mg/kg/day)	Animal number	Grip strength (g)		Motor activity (counts)	
		Forelimb	Hindlimb	$0\sim30_{min.}$	$0\sim60_{min.}$
0	513	573	253	9885	18047
	514	537	313	6831	11703
	515	624	357	7312	13911
	516	692	396	9088	15659
	517	625	311	6834	11338
	Mean	610	326	7990	14132
100	566	486	395	8661	15694
	567	580	277	9190	15248
	568	591	320	5896	10465
	569	425	313	7308	12098
	570	669	369	7820	13803
	Mean	550	335	7775	13462

Appendix 20-1 Individual body weights of male rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Animal number	Day	Administration period 1	7	14	21	28	35	42	Gain 1~42	Recovery period 42(0)	49(7)	56(14)	Gain 42~56
0	001		365	392	425	452	481	509	529	164	529	538	551	22
	002		366	389	413	447	479	501	513	147	513	533	546	33
	003		372	392	424	451	471	491	510	138	--	--	--	--
	004		382	407	435	457	472	483	491	109	--	--	--	--
	005		379	398	413	439	458	470	484	105	484	493	494	10
	006		370	393	424	445	455	480	496	126	--	--	--	--
	007		378	408	443	448	475	498	507	129	--	--	--	--
	008		389	418	448	472	492	522	532	143	532	548	546	14
	009		391	406	437	470	500	537	555	164	--	--	--	--
	010		404	427	463	498	526	553	579	175	--	--	--	--
	011		400	436	477	504	542	575	592	192	592	606	604	12
	012		422	449	488	515	539	563	574	152	--	--	--	--
	Mean		385	410	441	467	491	515	530	145	530	544	548	18
0.8	013		354	379	407	435	449	473	486	132	--	--	--	--
	014		365	385	398	427	447	471	483	118	--	--	--	--
	015		369	390	408	430	446	464	482	113	--	--	--	--
	016		377	398	427	450	484	518	525	148	--	--	--	--
	017		382	407	438	478	508	538	564	182	--	--	--	--
	018		377	401	423	453	482	507	527	150	--	--	--	--
	019		382	408	442	456	488	513	527	145	--	--	--	--
	020		396	421	462	454	508	538	570	174	--	--	--	--
	021		389	416	438	470	488	514	518	129	--	--	--	--
	022		399	427	459	471	489	506	531	132	--	--	--	--
	023		409	440	483	520	545	576	603	194	--	--	--	--
	024		418	449	495	525	550	572	586	168	--	--	--	--
	Mean		385	410	440	464	490	516	534	149	--	--	--	--
4	025		366	395	423	448	462	472	479	113	--	--	--	--
	026		367	399	432	455	483	507	525	158	--	--	--	--
	027		386	400	432	470	505	521	542	156	--	--	--	--
	028		364	387	416	440	463	488	506	142	--	--	--	--
	029		384	404	431	455	472	482	480	96	--	--	--	--
	030		384	416	454	494	513	538	562	178	--	--	--	--
	031		389	415	442	469	496	517	536	147	--	--	--	--
	032		393	431	468	494	521	546	562	169	--	--	--	--
	033		395	419	457	469	503	520	538	143	--	--	--	--
	034		399	422	455	463	484	509	515	116	--	--	--	--
	035		398	434	471	482	513	545	559	161	--	--	--	--
	036		417	449	486	489	522	546	570	153	--	--	--	--
	Mean		387	414	447	469	495	516	531	144	--	--	--	--

Appendix 20-2 Individual body weights of male rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Animal number	Day	Administration period 1	7	14	21	28	35	42	Gain 1~42	Recovery period 42(0)	49(7)	56(14)	Gain 42~56
20	037		357	383	407	440	465	500	519	162	--	--	--	--
	038		367	402	427	443	477	488	515	148	--	--	--	--
	039		375	409	449	486	508	536	568	193	--	--	--	--
	040		374	409	435	452	480	504	515	141	--	--	--	--
	041		381	404	438	461	485	502	501	120	--	--	--	--
	042		378	420	452	479	494	508	532	154	--	--	--	--
	043		380	410	433	441	477	501	510	130	--	--	--	--
	044		385	422	444	464	485	504	515	130	--	--	--	--
	045		396	422	456	483	514	536	547	151	--	--	--	--
	046		399	424	458	475	500	518	529	130	--	--	--	--
	047		409	443	478	492	508	529	535	126	--	--	--	--
	048		395	430	470	480	517	545	552	157	--	--	--	--
	Mean		383	415	446	466	493	514	528	145	--	--	--	--
100	049		362	411	444	464	495	524	542	180	--	--	--	--
	050		367	387	409	442	463	484	503	136	--	--	--	--
	051		381	420	455	475	499	523	527	146	--	--	--	--
	052		373	399	422	434	459	476	493	120	493	490	497	4
	053		373	408	428	452	474	495	515	142	515	525	528	13
	054		381	412	441	457	472	479	477	96	--	--	--	--
	055		384	410	439	459	477	497	501	117	--	--	--	--
	056		385	421	454	467	492	512	524	139	524	538	534	10
	057		394	427	466	482	512	534	537	143	--	--	--	--
	058		402	434	463	476	488	508	517	115	--	--	--	--
	059		397	425	455	469	493	525	541	144	541	565	564	23
	060		412	438	467	500	526	548	570	158	570	594	597	27
	Mean		384	416	445	465	488	509	521	136	529	542	544	15

Appendix 21-1 Individual body weights of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Animal number	Day	Premating period 1	7	14	Gain 1~14	Pregnancy period 0	7	14	20	Gain 0~20	Lactation period 0	4	Gain 0~4
0	501		236	247	262	26	273	309	352	430	157	328	347	19
	502		240	245	259	19	263	299	333	404	141	315	335	20
	503		244	251	263	19	269	306	349	442	173	333	352	19
	504		244	247	264	20	281	311	360	453	172	343	349	6
	505		248	257	264	16	269	303	336	409	140	305	334	29
	506		247	261	269	22	272	297	325	380	108	300	328	28
	507		249	248	268	19	279	313	355	463	184	328	353	25
	508		248	251	264	16	272	303	342	423	151	323	340	17
	509		254	246	259	5	279	302	344	422	143	327	363	36
	510		252	256	269	17	285	315	347	426	141	318	353	35
	511		256	255	276	20	303	323	355	425	122	352	366	14
	512		245	262	265	20	271	312	344	425	154	337	338	1
	Mean		247	252	265	18	276	308	345	425	149	326	347	21
0.8	518		234	243	252	18	253	293	326	421	168	309	327	18
	519		234	251	261	27	274	311	348	436	162	345	353	8
	520		244	257	266	22	268	291	321	408	140	300	317	17
	521		246	263	270	24	276	311	351	432	156	337	361	24
	522		247	260	271	24	287	324	371	471	184	354	370	16
	523		250	264	276	26	276	317	347	428	152	299	337	38
	524		254	259	258	4	281	316	348	444	163	370	359	-11
	525		255	273	285	30	290	336	375	448	158	351	361	10
	526		247	275	290	43	299	343	383	461	162	377	392	15
	527		256	255	275	19	279	320	355	451	172	346	368	22
	528		260	273	277	17	291	321	363	460	169	349	372	23
	529		262	273	277	15	288	328	362	447	159	354	363	9
	Mean		249	262	272	22	280	318	354	442	162	341	357	16
4	530		237	232	254	17	268	312	343	431	163	334	352	18
	531		229	248	259	30	265	299	338	409	144	321	340	19
	532		229	250	256	27	260	297	337	429	169	288	322	34
	533		251	263	280	29	288	333	371	464	176	365	372	7
	534		254	262	282	28	281	325	358	442	161	358	370	12
	535		250	262	278	28	283	313	339	413	130	328	355	27
	536		246	256	262	16	282	319	346	429	147	340	361	21
	537		245	248	264	19	312	338	371	457	145	342	370	28
	538		259	250	272	13	283	317	354	449	166	350	364	14
	539		252	257	274	22	282	314	349	432	150	333	363	30
	540		249	268	276	27	284	315	356	434	150	337	367	30
	541		261	262	281	20	294	325	360	427	133	336	371	35
	Mean		247	255	270	23	282	317	352	435	153	336	359	23

Appendix 21-2 Individual body weights of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Animal number	Day	Premating period 1	7	14	Gain 1~14	Pregnancy period 0	7	14	20	Gain 0~20	Lactation period 0	4	Gain 0~4
20	542 NP		227	243	252	25	(253)	(264)	(272)	(273)	(20)	--	--	--
	543		230	245	259	29	269	309	343	428	159	329	336	7
	544		235	242	251	16	267	293	319	391	124	301	316	15
	545		239	235	263	24	278	293	324	400	122	306	324	18
	546		243	249	277	34	289	322	361	433	144	353	360	7
	547		254	261	269	15	332	352	385	471	139	341	381	40
	548		251	253	273	22	288	317	348	434	146	346	366	20
	549		251	264	280	29	285	324	362	454	169	344	377	33
	550		249	251	273	24	271	305	341	403	132	351	351	0
	551		254	264	267	13	283	332	360	456	173	323	372	49
	552		261	265	259	-2	278	317	348	433	155	330	362	32
	553		251	270	276	25	289	315	350	438	149	341	367	26
	Mean		245	254	267	21	284	316	349	431	147	333	356	22
100	554		233	256	263	30	275	309	344	434	159	332	347	15
	555		237	247	261	24	260	298	328	410	150	324	339	15
	556		246	256	269	23	277	315	342	447	170	359	337	-22
	557		246	260	276	30	278	307	338	429	151	327	337	10
	558		239	248	259	20	278	312	346	438	160	339	345	6
	559		235	252	259	24	275	312	356	448	173	346	363	17
	560 KL		232	242	268	36	266	312	350	443	177	(289)	--	--
	561		247	261	283	36	279	323	358	413	134	363	372	9
	562		248	262	269	21	287	324	343	430	143	324	346	22
	563		251	268	271	20	294	329	360	450	156	345	359	14
	564		254	260	280	26	296	327	354	443	147	342	363	21
	565		256	269	276	20	282	314	352	459	177	336	343	7
	Mean		244	257	270	26	279	315	348	437	158	340	350	10

NP : Non-pregnant.
KL : Killed because all pups died after delivery.
( ) : Not included in statistics.

Appendix 21-3 Individual body weights of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg)	Animal number	Day	Administration period 1	7	14	21	28	35	42	Gain 1~42	Recovery period 42(0)	49(7)	56(14)	Gain 42~56
0	513		260	261	283	288	292	297	309	49	309	310	309	0
	514		239	268	267	290	289	300	296	57	296	309	314	18
	515		264	263	278	287	296	303	315	51	315	327	322	7
	516		258	261	283	298	311	307	321	63	321	329	332	11
	517		267	283	289	305	307	313	322	55	322	324	327	5
	Mean		258	267	280	294	299	304	313	55	313	320	321	8
100	566		255	270	272	301	306	320	314	59	314	326	331	17
	567		253	266	284	299	310	319	327	74	327	334	330	3
	568		255	265	289	306	316	322	336	81	336	345	343	7
	569		267	258	280	296	304	300	314	47	314	332	334	20
	570		262	274	295	302	324	328	344	82	344	352	356	12
	Mean		258	267	284	301	312	318	327	69	327	338	339	12

Appendix 22-1 Individual food consumption of male rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Animal number	Day	Administration period 1	7	14	21	28	35	41	Recovery period 42(0)	49(7)	55(13)
0	001		29	33	26	30	29	26	29	30	32	37
	002		28	24	25	28	29	28	23	33	35	34
	003		23	30	26	26	28	27	23	--	--	--
	004		31	31	24	30	23	26	23	--	--	--
	005		27	25	21	29	29	33	26	31	35	36
	006		29	24	23	21	24	24	26	--	--	--
	007		31	33	28	28	32	27	27	--	--	--
	008		29	29	25	29	27	26	26	32	32	32
	009		26	28	29	35	33	30	30	--	--	--
	010		32	31	29	31	31	34	27	--	--	--
	011		33	30	28	27	31	31	31	30	35	37
	012		34	32	32	27	33	32	23	--	--	--
	Mean		29	29	26	28	29	29	26	31	34	35
0.8	013		28	26	25	23	24	25	23	--	--	--
	014		29	24	22	27	26	23	25	--	--	--
	015		29	24	24	27	27	27	23	--	--	--
	016		31	26	28	32	32	26	26	--	--	--
	017		27	28	28	28	28	28	28	--	--	--
	018		27	25	26	24	27	27	26	--	--	--
	019		34	26	26	25	30	26	24	--	--	--
	020		32	30	32	31	30	35	32	--	--	--
	021		29	27	32	27	26	31	19	--	--	--
	022		26	27	27	20	28	27	22	--	--	--
	023		31	32	31	30	31	32	29	--	--	--
	024		28	28	26	23	29	26	25	--	--	--
	Mean		29	27	27	26	28	28	25	--	--	--
4	025		28	26	24	24	22	23	21	--	--	--
	026		33	27	27	25	25	25	26	--	--	--
	027		25	26	25	25	26	28	24	--	--	--
	028		27	24	23	28	27	27	25	--	--	--
	029		27	28	25	23	24	23	21	--	--	--
	030		26	28	30	28	22	29	30	--	--	--
	031		31	26	26	22	28	26	24	--	--	--
	032		30	26	24	--	--	29	24	--	--	--
	033		29	29	29	28	20	29	25	--	--	--
	034		40	38	34	35	32	30	27	--	--	--
	035		33	29	27	31	32	33	26	--	--	--
	036		29	30	27	31	24	28	29	--	--	--
	Mean		30	28	27	27	26	28	25	--	--	--

Appendix 22-2 Individual food consumption of male rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g)

Dose (mg/kg/day)	Animal number	Day	Administration period 1	7	14	21	28	35	41	Recovery period 42(0)	49(7)	55(13)
20	037		23	25	25	29	28	29	26	--	--	--
	038		31	27	27	30	22	27	25	--	--	--
	039		28	32	30	27	32	31	30	--	--	--
	040		32	27	26	27	27	29	22	--	--	--
	041		29	26	26	26	24	26	24	--	--	--
	042		32	27	28	--	--	26	26	--	--	--
	043		26	24	25	27	29	30	22	--	--	--
	044		28	26	25	27	24	24	21	--	--	--
	045		33	27	29	29	27	29	27	--	--	--
	046		29	29	27	27	30	27	29	--	--	--
	047		35	27	30	27	28	30	25	--	--	--
	048		35	30	33	34	29	27	28	--	--	--
	Mean		30	27	28	28	27	28	25	--	--	--
100	049		31	26	27	35	35	34	31	--	--	--
	050		23	30	27	28	27	29	30	--	--	--
	051		29	28	26	26	31	29	24	--	--	--
	052		28	33	32	27	30	32	28	34	30	34
	053		26	27	27	32	32	33	29	32	34	37
	054		34	29	19	29	24	27	24	--	--	--
	055		30	27	28	28	30	28	26	--	--	--
	056		27	25	27	29	27	28	24	30	34	35
	057		29	29	27	32	32	32	28	--	--	--
	058		29	34	29	32	31	29	28	--	--	--
	059		31	27	29	36	35	33	31	31	35	34
	060		27	27	30	32	33	32	32	29	35	36
	Mean		29	29	27	31	31	31	28	31	34	35

Appendix 23-1 Individual food consumption of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g/rat/day)

Dose (mg/kg/day)	Animal number	Day	Premating period 1	7	14	Pregnancy period 0	7	14	20	Lactation period 0	3
0	501		19	12	19	16	22	26	26	20	47
	502		20	13	21	18	22	21	22	25	43
	503		20	14	18	15	23	24	27	20	46
	504		18	21	15	19	24	27	28	24	43
	505		18	14	18	17	18	20	22	19	38
	506		18	15	16	13	19	18	15	17	41
	507		20	21	12	16	28	26	23	25	53
	508		24	20	13	12	23	22	24	24	42
	509		20	16	13	13	21	20	25	26	50
	510		22	18	18	13	20	20	15	25	46
	511		21	24	16	16	23	23	27	26	46
	512		19	21	21	22	28	26	25	21	42
	Mean		20	17	17	16	23	23	23	23	45
0.8	518		21	14	20	22	20	23	29	24	45
	519		24	23	22	14	28	24	26	16	36
	520		20	18	20	37	17	18	19	20	42
	521		23	16	19	18	24	22	22	22	44
	522		22	15	21	17	29	24	29	23	50
	523		20	16	19	17	22	21	17	19	58
	524		22	16	22	20	23	25	24	17	49
	525		25	16	24	19	18	20	25	17	43
	526		23	23	25	20	33	30	22	25	44
	527		18	21	23	18	27	26	24	28	57
	528		22	19	21	19	17	28	30	23	51
	529		16	21	23	16	25	27	24	21	50
	Mean		21	18	22	20	24	24	24	21	47
4	530		20	18	15	19	26	20	30	27	47
	531		19	21	19	16	27	22	24	20	36
	532		21	16	18	19	24	27	22	18	55
	533		22	15	21	21	26	27	30	26	41
	534		20	17	19	17	24	27	26	26	37
	535		20	16	21	13	20	22	25	23	45
	536		17	20	20	20	23	21	26	42	55
	537		18	21	13	17	21	22	28	24	53
	538		23	22	17	20	25	29	28	30	44
	539		21	21	15	12	22	26	24	20	42
	540		20	20	16	15	23	24	24	22	42
	541		22	21	23	15	24	27	24	35	58
	Mean		20	19	18	17	24	25	26	26	46

Appendix 23-2 Individual food consumption of female rats treated orally with 2-(2H-benzotriazol-2-yl) 6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g/rat/day)

Dose (mg/kg/day)	Animal number	Day	Premating period 1	7	14	Pregnancy period 0	7	14	20	Lactation period 0	3
20	542 NP		21	18	20	(17)	(15)	(18)	(18)	--	--
	543		24	23	23	17	28	29	29	11	35
	544		15	21	19	14	20	23	25	24	35
	545		19	21	12	12	16	19	24	24	38
	546		21	22	17	21	26	24	27	26	48
	547		20	19	22	20	28	23	26	9	56
	548		20	20	15	17	21	23	23	30	60
	549		20	20	17	16	24	29	24	22	64
	550		17	20	20	15	27	24	26	17	32
	551		17	20	20	20	21	26	26	19	53
	552		15	19	16	23	21	24	32	19	50
	553		17	22	21	12	24	24	27	32	53
	Mean		19	20	19	17	23	24	26	21	48
100	554		22	22	21	17	24	25	20	23	41
	555		19	15	19	16	19	23	29	23	44
	556		19	14	18	19	22	26	25	13	44
	557		20	19	19	15	15	24	26	21	36
	558		13	20	22	20	20	23	24	28	42
	559		20	20	20	17	27	27	31	18	42
	560 KL		13	19	21	15	28	27	22	(0)	--
	561		24	15	19	17	27	22	27	16	26
	562		15	22	20	18	22	22	29	24	50
	563		25	23	25	18	22	29	27	19	48
	564		19	21	16	18	20	24	19	26	48
	565		22	15	21	16	22	20	29	23	39
	Mean		19	19	20	17	22	24	26	21	42

NP : Non-pregnant.
KL : Killed because all pups died after delivery.
( ) : Not included in statistics.

Appendix 23-3 Individual food consumption of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(g/rat/day)

Dose (mg/kg/day)	Animal number	Day	Administration period 1	7	14	21	28	35	42	Recovery period 42(0)	49(7)	55(13)
0	513		21	20	16	20	23	20	24	24	24	20
	514		23	25	23	21	17	22	23	23	21	23
	515		23	24	17	23	23	24	24	24	25	26
	516		19	22	14	21	17	22	25	25	25	24
	517		23	21	15	21	18	22	23	23	23	26
	Mean		22	22	17	21	20	22	24	24	24	24
100	566		15	22	23	16	24	21	24	24	23	27
	567		20	21	21	16	22	21	22	22	23	22
	568		22	25	20	23	23	23	23	23	25	22
	569		19	22	13	20	22	23	21	21	26	27
	570		27	17	24	23	21	22	24	24	24	26
	Mean		21	21	20	20	22	22	23	23	24	25

Appendix 24 - 1 Individual urinary findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 6 of the administration period >

Dose (mg/kg/day)	Animal number	Color	Cloudy	Volume (mL/18hr)	Specific gravity	Na (mEq/18hr)	K (mEq/18hr)	pH	Protein	Glucose	Ketone body	Bilirubin	Occult blood	Urobilinogen
0	003	PY	−	9.0	1.060	1.21	4.24	8.5	2+	−	1+	−	−	0.1
	004	PY	−	4.7	1.078	0.60	2.23	8.5	1+	−	±	−	−	0.1
	007	PY	−	12.0	1.052	1.82	5.22	8.5	1+	−	±	−	−	0.1
	010	PY	−	7.7	1.074	1.04	3.50	7.5	2+	−	1+	−	−	0.1
	012	PY	−	13.4	1.050	1.86	5.88	8.5	±	−	±	−	−	0.1
0.8	013	PY	−	8.1	1.072	1.22	3.30	8.0	1+	−	±	−	−	0.1
	015	PY	−	4.3	1.078	0.71	1.63	8.5	1+	−	1+	−	−	0.1
	016	PY	−	10.8	1.064	1.50	4.16	8.0	1+	−	1+	−	−	0.1
	021	PY	−	14.8	1.050	1.82	5.09	8.5	2+	−	±	−	−	0.1
	024	PY	−	10.7	1.048	2.36	4.57	8.0	2+	−	1+	−	−	0.1
4	025	PY	−	7.9	1.060	1.52	3.37	8.5	3+	−	1+	−	−	0.1
	029	PY	−	5.9	1.072	1.00	2.48	8.5	1+	−	±	−	−	0.1
	032	PY	−	13.5	1.048	2.50	5.82	8.5	2+	−	±	−	−	0.1
	034	PY	−	9.6	1.064	1.82	3.73	8.5	2+	−	1+	−	−	0.1
	035	PY	−	10.9	1.050	2.07	4.21	8.5	±	−	±	−	−	0.1
20	040	PY	−	9.1	1.066	1.64	4.20	7.5	2+	−	1+	−	−	0.1
	041	PY	−	5.2	1.096	0.95	2.41	8.5	2+	−	1+	−	−	0.1
	043	PY	−	19.7	1.040	3.68	8.83	8.5	1+	−	±	−	−	0.1
	044	PY	−	11.6	1.048	2.29	5.01	8.5	2+	−	1+	−	−	0.1
	047	PY	−	8.7	1.066	1.71	3.40	8.5	1+	−	±	−	−	0.1
100	051	PY	−	8.1	1.070	1.40	3.36	8.5	2+	−	1+	−	−	0.1
	054	PY	−	5.2	1.078	0.87	2.12	8.5	2+	−	1+	−	−	0.1
	055	PY	−	8.9	1.064	1.51	3.69	7.5	2+	−	±	−	−	0.1
	057	PY	−	7.2	1.093	1.35	3.02	8.5	2+	−	1+	−	−	0.1
	058	PY	−	9.3	1.070	1.73	2.89	8.5	3+	−	1+	−	−	0.1

Color : PY(pale yellow).
Cloudy : −(negligible).
Protein : ±(15～30mg/dL), 1+(30mg/dL), 2+(100mg/dL), 3+(300mg/dL).
Glucose : −(negligible).
Ketone body : ±(5mg/dL), 1+(15mg/dL).
Bilirubin : −(negligible).
Occult blood : −(negligible).
Urobilinogen : Ehrlich unit/dL.

Appendix 24 - 2 Individual urinary findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 6 of the administration period >

Dose (mg/kg/day)	Animal number	Erythro-cytes	Leuko-cytes	Crystals			Epithelial cells			Casts			Fat globules
				Mg	Ca	Ams	Sq	R	S	G	H	W	
0	003	—	—	—	—	—	—	—	—	—	—	—	—
	004	—	—	1+	—	—	1+	—	—	—	—	—	—
	007	—	—	—	—	—	—	—	—	—	—	—	—
	010	—	—	1+	—	—	—	—	—	—	—	—	—
	012	—	—	—	—	—	—	—	—	—	—	—	—
0.8	013	—	—	—	—	—	—	—	—	—	—	—	—
	015	—	—	—	—	—	—	—	—	—	—	—	—
	016	—	—	1+	—	—	1+	—	—	—	—	—	—
	021	—	—	—	—	—	—	—	—	—	—	—	—
	024	—	—	—	—	—	—	—	—	—	—	—	—
4	025	—	—	1+	—	—	—	—	—	—	—	—	—
	029	—	—	1+	—	—	—	—	—	—	—	—	—
	032	—	—	—	—	—	—	—	—	—	—	—	—
	034	—	—	—	—	—	—	—	—	—	—	—	—
	035	—	—	—	—	—	—	—	—	—	—	—	—
20	040	—	—	1+	—	—	1+	—	—	—	—	—	—
	041	—	—	1+	—	—	—	—	—	—	—	—	—
	043	—	—	—	—	—	—	—	—	—	—	—	—
	044	—	—	—	—	—	—	—	—	—	—	—	—
	047	—	—	—	—	—	—	—	—	—	—	—	—
100	051	—	—	—	—	—	—	—	—	—	—	—	—
	054	—	—	1+	—	—	1+	—	—	—	—	—	—
	055	—	—	1+	—	—	—	—	—	—	—	—	—
	057	—	—	—	—	—	—	—	—	—	—	—	—
	058	—	—	—	—	—	—	—	—	—	—	—	—

— : Not observed, 1+ : A few in some fields.
Crystals : Mg (ammonium magnesium phosphate), Ca (calcium carbonate), Ams (amorphous).
Epithelial cells : Sq (squamous), R (round), S (spindle).
Casts : G (granule), H (hyaline), W (waxy).

Appendix 24 - 3 Individual urinary findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 2 of the recovery period >

Dose (mg/kg/day)	Animal number	Color	Cloudy	Volume (mL/18hr)	Specific gravity	Na (mEq/18hr)	K (mEq/18hr)	pH	Protein	Glucose	Ketone body	Bilirubin	Occult blood	Urobilinogen
0	001	PY	−	10.0	1.072	1.34	4.78	8.5	1+	−	1+	−	−	0.1
	002	PY	−	10.5	1.066	1.37	4.99	8.5	1+	−	−	−	−	0.1
	005	PY	−	10.3	1.070	1.55	4.27	8.5	2+	−	1+	−	−	0.1
	008	PY	−	7.9	1.058	0.97	2.74	8.0	±	−	−	−	−	0.1
	011	PY	−	13.8	1.066	3.01	5.96	8.5	1+	−	±	−	−	0.1
100	052	PY	−	5.7	1.070	1.00	2.47	8.5	2+	−	1+	−	−	0.1
	053	PY	−	11.9	1.066	2.28	4.36	8.5	2+	−	1+	−	−	0.1
	054	PY	−	7.1	1.078	1.29	3.39	8.5	1+	−	1+	−	−	0.1
	059	PY	−	8.3	1.074	1.54	3.45	8.5	2+	−	±	−	−	0.1
	060	PY	−	12.7	1.070	2.18	5.05	8.5	2+	−	1+	−	−	0.1

Color : PY(pale yellow).
Cloudy : −(negligible).
Protein : ±(15~30mg/dL), 1+(30mg/dL), 2+(100mg/dL).
Glucose : −(negligible).
Ketone body : −(negligible), ±(5mg/dL), 1+(15mg/dL).
Bilirubin : −(negligible).
Occult blood : −(negligible).
Urobilinogen : Ehrlich unit/dL.

Appendix 24 - 4 Individual urinary findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeated dose toxicity with the reproduction/developmental toxicity screening test

< On week 2 of the recovery period >

Dose (mg/kg/day)	Animal number	Erythro-cytes	Leuko-cytes	Crystals			Epithelial cells			Casts			Fat globules
				Mg	Ca	Ams	Sq	R	S	G	H	W	
0	001	—	—	—	—	—	—	—	—	—	—	—	—
	002	—	—	1+	—	—	—	—	—	—	—	—	—
	005	—	—	—	—	—	—	—	—	—	—	—	—
	008	—	—	—	—	—	—	—	—	—	—	—	—
	011	—	—	—	—	—	—	—	—	—	—	—	—
100	052	—	—	—	—	—	—	—	—	—	—	—	—
	053	—	—	—	—	—	—	—	—	—	—	—	—
	054	—	—	—	—	—	—	—	—	—	—	—	—
	059	—	—	—	—	—	—	—	—	—	—	—	—
	060	—	—	1+	—	—	—	—	—	—	—	—	—

— : Not observed, 1+ : A few in some fields.
Crystals : Mg (ammonium magnesium phosphate), Ca (calcium carbonate), Ams (amorphous).
Epithelial cells : Sq (squamous), R (round), S (spindle).
Casts : G (granule), H (hyaline), W (waxy).

Appendix 25 - 1 Individual hematological findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	RBC (10^4/μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	003	847	15.1	46.8	55	17.8	32.3	26.0	15.6
	004	931	16.5	52.2	56	17.7	31.6	26.9	15.7
	007	851	15.4	48.1	57	18.1	32.0	32.5	13.3
	010	839	14.9	46.6	56	17.8	32.0	29.9	16.8
	012	857	15.3	47.5	55	17.9	32.2	22.1	15.7
	Mean	865	15.4	48.2	56	17.9	32.0	27.5	15.4
0.8	013	813	15.2	46.5	57	18.7	32.7	25.4	15.2
	015	929	15.6	48.6	52	16.8	32.1	21.6	16.0
	016	865	15.7	49.8	58	18.2	31.5	43.5	15.2
	021	970	16.3	49.7	51	16.8	32.8	21.7	15.1
	024	920	15.6	48.1	52	17.0	32.4	21.1	15.7
	Mean	899	15.7	48.5	54	17.5	32.3	26.7	15.4
4	025	882	15.9	48.4	55	18.0	32.9	15.8	15.4
	029	968	16.4	51.2	53	16.9	32.0	12.8	16.0
	032	924	16.7	53.1	58	18.1	31.5	22.2	15.7
	034	869	15.2	47.4	55	17.5	32.1	25.8	14.7
	035	856	15.2	46.4	54	17.8	32.8	28.1	15.7
	Mean	900	15.9	49.3	55	17.7	32.3	20.9	15.5
20	040	837	15.2	47.9	57	18.2	31.7	22.8	14.8
	041	907	16.1	51.3	57	17.8	31.4	11.6	15.5
	043	818	14.8	46.8	57	18.1	31.6	25.9	15.0
	044	804	15.5	49.0	61	19.3	31.6	20.7	15.1
	047	862	15.5	48.2	56	18.0	32.2	18.9	13.6
	Mean	846	15.4	48.6	58	18.3	31.7	20.0	14.8
100	051	836	14.2	46.3	55	17.0	30.7	31.7	14.8
	054	809	14.0	45.0	56	17.3	31.1	22.7	14.6
	055	905	15.2	48.5	54	16.8	31.3	28.1	15.0
	057	844	14.5	45.1	53	17.2	32.2	29.2	14.9
	058	828	14.0	44.6	54	16.9	31.4	26.2	14.3
	Mean	844	14.4	45.9	54	17.0	31.3	27.6	14.7

Appendix 25 - 2 Individual hematological findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	003	20.2	129	69	0.0	1.3	25.5	67.0	6.2
	004	19.4	119	63	0.0	1.4	14.4	79.5	4.7
	007	16.9	151	81	0.0	1.7	30.5	63.9	3.9
	010	18.4	118	85	0.0	1.4	19.0	73.5	6.1
	012	18.4	118	101	0.0	0.9	20.7	73.0	5.4
	Mean	18.7	127	80	0.0	1.3	22.0	71.4	5.3
0.8	013	17.5	108	64	0.0	1.6	18.2	75.9	4.3
	015	18.3	135	61	0.0	0.8	27.4	67.9	3.9
	016	18.3	118	107	0.0	0.5	8.9	84.2	6.4
	021	16.1	113	89	0.0	0.8	24.9	67.9	6.4
	024	19.6	147	145	0.0	1.3	13.1	81.7	3.9
	Mean	18.0	124	93	0.0	1.0	18.5	75.5	5.0
4	025	21.2	134	60	0.0	0.7	18.7	76.9	3.7
	029	18.0	163	64	0.0	1.1	17.8	77.0	4.1
	032	19.5	118	63	0.0	1.8	19.4	75.1	3.7
	034	16.4	123	100	0.0	0.5	10.8	83.7	5.0
	035	18.4	163	135	0.0	1.1	23.5	69.0	6.4
	Mean	18.7	140	84	0.0	1.0	18.0	76.3	4.6
20	040	18.4	139	72	0.0	0.8	13.1	82.6	3.5
	041	19.8	124	99	0.0	1.0	22.5	72.6	3.9
	043	16.9	152	114	0.0	1.0	12.3	83.6	3.1
	044	16.4	140	73	0.0	1.8	13.6	79.9	4.7
	047	14.6	140	81	0.0	1.4	9.3	83.2	6.1
	Mean	17.2	139	88	0.0	1.2	14.2	80.4	4.3
100	051	21.2	130	110	0.0	1.0	20.1	74.1	4.8
	054	18.6	146	91	0.0	0.6	13.3	81.5	4.6
	055	17.9	144	88	0.0	0.7	20.3	73.8	5.2
	057	18.2	142	114	0.0	0.9	19.0	74.8	5.3
	058	17.8	150	78	0.0	0.6	21.6	72.7	5.1
	Mean	18.7	142	96	0.0	0.8	18.9	75.4	5.0

Appendix 25 - 3 Individual hematological findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	RBC (10^4/μL)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	001	905	15.5	48.0	53	17.1	32.3	15.9	14.8
	002	839	14.5	46.3	55	17.3	31.3	36.2	15.6
	005	908	15.6	47.5	52	17.2	32.8	25.1	16.0
	008	939	15.7	48.0	51	16.7	32.7	23.8	15.1
	011	872	15.9	49.6	57	18.2	32.1	18.0	17.0
	Mean	893	15.4	47.9	54	17.3	32.2	23.8	15.7
100	052	797	13.9	43.8	55	17.4	31.7	56.9	14.9
	053	835	13.9	44.2	53	16.6	31.4	37.6	15.8
	056	840	13.9	43.8	52	16.5	31.7	39.1	14.2
	059	772	14.0	44.4	58	18.1	31.5	54.4	15.5
	060	756	13.7	43.9	58	18.1	31.2	59.9	13.4
	Mean	800	13.9	44.0	55	17.3	31.5	49.6	14.8

Appendix 25 - 4 Individual hematological findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	001	20.0	116	129	0.0	0.9	20.1	75.0	5.1
	002	20.0	125	102	0.0	1.0	14.9	77.5	6.6
	005	17.5	106	74	0.0	0.8	15.9	79.5	3.8
	008	19.4	165	92	0.0	1.6	18.8	75.6	4.0
	011	18.4	97	88	0.0	1.3	27.2	63.9	7.6
	Mean	19.1	122	97	0.0	1.1	19.4	74.3	5.4
100	052	18.6	147	77	0.0	1.4	16.6	77.7	4.3
	053	18.6	166	114	0.0	1.0	20.4	73.9	4.7
	056	18.2	167	86	0.0	0.7	9.8	85.1	4.4
	059	19.3	137	88	0.0	0.7	26.3	68.8	4.2
	060	15.8	105	91	0.0	14.8	23.7	56.3	5.2
	Mean	18.1	144	91	0.0	3.7	19.4	72.4	4.6

Appendix 26 - 1 Individual hematological findings of female rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	504	680	13.3	42.5	63	19.6	31.3	97.4	17.5
	505	731	13.3	43.7	60	18.2	30.4	72.7	16.5
	507	708	13.6	43.4	61	19.2	31.3	82.1	16.6
	508	714	13.6	43.2	61	19.0	31.5	96.0	17.8
	511	733	13.6	43.7	60	18.6	31.1	59.3	17.2
	Mean	713	13.5	43.3	61	18.9	31.1	81.5	17.1
0.8	519	694	12.9	41.5	60	18.6	31.1	92.8	18.9
	520	652	13.1	42.3	65	20.1	31.0	106.5	18.9
	523	722	14.4	45.2	63	19.9	31.9	98.4	16.4
	525	702	13.4	40.8	58	19.1	32.8	61.4	16.8
	528	684	13.2	41.2	60	19.3	32.0	73.8	17.8
	Mean	691	13.4	42.2	61	19.4	31.8	86.6	17.8
4	532	689	13.1	42.6	62	19.0	30.8	83.1	18.8
	534	674	13.3	42.1	63	19.7	31.6	72.8	17.4
	535	687	13.3	41.3	60	19.4	32.2	80.2	16.8
	536	713	13.4	42.1	59	18.8	31.8	71.9	18.4
	538	696	13.6	43.6	63	19.5	31.2	86.7	18.1
	Mean	692	13.3	42.3	61	19.3	31.5	78.9	17.9
20	544	701	13.1	42.6	61	18.7	30.8	68.1	17.9
	545	737	13.6	43.3	59	18.5	31.4	55.0	17.5
	546	657	13.0	42.2	64	19.8	30.8	91.7	16.7
	548	587	12.1	40.0	68	20.6	30.3	141.2	17.2
	551	624	11.9	38.6	62	19.1	30.8	127.5	18.5
	Mean	661	12.7	41.3	63	19.3	30.8	96.7	17.6
100	554	624	12.1	40.4	65	19.4	30.0	128.2	18.0
	557	592	12.2	40.2	68	20.6	30.3	108.4	18.1
	558	682	12.9	42.4	62	18.9	30.4	77.9	18.1
	561	621	12.1	39.9	64	19.5	30.3	80.1	18.2
	564	626	11.6	37.9	61	18.5	30.6	114.5	17.4
	Mean	629	12.2	40.2	64	19.4	30.3	101.8	18.0

Appendix 26 - 2 Individual hematological findings of female rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	504	16.3	148	65	0.0	0.5	27.7	69.2	1.7
	505	18.4	190	64	0.0	0.6	17.3	76.2	5.9
	507	16.0	192	120	0.0	1.3	27.2	67.7	4.6
	508	16.3	156	75	0.0	0.4	18.2	78.1	3.3
	511	16.6	152	57	0.0	0.7	31.8	64.9	2.6
	Mean	16.7	168	76	0.0	0.7	24.4	71.2	3.6
0.8	519	17.0	169	73	0.0	1.0	26.9	66.5	5.6
	520	17.6	137	75	0.0	0.4	26.3	68.1	5.2
	523	16.9	125	51	0.0	1.0	28.3	62.3	8.4
	525	15.6	141	73	0.0	1.5	25.8	62.7	10.0
	528	17.4	152	70	0.0	0.6	30.1	65.0	4.3
	Mean	16.9	145	68	0.0	0.9	27.5	64.9	6.7
4	532	16.3	146	97	0.0	0.5	34.9	60.2	4.4
	534	17.1	130	82	0.0	0.2	33.0	64.8	2.0
	535	16.9	154	72	0.0	0.6	30.6	64.5	4.3
	536	16.2	146	66	0.0	1.2	30.1	64.6	4.1
	538	15.6	143	90	0.0	0.7	19.6	77.0	2.7
	Mean	16.4	144	81	0.0	0.6	29.6	66.2	3.5
20	544	15.9	143	53	0.0	0.6	29.2	61.9	8.3
	545	17.0	144	68	0.0	1.0	30.0	64.3	4.7
	546	14.2	172	111	0.0	0.5	39.8	56.4	3.3
	548	16.0	140	81	0.0	0.7	50.3	45.4	3.6
	551	16.5	134	76	0.0	0.3	34.5	63.6	1.6
	Mean	15.9	147	78	0.0	0.6	36.8	58.3	4.3
100	554	16.0	157	117	0.0	0.8	37.7	60.0	1.5
	557	16.4	141	105	0.0	0.7	36.4	59.3	3.6
	558	16.1	112	87	0.0	0.5	27.5	68.8	3.2
	561	16.3	136	60	0.0	0.7	31.4	64.4	3.5
	564	16.2	132	71	0.0	1.8	41.3	52.0	4.9
	Mean	16.2	136	88	0.0	0.9	34.9	60.9	3.3

Appendix 26 - 3 Individual hematological findings of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)
0	513	847	14.8	44.0	52	17.5	33.6	24.4	15.5
	514	744	13.6	41.2	55	18.3	33.0	37.0	14.9
	515	761	13.5	41.5	55	17.7	32.5	27.7	16.2
	516	813	15.0	45.7	56	18.5	32.8	23.2	15.4
	517	858	14.9	45.5	53	17.4	32.7	31.2	16.5
	Mean	805	14.4	43.6	54	17.9	32.9	28.7	15.7
100	566	786	14.5	45.0	57	18.4	32.2	25.3	16.7
	567	831	15.5	48.6	59	18.7	31.9	22.9	17.3
	568	799	15.0	45.8	57	18.8	32.8	29.5	15.2
	569	826	15.7	47.9	58	19.0	32.8	27.6	15.8
	570	744	14.2	44.0	59	19.1	32.3	54.8	15.8
	Mean	797	15.0	46.3	58	18.8	32.4	32.0	16.2

Appendix 26 - 4 Individual hematological findings of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	APTT (sec)	Plat. (10^4/μL)	WBC (10^2/μL)	Differential leukocyte counts (%)				
					Baso.	Eosin.	Neutro.	Lymph.	Mono.
0	513	17.7	129	38	0.0	1.6	24.0	71.5	1.1
	514	16.7	134	33	0.0	1.5	32.5	63.9	2.1
	515	14.8	135	35	0.0	1.7	22.7	73.6	2.0
	516	17.5	122	44	0.0	2.5	21.4	73.6	2.5
	517	16.6	119	41	0.0	1.5	26.3	70.0	2.2
	Mean	16.7	128	38	0.0	1.8	25.4	70.5	2.0
100	566	17.4	113	34	0.0	2.4	16.5	78.7	2.4
	567	16.7	92	31	0.0	2.6	27.3	66.2	3.9
	568	16.0	118	57	0.0	1.2	19.1	77.6	2.1
	569	17.5	124	33	0.0	0.9	23.5	73.8	1.8
	570	16.4	131	39	0.0	1.8	23.7	68.9	5.6
	Mean	16.8	116	39	0.0	1.8	22.0	73.0	3.2

Appendix 27 - 1 Individual blood biochemical findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	003	269	60	36	283	0.78	13	5.72	2.60	0.83	65
	004	231	61	31	337	0.66	35	6.35	3.40	1.15	81
	007	351	69	32	442	0.83	30	5.78	2.88	0.99	65
	010	276	80	35	415	1.07	36	5.49	2.33	0.74	63
	012	301	65	30	264	0.62	43	5.33	2.50	0.88	76
	Mean	286	67	33	348	0.79	31	5.73	2.74	0.92	70
0.8	013	606	90	44	454	1.65	28	5.41	2.48	0.85	44
	015	359	64	42	603	0.94	18	5.78	2.68	0.86	61
	016	293	68	38	513	1.15	49	5.86	3.00	1.05	53
	021	569	86	32	273	1.84	30	5.98	2.92	0.95	69
	024	264	59	22	341	0.97	55	5.67	2.54	0.81	67
	Mean	418	73	36	437	1.31	36	5.74	2.72	0.90	59
4	025	327	73	31	400	0.42	36	5.47	2.65	0.94	61
	029	302	54	27	479	1.19	25	5.52	2.82	1.04	56
	032	277	63	27	432	1.51	52	6.12	2.89	0.89	56
	034	376	70	29	429	1.70	37	5.72	2.93	1.05	74
	035	321	74	24	354	1.11	35	5.64	2.69	0.91	48
	Mean	321	67	28	419	1.19	37	5.69	2.80	0.97	59
20	040	424	68	36	998	0.88	79	5.35	2.83	1.12	72
	041	368	61	25	613	1.21	39	5.59	2.91	1.09	41
	043	288	69	31	911	0.90	112	5.84	3.19	1.20	52
	044	338	66	27	508	1.40	80	5.62	2.63	0.88	69
	047	641	98	54	837	1.88	140	5.57	2.71	0.95	62
	Mean	412	72	35	773	1.25	90	5.59	2.85	1.05	59
100	051	485	88	67	1077	1.16	210	7.04	4.18	1.46	100
	054	378	77	47	972	1.32	121	6.04	3.59	1.47	73
	055	479	103	71	855	1.10	83	6.19	3.53	1.33	56
	057	369	88	46	938	1.35	168	6.20	3.62	1.40	61
	058	304	82	35	1037	0.78	230	5.91	3.32	1.28	60
	Mean	403	88	53	976	1.14	162	6.28	3.65	1.39	70

Appendix 27 - 2 Individual blood biochemical findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	003	79	160	13.0	0.38	0.24	9.6	7.1	147	4.43	107
	004	82	153	12.7	0.36	0.28	10.8	8.9	150	6.54	103
	007	34	131	12.3	0.27	0.25	9.6	7.1	146	4.88	107
	010	50	145	13.7	0.43	0.26	9.8	7.6	147	4.69	107
	012	51	146	11.5	0.33	0.24	10.0	6.9	146	4.46	108
	Mean	59	147	12.6	0.35	0.25	10.0	7.5	147	5.00	106
0.8	013	36	150	11.1	0.38	0.30	9.7	7.4	148	4.62	107
	015	32	140	8.7	0.31	0.28	9.3	6.8	148	4.41	108
	016	53	152	11.9	0.31	0.23	10.1	7.6	147	4.23	105
	021	70	185	9.8	0.31	0.27	11.1	9.4	149	6.07	102
	024	32	171	10.1	0.37	0.25	9.9	7.4	145	4.89	105
	Mean	45	160	10.3	0.34	0.27	10.0	7.7	147	4.84	105
4	025	21	150	13.1	0.35	0.27	9.4	6.7	146	4.21	107
	029	29	135	11.5	0.31	0.27	9.7	7.7	148	4.21	105
	032	22	144	11.5	0.38	0.29	10.5	8.4	150	6.48	104
	034	33	143	12.1	0.26	0.24	10.1	7.6	147	4.92	104
	035	38	155	9.7	0.29	0.24	9.8	6.7	145	4.75	106
	Mean	29	145	11.6	0.32	0.26	9.9	7.4	147	4.91	105
20	040	41	157	11.9	0.28	0.24	10.0	7.9	146	4.23	105
	041	27	159	14.8	0.29	0.24	9.9	7.1	147	5.06	106
	043	38	169	11.0	0.33	0.27	10.8	8.7	150	5.50	104
	044	21	156	12.0	0.37	0.30	10.3	8.1	147	5.12	106
	047	42	165	15.5	0.33	0.25	9.8	8.7	145	5.39	104
	Mean	34	161	13.0	0.32	0.26	10.2	8.1	147	5.06	105
100	051	124	160	11.5	0.32	0.23	11.5	8.7	149	5.79	100
	054	22	178	12.3	0.30	0.28	10.7	9.2	148	5.58	104
	055	40	167	13.1	0.26	0.23	10.1	8.2	146	5.31	104
	057	49	165	13.5	0.33	0.26	9.9	8.6	146	5.18	104
	058	46	158	13.7	0.28	0.26	9.5	7.5	146	4.83	104
	Mean	56	166	12.8	0.30	0.25	10.3	8.4	147	5.34	103

Appendix 27 - 3 Individual blood biochemical findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	001	264	74	51	384	0.71	45	5.56	2.49	0.81	70
	002	250	75	41	231	1.34	15	5.23	2.66	1.04	31
	005	424	87	39	316	0.76	23	5.20	2.48	0.91	61
	008	368	88	44	400	1.40	42	5.86	2.57	0.78	64
	011	287	104	58	277	0.91	26	5.27	2.50	0.90	46
	Mean	319	86	47	322	1.02	30	5.42	2.54	0.89	54
100	052	354	80	65	349	0.67	53	6.28	3.18	1.03	105
	053	305	66	41	432	1.09	94	6.03	2.83	0.88	122
	056	412	141	103	433	0.43	34	6.10	3.52	1.36	136
	059	417	97	74	327	0.68	29	5.94	3.11	1.10	117
	060	633	247	274	502	1.72	39	6.42	3.34	1.08	134
	Mean	424	126	111	409	0.92	50	6.15	3.20	1.09	123

Appendix 27 - 4 Individual blood biochemical findings of male rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	001	39	144	14.6	0.33	0.20	9.4	6.6	148	4.14	109
	002	22	130	8.7	0.38	0.26	10.2	7.3	149	4.25	106
	005	47	137	18.4	0.33	0.25	9.0	5.6	146	4.56	110
	008	39	149	14.5	0.33	0.22	9.8	5.7	148	4.31	107
	011	11	146	13.9	0.37	0.24	9.8	7.4	149	4.16	108
	Mean	32	141	14.0	0.35	0.23	9.6	6.5	148	4.28	108
100	052	37	143	16.4	0.31	0.28	10.0	6.8	147	5.25	108
	053	74	171	19.3	0.41	0.26	9.8	6.7	145	4.76	106
	056	72	160	13.0	0.30	0.24	10.3	6.9	147	4.60	106
	059	55	162	15.5	0.28	0.27	10.0	7.2	148	5.05	108
	060	68	139	19.3	0.30	0.30	10.5	7.5	146	5.30	105
	Mean	61	155	16.7	0.32	0.27	10.1	7.0	147	4.99	107

Appendix 28 - 1 Individual blood biochemical findings of female rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	504	583	92	77	337	0.80	303	5.85	3.15	1.17	81
	505	356	74	75	646	0.94	152	5.88	3.02	1.06	66
	507	475	98	65	332	1.06	365	5.48	2.63	0.92	52
	508	343	63	56	389	0.72	252	6.16	3.30	1.15	67
	511	284	217	81	547	1.31	378	6.55	3.37	1.06	91
	Mean	408	109	71	450	0.97	290	5.98	3.09	1.07	71
0.8	519	333	76	39	318	0.57	326	5.69	3.08	1.18	70
	520	483	105	84	533	0.76	144	5.12	2.36	0.86	59
	523	299	70	56	283	1.05	580	6.21	3.29	1.13	82
	525	399	96	61	324	0.77	303	6.18	3.39	1.22	67
	528	366	90	49	157	0.91	213	6.21	3.24	1.09	46
	Mean	376	87	58	323	0.81	313	5.88	3.07	1.10	65
4	532	307	98	102	312	1.26	465	5.79	2.65	0.84	67
	534	389	124	92	531	0.87	304	5.69	2.70	0.90	97
	535	627	111	55	284	1.30	313	6.05	2.85	0.89	66
	536	348	89	89	350	0.80	184	5.30	2.64	0.99	71
	538	339	75	47	360	0.84	334	5.33	2.42	0.83	66
	Mean	402	99	77	367	1.01	320	5.63	2.65	0.89	73
20	544	343	71	46	417	0.72	207	5.73	2.78	0.94	64
	545	282	88	68	459	1.50	236	5.64	2.72	0.93	74
	546	293	71	71	446	0.75	179	5.52	2.88	1.09	74
	548	410	105	66	330	0.73	322	5.51	2.77	1.01	71
	551	509	153	92	598	0.74	199	5.89	3.08	1.10	61
	Mean	367	98	69	450	0.89	229	5.66	2.85	1.01	69
100	554	321	94	65	405	0.71	212	5.50	2.68	0.95	65
	557	337	96	76	356	1.21	162	5.28	2.60	0.97	60
	558	567	89	67	297	0.57	146	5.44	2.62	0.93	68
	561	283	64	44	302	0.47	289	5.61	3.17	1.30	53
	564	322	105	70	353	0.70	327	5.88	3.06	1.09	87
	Mean	366	90	64	343	0.73	227	5.54	2.83	1.05	67

Appendix 28 - 2 Individual blood biochemical findings of female rats treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	504	52	121	19.4	0.46	0.27	10.5	9.4	146	4.66	109
	505	108	157	20.4	0.46	0.22	10.9	8.7	149	4.53	105
	507	83	143	16.4	0.37	0.27	10.0	8.3	148	4.21	111
	508	168	159	21.6	0.49	0.30	10.8	8.0	144	4.62	104
	511	110	152	25.4	0.50	0.36	11.2	8.8	151	4.40	103
	Mean	104	146	20.6	0.46	0.28	10.7	8.6	148	4.48	106
0.8	519	112	163	22.5	0.45	0.21	10.6	7.2	148	4.14	112
	520	174	148	24.7	0.50	0.31	10.9	11.1	146	4.08	103
	523	73	157	17.8	0.42	0.24	10.5	9.1	147	4.57	105
	525	95	149	23.1	0.45	0.25	11.8	11.6	147	4.24	107
	528	77	140	12.0	0.41	0.26	10.3	7.7	148	3.97	109
	Mean	106	151	20.0	0.45	0.25	10.8	9.3	147	4.20	107
4	532	75	143	15.1	0.45	0.28	10.0	7.6	147	4.24	109
	534	91	154	19.0	0.42	0.24	11.1	9.4	149	3.90	106
	535	81	124	15.4	0.41	0.28	10.7	9.0	149	6.34	109
	536	99	143	16.8	0.41	0.28	9.9	7.4	145	4.76	110
	538	61	152	16.2	0.36	0.25	10.5	9.3	150	4.39	112
	Mean	81	143	16.5	0.41	0.27	10.4	8.5	148	4.73	109
20	544	74	143	19.8	0.43	0.22	10.2	8.3	148	4.16	111
	545	72	150	29.8	0.56	0.32	10.8	8.2	148	3.78	109
	546	165	151	25.4	0.53	0.28	10.8	8.3	148	4.05	109
	548	66	164	22.0	0.48	0.27	11.6	11.3	149	4.70	109
	551	94	144	23.0	0.54	0.28	11.5	9.8	145	4.78	105
	Mean	94	150	24.0	0.51	0.27	11.0	9.2	148	4.29	109
100	554	58	142	19.3	0.38	0.33	10.1	9.1	143	4.55	107
	557	120	142	22.2	0.44	0.21	10.5	9.6	149	3.58	109
	558	56	146	21.3	0.43	0.23	10.5	9.7	146	4.22	108
	561	77	162	16.6	0.38	0.30	10.1	7.6	146	3.57	110
	564	79	146	19.6	0.46	0.22	10.6	8.2	144	5.14	108
	Mean	78	148	19.8	0.42	0.26	10.4	8.8	146	4.21	108

Appendix 28 - 3 Individual blood biochemical findings of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	LDH (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	γ-GTP (IU/L)	ChE (IU/L)	T.P. (g/dL)	Alb. (g/dL)	A/G	T-Cho. (mg/dL)
0	513	357	82	36	86	0.87	528	6.69	3.68	1.22	83
	514	358	82	41	142	0.99	1330	6.62	3.61	1.20	87
	515	338	106	60	286	1.07	620	6.37	3.28	1.06	79
	516	320	74	35	134	1.29	818	6.59	3.32	1.02	91
	517	349	67	22	129	2.28	494	6.03	3.22	1.15	97
	Mean	344	82	39	155	1.30	758	6.46	3.42	1.13	87
100	566	334	65	25	240	2.23	379	5.67	2.72	0.92	70
	567	288	70	33	225	2.45	244	6.21	3.00	0.93	72
	568	359	61	35	109	0.69	592	5.68	3.02	1.14	112
	569	387	101	49	146	1.03	505	6.78	3.90	1.35	105
	570	374	59	31	170	1.53	280	6.09	3.21	1.11	88
	Mean	348	71	35	178	1.59	400	6.09	3.17	1.09	89

Appendix 28 - 4 Individual blood biochemical findings of female rats of the satellite group treated orally with 2-(2H-benzotriazol-2-yl)-6-sec-buty-4-tert-butylphenol in the combined repeat dose and reproductive/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	T.G. (mg/dL)	Glu. (mg/dL)	BUN (mg/dL)	Crea. (mg/dL)	T-Bil. (mg/dL)	Ca (mg/dL)	P (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
0	513	23	161	16.1	0.35	0.26	10.5	5.3	147	4.64	104
	514	27	149	14.6	0.31	0.27	10.1	5.2	146	4.67	106
	515	20	146	21.2	0.45	0.26	10.3	6.1	149	4.52	108
	516	25	154	15.7	0.39	0.27	10.1	5.6	147	4.61	105
	517	11	137	16.5	0.41	0.28	9.8	6.3	146	4.63	104
	Mean	21	149	16.8	0.38	0.27	10.2	5.7	147	4.61	105
100	566	17	143	18.0	0.38	0.30	9.6	6.0	148	5.13	106
	567	32	156	19.2	0.45	0.22	9.8	5.0	148	5.05	101
	568	55	146	17.9	0.37	0.26	10.0	5.1	145	4.91	107
	569	17	162	20.9	0.41	0.23	10.7	6.8	147	4.61	103
	570	20	149	19.5	0.38	0.30	9.7	6.3	147	4.80	104
	Mean	28	151	19.1	0.40	0.26	10.0	5.8	147	4.90	104

Appendix 29-1 Individual pathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy			Histology
0	001	NAD			Not examined
	002	NAD			Not examined
	003	NAD	a	Heart	: Myocardial degeneration/fibrosis +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, pigment, brown +
	004	NAD	a	Lung	: Hemorrhage +
				Kidney	: Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, pigment, brown +
	005	NAD			Not examined
	006	NAD			Not examined
	007	NAD	a	Liver	: Microgranuloma +
				Kidney	: Hyaline droplet, proximal tubular epithelium +
					Cast, hyaline, unilateral +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, pigment, brown +
	008	NAD			Not examined
	009	NAD			Not examined
	010	NAD	a	Lung	: Accumulation, foam cell +
				Kidney	: Basophilic tubule +
					Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, pigment, brown +
	011	NAD			Not examined
	012	NAD	a	Heart	: Myocardial degeneration/fibrosis +
				Glandular stomach	: Dilatation, fundic gland +
				Kidney	: Hyaline droplet, proximal tubular epithelium +
					Cyst, solitary, unilateral +
				Prostate	: Cellular infiltration, lymphocyte, interstitium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, pigment, brown +

NAD : No abnormalities were detected. + : Slight.

a : Organs of the brain, pituitary, thyroid, parathyroid, thymus, trachea, lung, heart, stomach, small intestine, large intestine, liver, spleen, kidney, adrenal, urinary bladder, testis, epididymis, prostate, seminal vesicle, spinal cord, sciatic nerve, bone marrow and lymph nodes were examined.

Appendix 29-2 Individual pathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy		Not examined
0.8	013	NAD	Liver	: Necrosis, focal +
	014	NAD		Not examined
	015	NAD	Liver	: NAD
	016	NAD	Liver	: NAD
	017	NAD		Not examined
	018	NAD		Not examined
	019	NAD		Not examined
	020	NAD		Not examined
	021	NAD	Liver	: NAD
	022	NAD		Not examined
	023	NAD		Not examined
	024	NAD	Liver	: NAD

NAD : No abnormalities were detected. + : Slight.

Appendix 29-3 Individual pathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy	Histology	
4	025	NAD	Liver	: NAD
	026	NAD		Not examined
	027	NAD		Not examined
	028	NAD		Not examined
	029	NAD	Liver	: NAD
	030	NAD		Not examined
	031	NAD		Not examined
	032	NAD	Liver	: Microgranuloma +
	033	NAD		Not examined
	034	NAD	Liver	: Necrosis, focal +
	035	NAD	Liver	: NAD
	036	NAD		Not examined

NAD : No abnormalities were detected. + : Slight.

Appendix 29-4 Individual pathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number		Necropsy			Histology
20	037	FP	NAD		Testis	: NAD
					Epididymis	: NAD
					Prostate	: NAD
					Seminal vesicle	: NAD
					Pituitary	: NAD
	038		NAD			Not examined
	039		NAD			Not examined
	040		NAD	c	Liver	:
	041		NAD	c	Liver	:
	042		NAD			Not examined
	043		NAD	c	Liver	:
	044		NAD	c	Liver	:
	045		NAD			Not examined
	046		NAD			Not examined
	047		NAD	c	Liver	:
	048		NAD			Not examined

NAD : No abnormalities were detected. + : Slight.; ++ : Moderate. FP : Failed to cause pregnancy.
c : Organs of the liver was examined.

Appendix 29-5 Individual pathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy		Histology
100	049	NAD		Not examined
	050	NAD		Not examined
	051	Liver : Large +	a Lung	: Accumulation, foam cell +
			Liver	: Hypertrophy, hepatocyte, centrilobular ++
			Kidney	: Hyaline droplet, proximal tubular epithelium +
				Basophilic tubule, unilateral +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	052	NAD		Not examined
	053	NAD		Not examined
	054	Liver : Large +	a Heart	: Myocardial degeneration/fibrosis +
			Liver	: Hypertrophy, hepatocyte, centrilobular ++
				Necrosis, focal +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	055	NAD	a Liver	: Hypertrophy, hepatocyte, centrilobular ++
				Necrosis, focal +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	056	NAD		Not examined
	057	NAD	a Lung	: Accumulation, foam cell +
			Liver	: Hypertrophy, hepatocyte, centrilobular ++
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	058	NAD	a Heart	: Myocardial degeneration/fibrosis +
			Glandular stomach	: Dilatation, fundic gland +
			Liver	: Hypertrophy, hepatocyte, centrilobular ++
			Kidney	: Hyaline droplet, proximal tubular epithelium +
				Cast, hyaline, unilateral +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	059	NAD		Not examined
	060	NAD		Not examined

NAD : No abnormalities were detected. + : Slight; ++ : Moderate.

a : Organs of the brain, pituitary, thyroid, parathyroid, thymus, trachea, lung, heart, stomach, small intestine, large intestine, liver, spleen, kidney, adrenal, urinary bladder, testis, epididymis, prostate, seminal vesicle, spinal cord, sciatic nerve, bone marrow and lymph nodes were examined.

Appendix 29-6 Individual pathological findings of male rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthy-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	Necropsy	Histology	
0	001	NAD	Liver	: NAD
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	002	NAD	Liver	: Necrosis, focal +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	005	NAD	Liver	: NAD
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	008	NAD	Liver	: Microgranuloma +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	011	NAD	Liver	: NAD
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
100	052	NAD	Liver	: Microgranuloma +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	053	NAD	Liver	: NAD
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +
	056	NAD	Liver	: Hypertrophy, hepatocyte, centrilobular +
			Spleen	: Hematopoiesis, extramedullary ++
				Deposit, pigment, brown +
	059	NAD	Liver	: Hypertrophy, hepatocyte, centrilobular +
			Spleen	: Hematopoiesis, extramedullary ++
				Deposit, pigment, brown +
	060	NAD	Liver	: NAD
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, pigment, brown +

NAD : No abnormalities were detected. + : Slight.

Appendix 30-1 Individual pathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthyl-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy			Histology
0	501	NAD			Not examined
	502	NAD			Not examined
	503	NAD			Not examined
	504	NAD	b	Spleen	: Hematopoiesis, extramedullary ++ Deposit, pigment, brown +
	505	NAD	b	Spleen	: Hematopoiesis, extramedullary + Deposit, pigment, brown +
	506	NAD			Not examined
	507	NAD	b	Kidney Spleen	: Dilatation, distal tubular, unilateral + : Hematopoiesis, extramedullary + Deposit, pigment, brown ++
	508	NAD	b	Lung Spleen	: Mineralization, artery + : Hematopoiesis, extramedullary + Deposit, pigment, brown ++
	509	NAD			Not examined
	510	NAD			Not examined
	511	NAD	b	Spleen	: Hematopoiesis, extramedullary + Deposit, pigment, brown +
	512	NAD			Not examined

NAD : No abnormalities were detected. + : Slight. ++ : Moderate.

b : Organs of the brain, pituitary, thyroid, parathyroid, thymus, trachea, lung, heart, stomach, small intestine, large intestine, liver, spleen, kidney, adrenal, urinary bladder, ovary, uterus, mammary gland, testis, spinal cord, sciatic nerve, bone marrow and lymph nodes were examined.

Appendix 30-2 Individual pathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthyl-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy	Histology
0.8	518	NAD	Not examined
	519	NAD	Liver : NAD
	520	NAD	Liver : NAD
	521	NAD	Not examined
	522	NAD	Not examined
	523	NAD	Liver : Microgranuloma +
	524	NAD	Not examined
	525	NAD	Liver : NAD
	526	NAD	Not examined
	527	NAD	Not examined
	528	NAD	Liver : NAD
	529	NAD	Not examined

NAD : No abnormalities were detected. + : Slight.

Appendix 30-3 Individual pathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthyl-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	Necropsy		Histology
4	530	NAD		Not examined
	531	NAD		Not examined
	532	NAD	Liver	: NAD
	533	NAD		Not examined
	534	NAD	Liver	: NAD
	535	NAD	Liver	: NAD
	536	NAD	Liver	: NAD
	537	NAD		Not examined
	538	NAD	Liver	: NAD
	539	NAD		Not examined
	540	NAD		Not examined
	541	NAD		Not examined

NAD : No abnormalities were detected. + : Slight.

Appendix 30-4 Individual pathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthyl-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number		Necropsy			Histology
20	542	NP	NAD		Overy	: NAD
					Uterus	: NAD
					Pituitary	: NAD
	543		NAD			Not examined
	544		NAD	c	Liver	:
	545		NAD	c	Liver	:
	546		NAD	c	Liver	:
	547		NAD			Not examined
	548		NAD	c	Liver	:
	549		NAD			Not examined
	550		NAD			Not examined
	551		NAD	c	Liver	:
	552		NAD			Not examined
	553		NAD			Not examined

NAD : No abnormalities were detected. + : Slight. ++ : Moderate.
c : Organs of the liver was examined.
NP : Non-pregnant.

Appendix 30-5 Individual pathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthyl-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number		Necropsy			Histology
100	554		NAD	b	Lung	: Accumulation, foam cell +
					Spleen	: Hematopoiesis, extramedullary +
						Deposit, pigment, brown +
	555		NAD			Not examined
	556		NAD			Not examined
	557		NAD	b	Liver	: Hypertrophy, hepatocyte, centrilobular +
					Spleen	: Hematopoiesis, extramedullary ++
						Deposit, pigment, brown ++
	558		NAD	b	Lung	: Accumulation, foam cell +
					Spleen	: Hematopoiesis, extramedullary +
						Deposit, pigment, brown +
	559		NAD			Not examined
	560	KL	NAD		Overy	: NAD
					Uterus	: NAD
					Pituitary	: NAD
					Mammary gland	: NAD
	561		NAD	b	Spleen	: Hematopoiesis, extramedullary +
						Deposit, pigment, brown ++
	562		NAD			Not examined
	563		NAD			Not examined
	564		NAD	b	Liver	: Hypertrophy, hepatocyte, centrilobular +
					Kidney	: Dilatation, distal tubular, unilateral +
					Spleen	: Hematopoiesis, extramedullary +
						Deposit, pigment, brown +
	565		NAD			Not examined

NAD : No abnormalities were detected. + : Slight. ++ : Moderate.

b : Organs of the brain, pituitary, thyroid, parathyroid, thymus, trachea, lung, heart, stomach, small intestine, large intestine, liver, spleen, kidney, adrenal, urinary bladder, ovary, uterus, mammary gland, spinal cord, sciatic nerve, bone marrow and lymph nodes were examined.

KL : Killed because all pups died after delivery.

Appendix 30-6 Individual pathological findings of female rats treated orally with 2-(2H-Benzotriazole-2-yl)-6-sec-buthyl-4-ter-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	Necropsy	Histology	
0	513	NAD	Liver	: NAD
	514	NAD	Liver	: Microgranuloma +
	515	NAD	Liver	: NAD
	516	NAD	Liver	: NAD
	517	NAD	Liver	: NAD
100	566	NAD	Liver	: NAD
	567	NAD	Liver	: NAD
	568	NAD	Liver	: NAD
	569	NAD	Liver	: NAD
	570	NAD	Liver	: NAD

NAD : No abnormalities were detected. + : Slight.

Appendix 31 The number of cells in seminiferous epithelia assessed by the individual examination in individual male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal No.	Stage II-III			Stage V			Stage VII			Stage XII	
		G	P	T	G	P	T	G	R/P	T	G	Z/P
0	003	0.52	1.75	5.46	0.63	2.02	6.48	0.06	3.13	6.17	0.05	4.72
	004	0.44	1.92	5.92	0.52	2.00	6.19	0.05	3.25	6.46	0.06	4.58
	007	0.44	1.97	6.22	0.60	1.77	5.69	0.07	3.06	5.96	0.06	4.83
	010	0.52	1.93	5.86	0.59	1.80	6.12	0.05	3.16	6.18	0.05	4.59
	012	0.44	1.75	5.33	0.58	1.98	5.82	0.05	3.12	5.48	0.06	4.58
	Mean	0.47	1.86	5.76	0.58	1.91	6.06	0.06	3.14	6.05	0.06	4.66
100	051	0.47	2.03	6.02	0.55	1.87	6.40	0.05	3.16	5.72	0.05	4.06
	054	0.49	1.77	6.18	0.54	2.00	6.07	0.05	3.55	6.38	0.06	4.62
	055	0.49	1.90	6.29	0.63	1.91	6.41	0.05	3.39	6.23	0.06	4.51
	057	0.51	1.90	5.77	0.59	1.82	5.90	0.06	3.13	5.90	0.07	4.73
	058	0.48	1.98	5.99	0.57	1.86	6.07	0.05	3.47	6.34	0.05	4.62
	Mean	0.49	1.92	6.05	0.58	1.89	6.17	0.05	3.34	6.11	0.06	4.51

G : spermatogonia.
P : pachytene spermatocyte.
R : preleptotene spermatocyte.
Z : zygotene spermatocyte.
T : round spermatid.
Each value represents the mean for data from 3 seminiferous epithelia.

Appendix 32-1 Individual absolute organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Seminal vesicle (g)	Testis (g)	Epididy-mis (g)	Pituitary (mg)	Thyroid (mg)
0	003	489	2.06	0.33	1.28	12.77	2.93	72.9	0.73	2.23	3.42	1.38	13.9	27.9
	004	467	2.08	0.36	1.32	12.67	2.77	52.2	0.74	2.83	3.40	1.38	11.7	28.5
	006	479	---	---	---	---	---	---	---	---	3.32	1.30	---	---
	007	485	2.05	0.24	1.58	12.61	3.23	58.0	1.11	2.90	3.59	1.35	12.3	34.8
	009	520	---	---	---	---	---	---	---	---	3.77	1.49	---	---
	010	550	2.06	0.33	1.35	12.92	3.16	60.6	0.83	2.38	3.16	1.32	15.7	28.1
	012	554	2.11	0.37	1.36	13.71	3.06	69.9	0.87	1.92	3.20	1.19	14.2	40.8
	Mean	506	2.07	0.33	1.38	12.94	3.03	62.7	0.86	2.45	3.41	1.34	13.6	32.0
0.8	013	467	2.08	1.30	1.29	12.18	2.35	55.9	1.15	2.50	2.94	1.31	13.5	28.9
	014	456	---	---	---	---	---	---	---	---	3.42	1.44	---	---
	015	464	2.08	0.32	1.32	10.56	2.86	61.4	0.59	2.45	3.36	1.36	11.6	24.4
	016	495	2.15	0.29	1.51	13.57	3.43	73.6	0.92	2.28	3.49	1.58	13.0	35.4
	017	534	---	---	---	---	---	---	---	---	3.45	1.39	---	---
	018	504	---	---	---	---	---	---	---	---	3.20	1.42	---	---
	019	506	---	---	---	---	---	---	---	---	4.05	1.56	---	---
	020	531	---	---	---	---	---	---	---	---	3.54	1.60	---	---
	021	507	1.96	0.41	1.47	14.41	2.91	57.8	0.75	2.23	3.59	1.28	13.5	28.7
	022	508	---	---	---	---	---	---	---	---	4.03	1.53	---	---
	023	572	---	---	---	---	---	---	---	---	3.44	1.46	---	---
	024	559	2.05	0.49	1.27	14.93	2.73	62.7	0.86	2.01	3.19	1.29	16.1	32.5
	Mean	509	2.06	0.56	1.37	13.13	2.86	62.3	0.85	2.29	3.48	1.44	13.5	30.0
4	025	462	2.11	0.29	1.38	12.25	3.32	54.4	0.62	2.51	3.22	1.32	14.0	34.8
	026	506	---	---	---	---	---	---	---	---	3.59	1.30	---	---
	027	523	---	---	---	---	---	---	---	---	2.94	1.07	---	---
	028	484	---	---	---	---	---	---	---	---	3.66	1.30	---	---
	029	458	2.10	0.29	1.34	12.17	3.16	65.4	0.74	2.70	3.45	1.38	11.4	36.6
	030	538	---	---	---	---	---	---	---	---	3.83	1.53	---	---
	031	511	---	---	---	---	---	---	---	---	3.93	1.50	---	---
	032	541	2.17	0.34	1.47	15.07	3.17	75.1	0.79	2.29	3.57	1.35	16.3	37.4
	033	523	---	---	---	---	---	---	---	---	3.48	1.36	---	---
	034	495	2.20	0.27	1.43	14.62	3.56	53.4	0.86	3.36	3.25	1.38	14.4	33.1
	035	538	2.08	0.43	1.59	15.55	3.51	70.9	0.74	2.43	3.37	1.46	15.4	36.0
	036	541	---	---	---	---	---	---	---	---	3.82	1.34	---	---
	Mean	510	2.13	0.32	1.44	13.93	3.34	63.8	0.75	2.66	3.51	1.36	14.3	35.6

--- : Not examined.

Appendix 32-2 Individual absolute organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Seminal vesicle (g)	Testis (g)	Epididy-mis (g)	Pituitary (mg)	Thyroid (mg)
20	037	493	---	---	---	---	---	---	---	---	3.53	1.38	---	---
	038	494	---	---	---	---	---	---	---	---	3.53	1.43	---	---
	039	549	---	---	---	---	---	---	---	---	3.06	1.06	---	---
	040	494	1.84	0.35	1.31	19.09	3.39	64.3	0.60	2.52	3.36	1.33	16.0	26.6
	041	479	2.02	0.30	1.44	16.26	3.54	68.7	0.82	2.35	3.69	1.46	16.4	37.7
	042	509	---	---	---	---	---	---	---	---	3.71	1.31	---	---
	043	490	2.14	0.36	1.43	20.90	3.16	50.4	0.77	2.17	3.28	1.32	15.2	35.0
	044	499	2.06	0.30	1.45	15.44	2.97	59.0	0.90	2.44	3.80	1.33	15.1	32.9
	045	519	---	---	---	---	---	---	---	---	3.70	1.47	---	---
	046	506	---	---	---	---	---	---	---	---	3.33	1.31	---	---
	047	513	2.24	0.36	1.60	22.88	3.20	66.5	0.80	1.86	3.01	1.09	15.3	34.0
	048	529	---	---	---	---	---	---	---	---	3.65	1.48	---	---
	Mean	506	2.06	0.33	1.45	18.91	3.25	61.8	0.78	2.27	3.47	1.33	15.6	33.2
100	049	519	---	---	---	---	---	---	---	---	4.05	1.45	---	---
	050	473	---	---	---	---	---	---	---	---	3.35	1.21	---	---
	051	503	1.99	0.32	1.43	30.95	3.14	67.5	0.87	2.62	3.34	1.21	14.8	30.4
	054	456	1.98	0.29	1.42	26.43	3.18	57.5	0.84	1.59	3.56	1.38	14.7	37.0
	055	476	2.04	0.35	1.32	25.22	3.30	64.7	0.76	2.44	4.38	1.48	14.8	41.4
	057	515	2.05	0.30	1.52	25.23	3.19	62.5	0.93	2.41	3.56	1.35	13.3	39.3
	058	494	2.13	0.26	1.51	25.50	3.50	61.4	0.79	2.12	3.76	1.37	13.1	33.6
	Mean	491	2.04	0.30	1.44	26.67	3.26	62.7	0.84	2.24	3.71	1.35	14.1	36.3

--- : Not examined.

Appendix 32-3 Individual absolute organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Seminal vesicle (g)	Testis (g)	Epididy-mis (g)	Pituitary (mg)	Thyroid (mg)
0	001	513	2.16	0.32	1.54	13.53	3.35	75.5	0.99	2.65	3.50	1.58	15.9	42.0
	002	502	2.11	0.38	1.38	12.99	3.38	72.8	0.89	2.60	3.26	1.44	15.9	37.0
	005	460	2.19	0.21	1.46	11.13	3.37	68.7	0.77	2.62	3.20	1.27	12.5	31.9
	008	514	2.11	0.39	1.55	12.08	3.09	68.1	0.80	2.68	3.31	1.36	14.7	46.3
	011	558	2.14	0.25	1.57	11.44	3.71	101.3	0.89	3.34	3.80	1.61	18.6	30.6
	Mean	509	2.14	0.31	1.50	12.23	3.38	77.3	0.87	2.78	3.41	1.45	15.5	37.6
100	052	462	2.17	0.30	1.29	14.93	3.03	69.6	0.86	2.62	3.20	1.39	13.6	39.7
	053	495	2.07	0.41	1.28	14.96	3.05	61.8	0.90	2.69	3.20	1.31	13.8	25.4
	056	504	2.02	0.32	1.44	17.41	3.48	66.8	0.90	2.63	3.79	1.52	14.7	35.1
	059	508	2.15	0.19	1.58	17.34	3.82	63.7	1.10	3.15	3.37	1.65	16.4	38.6
	060	555	1.93	0.44	1.61	18.28	3.84	70.4	1.10	2.64	3.75	1.46	16.7	42.6
	Mean	505	2.07	0.33	1.44	16.58	3.44	66.5	0.97	2.75	3.46	1.47	15.0	36.3

Appendix 33-1 Individual relative organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (%)	Thymus (%)	Heart (%)	Liver (%)	Kidney (%)	Adrenal gland (mg%)	Spleen (%)	Seminal vesicle (%)	Testis (%)	Epididy-mis (%)	Pituitary (mg%)	Thyroid (mg%)
0	003	489	0.42	0.07	0.26	2.61	0.60	14.9	0.15	0.46	0.70	0.28	2.8	5.7
	004	467	0.45	0.08	0.28	2.71	0.59	11.2	0.16	0.61	0.73	0.30	2.5	6.1
	006	479	---	---	---	---	---	---	---	---	0.69	0.27	---	---
	007	485	0.42	0.05	0.33	2.60	0.67	12.0	0.23	0.60	0.74	0.28	2.5	7.2
	009	520	---	---	---	---	---	---	---	---	0.73	0.29	---	---
	010	550	0.37	0.06	0.25	2.35	0.57	11.0	0.15	0.43	0.57	0.24	2.9	5.1
	012	554	0.38	0.07	0.25	2.47	0.55	12.6	0.16	0.35	0.58	0.21	2.6	7.4
	Mean	506	0.41	0.07	0.27	2.55	0.60	12.3	0.17	0.49	0.68	0.27	2.7	6.3
0.8	013	467	0.45	0.28	0.28	2.61	0.50	12.0	0.25	0.54	0.63	0.28	2.9	6.2
	014	456	---	---	---	---	---	---	---	---	0.75	0.32	---	---
	015	464	0.45	0.07	0.28	2.28	0.62	13.2	0.13	0.53	0.72	0.29	2.5	5.3
	016	495	0.43	0.06	0.31	2.74	0.69	14.9	0.19	0.46	0.71	0.32	2.6	7.2
	017	534	---	---	---	---	---	---	---	---	0.65	0.26	---	---
	018	504	---	---	---	---	---	---	---	---	0.63	0.28	---	---
	019	506	---	---	---	---	---	---	---	---	0.80	0.31	---	---
	020	531	---	---	---	---	---	---	---	---	0.67	0.30	---	---
	021	507	0.39	0.08	0.29	2.84	0.57	11.4	0.15	0.44	0.71	0.25	2.7	5.7
	022	508	---	---	---	---	---	---	---	---	0.79	0.30	---	---
	023	572	---	---	---	---	---	---	---	---	0.60	0.26	---	---
	024	559	0.37	0.09	0.23	2.67	0.49	11.2	0.15	0.36	0.57	0.23	2.9	5.8
	Mean	509	0.42	0.12	0.28	2.63	0.57	12.5	0.17	0.47	0.69	0.28	2.7	6.0
4	025	462	0.46	0.06	0.30	2.65	0.72	11.8	0.13	0.54	0.70	0.29	3.0	7.5
	026	506	---	---	---	---	---	---	---	---	0.71	0.26	---	---
	027	523	---	---	---	---	---	---	---	---	0.56	0.20	---	---
	028	484	---	---	---	---	---	---	---	---	0.76	0.27	---	---
	029	458	0.46	0.06	0.29	2.66	0.69	14.3	0.16	0.59	0.75	0.30	2.5	8.0
	030	538	---	---	---	---	---	---	---	---	0.71	0.28	---	---
	031	511	---	---	---	---	---	---	---	---	0.77	0.29	---	---
	032	541	0.40	0.06	0.27	2.79	0.59	13.9	0.15	0.42	0.66	0.25	3.0	6.9
	033	523	---	---	---	---	---	---	---	---	0.67	0.26	---	---
	034	495	0.44	0.05	0.29	2.95	0.72	10.8	0.17	0.68	0.66	0.28	2.9	6.7
	035	538	0.39	0.08	0.30	2.89	0.65	13.2	0.14	0.45	0.63	0.27	2.9	6.7
	036	541	---	---	---	---	---	---	---	---	0.71	0.25	---	---
	Mean	510	0.43	0.06	0.29	2.79	0.67	12.8	0.15	0.54	0.69	0.27	2.9	7.2

--- : Not examined.

Appendix 33-2 Individual relative organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (%)	Thymus (%)	Heart (%)	Liver (%)	Kidney (%)	Adrenal gland (mg%)	Spleen (%)	Seminal vesicle (%)	Testis (%)	Epididy-mis (%)	Pituitary (mg%)	Thyroid (mg%)
20	037	493	---	---	---	---	---	---	---	---	0.72	0.28	---	---
	038	494	---	---	---	---	---	---	---	---	0.71	0.29	---	---
	039	549	---	---	---	---	---	---	---	---	0.56	0.19	---	---
	040	494	0.37	0.07	0.27	3.86	0.69	13.0	0.12	0.51	0.68	0.27	3.2	5.4
	041	479	0.42	0.06	0.30	3.39	0.74	14.3	0.17	0.49	0.77	0.30	3.4	7.9
	042	509	---	---	---	---	---	---	---	---	0.73	0.26	---	---
	043	490	0.44	0.07	0.29	4.27	0.64	10.3	0.16	0.44	0.67	0.27	3.1	7.1
	044	499	0.41	0.06	0.29	3.09	0.60	11.8	0.18	0.49	0.76	0.27	3.0	6.6
	045	519	---	---	---	---	---	---	---	---	0.71	0.28	---	---
	046	506	---	---	---	---	---	---	---	---	0.66	0.26	---	---
	047	513	0.44	0.07	0.31	4.46	0.62	13.0	0.16	0.36	0.59	0.21	3.0	6.6
	048	529	---	---	---	---	---	---	---	---	0.69	0.28	---	---
	Mean	506	0.42	0.07	0.29	3.81	0.66	12.5	0.16	0.46	0.69	0.26	3.1	6.7
100	049	519	---	---	---	---	---	---	---	---	0.78	0.28	---	---
	050	473	---	---	---	---	---	---	---	---	0.71	0.26	---	---
	051	503	0.40	0.06	0.28	6.15	0.62	13.4	0.17	0.52	0.66	0.24	2.9	6.0
	054	456	0.43	0.06	0.31	5.80	0.70	12.6	0.18	0.35	0.78	0.30	3.2	8.1
	055	476	0.43	0.07	0.28	5.30	0.69	13.6	0.16	0.51	0.92	0.31	3.1	8.7
	057	515	0.40	0.06	0.30	4.90	0.62	12.1	0.18	0.47	0.69	0.26	2.6	7.6
	058	494	0.43	0.05	0.31	5.16	0.71	12.4	0.16	0.43	0.76	0.28	2.7	6.8
	Mean	491	0.42	0.06	0.30	5.46	0.67	12.8	0.17	0.46	0.76	0.28	2.9	7.4

--- : Not examined.

Appendix 33-3 Individual relative organ weights of male rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol with the reproduction/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (%)	Thymus (%)	Heart (%)	Liver (%)	Kidney (%)	Adrenal gland (mg%)	Spleen (%)	Seminal vesicle (%)	Testis (%)	Epididy-mis (%)	Pituitary (mg%)	Thyroid (mg%)
0	001	513	0.42	0.06	0.30	2.64	0.65	14.7	0.19	0.52	0.68	0.31	3.1	8.2
	002	502	0.42	0.08	0.27	2.59	0.67	14.5	0.18	0.52	0.65	0.29	3.2	7.4
	005	460	0.48	0.05	0.32	2.42	0.73	14.9	0.17	0.57	0.70	0.28	2.7	6.9
	008	514	0.41	0.08	0.30	2.35	0.60	13.2	0.16	0.52	0.64	0.26	2.9	9.0
	011	558	0.38	0.04	0.28	2.05	0.66	18.2	0.16	0.60	0.68	0.29	3.3	5.5
	Mean	509	0.42	0.06	0.29	2.41	0.66	15.1	0.17	0.55	0.67	0.29	3.0	7.4
100	052	462	0.47	0.06	0.28	3.23	0.66	15.1	0.19	0.57	0.69	0.30	2.9	8.6
	053	495	0.42	0.08	0.26	3.02	0.62	12.5	0.18	0.54	0.65	0.26	2.8	5.1
	056	504	0.40	0.06	0.29	3.45	0.69	13.3	0.18	0.52	0.75	0.30	2.9	7.0
	059	508	0.42	0.04	0.31	3.41	0.75	12.5	0.22	0.62	0.66	0.32	3.2	7.6
	060	555	0.35	0.08	0.29	3.29	0.69	12.7	0.20	0.48	0.68	0.26	3.0	7.7
	Mean	505	0.41	0.06	0.29	3.28	0.68	13.2	0.19	0.55	0.69	0.29	3.0	7.2

Appendix 34-1 Individual absolute organ weights of female rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Pituitary (mg)	Thyroid (mg)
0	504	321	1.93	0.34	1.11	10.96	1.78	72.4	1.00	18.1	18.7
	505	316	1.83	0.40	0.95	9.88	1.76	56.0	0.56	20.6	17.2
	507	322	1.83	0.25	1.04	10.98	2.29	92.5	0.69	19.9	22.9
	508	313	1.77	0.32	0.95	10.55	1.66	70.2	0.60	16.9	26.5
	511	346	1.93	0.19	1.00	11.83	1.85	68.5	0.62	18.6	25.2
	Mean	324	1.86	0.30	1.01	10.84	1.87	71.9	0.69	18.8	22.1
0.8	519	329	1.88	0.39	0.94	10.74	1.77	71.5	0.64	18.8	28.3
	520	303	1.76	0.19	0.84	10.13	1.80	68.5	0.80	19.5	18.4
	523	317	1.89	0.19	0.94	10.24	1.83	83.4	0.78	16.0	23.5
	525	350	1.92	0.38	0.88	10.77	1.91	92.1	0.60	17.1	25.1
	528	346	1.85	0.33	0.96	10.97	1.91	79.6	0.68	22.2	25.4
	Mean	329	1.86	0.30	0.91	10.57	1.84	79.0	0.70	18.7	24.1
4	532	304	1.86	0.19	0.89	9.92	1.76	78.3	0.73	16.2	18.3
	534	350	1.89	0.29	0.91	11.81	1.76	64.0	0.73	16.2	22.1
	535	337	1.90	0.34	0.95	10.94	2.19	90.2	0.77	20.1	22.4
	536	326	1.91	0.25	0.93	10.33	1.93	75.4	0.82	14.8	25.1
	538	337	1.80	0.28	0.98	11.30	2.42	71.6	0.82	24.0	25.7
	Mean	331	1.87	0.27	0.93	10.86	2.01	75.9	0.77	18.3	22.7
20	544	293	2.06	0.21	0.93	9.81	1.94	67.7	0.65	18.8	23.4
	545	293	1.89	0.24	0.88	9.63	1.65	71.1	0.54	15.7	27.5
	546	345	1.94	0.34	0.97	12.25	1.98	81.7	0.70	16.4	21.9
	548	332	1.85	0.16	1.02	11.66	1.91	70.9	0.79	15.1	24.0
	551	342	2.02	0.19	1.00	12.17	1.92	69.0	0.71	17.7	23.2
	Mean	321	1.95	0.23	0.96	11.10	1.88	72.1	0.68	16.7	24.0
100	554	328	1.86	0.27	0.90	11.04	1.97	82.4	0.68	20.6	23.2
	557	324	1.85	0.35	0.91	12.18	2.00	62.8	0.69	16.8	25.2
	558	316	1.90	0.27	0.99	11.61	1.89	84.4	0.75	16.4	27.7
	561	352	1.84	0.38	1.00	12.20	2.12	63.1	0.86	16.9	26.0
	564	327	1.92	0.28	1.02	12.72	1.90	76.5	0.71	21.7	25.0
	Mean	329	1.87	0.31	0.96	11.95	1.98	73.8	0.74	18.5	25.4

Appendix 34-2 Individual absolute organ weights of female rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (g)	Thymus (g)	Heart (g)	Liver (g)	Kidney (g)	Adrenal gland (mg)	Spleen (g)	Pituitary (mg)	Thyroid (mg)
0	513	290	1.96	0.32	0.91	7.55	1.84	78.7	0.49	14.2	21.5
	514	293	1.91	0.30	1.10	7.78	2.12	61.2	0.61	23.2	23.4
	515	306	2.09	0.19	0.93	7.66	1.73	71.4	0.52	21.8	25.5
	516	310	1.88	0.41	1.08	8.42	1.85	71.2	0.64	17.6	17.9
	517	306	1.81	0.37	0.91	7.36	2.02	86.6	0.60	19.7	30.6
	Mean	301	1.93	0.32	0.99	7.75	1.91	73.8	0.57	19.3	23.8
100	566	302	2.01	0.44	0.93	6.94	1.93	76.9	0.56	16.3	23.4
	567	306	1.98	0.32	1.06	7.94	2.00	64.2	0.53	19.1	30.1
	568	321	1.96	0.38	1.05	8.45	1.99	85.2	0.83	14.5	25.6
	569	303	1.82	0.40	1.04	8.11	1.87	81.7	0.58	18.5	29.2
	570	328	1.98	0.30	0.98	8.39	2.01	55.6	0.74	18.5	31.6
	Mean	312	1.95	0.37	1.01	7.97	1.96	72.7	0.65	17.4	28.0

Appendix 35-1 Individual relative organ weights of female rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of administration period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (%)	Thymus (%)	Heart (%)	Liver (%)	Kidney (%)	Adrenal gland (mg%)	Spleen (%)	Pituitary (mg%)	Thyroid (mg%)
0	504	321	0.60	0.11	0.35	3.41	0.55	22.6	0.31	5.6	5.8
	505	316	0.58	0.13	0.30	3.13	0.56	17.7	0.18	6.5	5.4
	507	322	0.57	0.08	0.32	3.41	0.71	28.7	0.21	6.2	7.1
	508	313	0.57	0.10	0.30	3.37	0.53	22.4	0.19	5.4	8.5
	511	346	0.56	0.05	0.29	3.42	0.53	19.8	0.18	5.4	7.3
	Mean	324	0.58	0.09	0.31	3.35	0.58	22.2	0.21	5.8	6.8
0.8	519	329	0.57	0.12	0.29	3.26	0.54	21.7	0.19	5.7	8.6
	520	303	0.58	0.06	0.28	3.34	0.59	22.6	0.26	6.4	6.1
	523	317	0.60	0.06	0.30	3.23	0.58	26.3	0.25	5.0	7.4
	525	350	0.55	0.11	0.25	3.08	0.55	26.3	0.17	4.9	7.2
	528	346	0.53	0.10	0.28	3.17	0.55	23.0	0.20	6.4	7.3
	Mean	329	0.57	0.09	0.28	3.22	0.56	24.0	0.21	5.7	7.3
4	532	304	0.61	0.06	0.29	3.26	0.58	25.8	0.24	5.3	6.0
	534	350	0.54	0.08	0.26	3.37	0.50	18.3	0.21	4.6	6.3
	535	337	0.56	0.10	0.28	3.25	0.65	26.8	0.23	6.0	6.6
	536	326	0.59	0.08	0.29	3.17	0.59	23.1	0.25	4.5	7.7
	538	337	0.53	0.08	0.29	3.35	0.72	21.2	0.24	7.1	7.6
	Mean	331	0.57	0.08	0.28	3.28	0.61	23.0	0.23	5.5	6.8
20	544	293	0.70	0.07	0.32	3.35	0.66	23.1	0.22	6.4	8.0
	545	293	0.65	0.08	0.30	3.29	0.56	24.3	0.18	5.4	9.4
	546	345	0.56	0.10	0.28	3.55	0.57	23.7	0.20	4.8	6.3
	548	332	0.56	0.05	0.31	3.51	0.58	21.4	0.24	4.5	7.2
	551	342	0.59	0.06	0.29	3.56	0.56	20.2	0.21	5.2	6.8
	Mean	321	0.61	0.07	0.30	3.45	0.59	22.5	0.21	5.3	7.5
100	554	328	0.57	0.08	0.27	3.37	0.60	25.1	0.21	6.3	7.1
	557	324	0.57	0.11	0.28	3.76	0.62	19.4	0.21	5.2	7.8
	558	316	0.60	0.09	0.31	3.67	0.60	26.7	0.24	5.2	8.8
	561	352	0.52	0.11	0.28	3.47	0.60	17.9	0.24	4.8	7.4
	564	327	0.59	0.09	0.31	3.89	0.58	23.4	0.22	6.6	7.6
	Mean	329	0.57	0.10	0.29	3.63	0.60	22.5	0.22	5.6	7.7

Appendix 35-2 Individual relative organ weights of female rats treated orally with 2-(2*H*-benzotriazol-2-yl)-6-sec-buthyl-4-*tert*-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

< At the end of recovery period >

Dose (mg/kg/day)	Animal number	B.W. (g)	Brain (%)	Thymus (%)	Heart (%)	Liver (%)	Kidney (%)	Adrenal gland (mg%)	Spleen (%)	Pituitary (mg%)	Thyroid (mg%)
0	513	290	0.68	0.11	0.31	2.60	0.63	27.1	0.17	4.9	7.4
	514	293	0.65	0.10	0.38	2.66	0.72	20.9	0.21	7.9	8.0
	515	306	0.68	0.06	0.30	2.50	0.57	23.3	0.17	7.1	8.3
	516	310	0.61	0.13	0.35	2.72	0.60	23.0	0.21	5.7	5.8
	517	306	0.59	0.12	0.30	2.41	0.66	28.3	0.20	6.4	10.0
	Mean	301	0.64	0.10	0.33	2.58	0.64	24.5	0.19	6.4	7.9
100	566	302	0.67	0.15	0.31	2.30	0.64	25.5	0.19	5.4	7.7
	567	306	0.65	0.10	0.35	2.59	0.65	21.0	0.17	6.2	9.8
	568	321	0.61	0.12	0.33	2.63	0.62	26.5	0.26	4.5	8.0
	569	303	0.60	0.13	0.34	2.68	0.62	27.0	0.19	6.1	9.6
	570	328	0.60	0.09	0.30	2.56	0.61	17.0	0.23	5.6	9.6
	Mean	312	0.63	0.12	0.33	2.55	0.63	23.4	0.21	5.6	8.9

Appendix 36-1 Individual estrous cycle of rats before mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Day of the inspection period 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Mean estrous cycle# (day)	Group mean estrous cycle (day)
0	501	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	502	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	503	IV	I	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	504	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	505	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	506	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	507	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	508	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	509	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	4.1
	510	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	511	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	512	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	513	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	514	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	515	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	516	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	517	IV	V	I	III	IV	V	V	I	III	III	IV	V	I	III	IV	5.0	
0.8	518	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	519	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	520	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	521	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	522	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	523	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	4.2
	524	V	I	III	III	IV	V	I	III	III	IV	V	I	III	III	IV	5.0	
	525	IV	IV	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	526	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	527	III	III	IV	V	I	III	III	IV	V	I	III	III	IV	V	V	5.0	
	528	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	529	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
4	530	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	531	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	532	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	533	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	534	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	535	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	4.1
	536	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
	537	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	538	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	539	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	540	III	IV	V	I	III	III	IV	V	V	I	III	IV	V	I	III	4.7	
	541	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V: Diestrus. # : Mean days from III to next III.

Appendix 36-2 Individual estrous cycle of rats before mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

Dose (mg/kg/day)	Animal number	Day of the inspection period															Mean estrous cycle# (day)	Group mean estrous cycle (day)
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15		
20	542	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	543	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	544	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
	545	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	546	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	547	IV	V	I	III	IV	V	I	III	III	IV	V	I	III	III	IV	4.5	4.1
	548	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	549	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	550	I	III	IV	V	I	I	III	IV	V	I	III	III	IV	V	V	4.5	
	551	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
	552	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
	553	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
100	554	V	I	III	IV	V	V	V	I	III	IV	V	I	III	IV	V	5.0	
	555	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	556	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	557	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	558	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
	559	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	4.0	
	560	I	III	IV	V	I	I	III	IV	V	V	V	I	IV	V	I	5.5	
	561	IV	V	I	III	IV	V	I	III	IV	V	I	III	III	V	I	4.0	
	562	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	4.3
	563	V	I	III	IV	V	V	V	I	III	IV	V	V	I	III	IV	5.5	
	564	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	565	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	4.0	
	566	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	IV	4.0	
	567	III	IV	V	V	I	III	IV	V	I	I	III	IV	V	V	V	5.0	
	568	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	569	V	I	III	IV	V	I	III	IV	V	I	III	IV	V	I	III	4.0	
	570	V	I	III	IV	V	I	III	IV	V	V	I	III	IV	V	I	4.5	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V : Diestrus. # : Mean days from III to next III.

Appendix 37-1 Individual estrous cycle of rats in mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0 mg/kg/day)

Female number	Paired male number	Day of the mating period 1 Vaginal plug	1 Estrous cycle	1 Sperm	2 Vaginal plug	2 Estrous cycle	2 Sperm	3 Vaginal plug	3 Estrous cycle	3 Sperm	4 Vaginal plug	4 Estrous cycle	4 Sperm
501	001	+	III	+									
502	002	+	III	+									
503	003	+	III	+									
504	004	-	IV	-	-	V	-	-	I	-	+	III	+
505	005	+	III	+									
506	006	+	III	+									
507	007	-	IV	-	-	V	-	-	I	-	+	III	+
508	008	-	IV	-	-	V	-	-	I	-	+	III	+
509	009	-	IV	-	-	V	-	-	I	-	+	III	+
510	010	-	IV	-	-	V	-	-	I	-	+	III	+
511	011	-	IV	-	-	V	-	-	I	-	+	III	+
512	012	-	I	-	+	III	+						

Female number	Paired male number	Day of the mating period 5 Vaginal plug	5 Estrous cycle	5 Sperm	6 Vaginal plug	6 Estrous cycle	6 Sperm	7 Vaginal plug	7 Estrous cycle	7 Sperm	8 Vaginal plug	8 Estrous cycle	8 Sperm
501	001												
502	002												
503	003												
504	004												
505	005												
506	006												
507	007												
508	008												
509	009												
510	010												
511	011												
512	012												

Female number	Paired male number	Day of the mating period 9 Vaginal plug	9 Estrous cycle	9 Sperm	10 Vaginal plug	10 Estrous cycle	10 Sperm	11 Vaginal plug	11 Estrous cycle	11 Sperm	12 Vaginal plug	12 Estrous cycle	12 Sperm
501	001												
502	002												
503	003												
504	004												
505	005												
506	006												
507	007												
508	008												
509	009												
510	010												
511	011												
512	012												

Female number	Paired male number	Day of the mating period 13 Vaginal plug	13 Estrous cycle	13 Sperm	14 Vaginal plug	14 Estrous cycle	14 Sperm	Pairing Day until copulation (Day)	Group mean pairing Day until copulation (Day)
501	001							1	
502	002							1	
503	003							1	
504	004							4	
505	005							1	
506	006							1	2.6
507	007							4	
508	008							4	
509	009							4	
510	010							4	
511	011							4	
512	012							2	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V: Diestrus. + : Confirmed. - : Not confirmed.

Appendix 37-2 Individual estrous cycle of rats in mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0.8 mg/kg/day)

Female number	Paired male number	Day of the mating period 1 Vaginal plug	1 Estrous cycle	1 Sperm	2 Vaginal plug	2 Estrous cycle	2 Sperm	3 Vaginal plug	3 Estrous cycle	3 Sperm	4 Vaginal plug	4 Estrous cycle	4 Sperm
518	013	+	III	+									
519	014	-	I	-	+	III	+						
520	015	+	III	+									
521	016	+	III	+									
522	017	+	III	+									
523	018	+	III	+									
524	019	-	V	-	-	I	-	+	III	+			
525	020	+	III	+									
526	021	-	I	-	+	III	+						
527	022	-	I	-	+	III	+						
528	023	+	III	+									
529	024	-	V	-	-	I	-	+	III	+			

Female number	Paired male number	Day of the mating period 5 Vaginal plug	5 Estrous cycle	5 Sperm	6 Vaginal plug	6 Estrous cycle	6 Sperm	7 Vaginal plug	7 Estrous cycle	7 Sperm	8 Vaginal plug	8 Estrous cycle	8 Sperm
518	013												
519	014												
520	015												
521	016												
522	017												
523	018												
524	019												
525	020												
526	021												
527	022												
528	023												
529	024												

Female number	Paired male number	Day of the mating period 9 Vaginal plug	9 Estrous cycle	9 Sperm	10 Vaginal plug	10 Estrous cycle	10 Sperm	11 Vaginal plug	11 Estrous cycle	11 Sperm	12 Vaginal plug	12 Estrous cycle	12 Sperm
518	013												
519	014												
520	015												
521	016												
522	017												
523	018												
524	019												
525	020												
526	021												
527	022												
528	023												
529	024												

Female number	Paired male number	Day of the mating period 13 Vaginal plug	13 Estrous cycle	13 Sperm	14 Vaginal plug	14 Estrous cycle	14 Sperm	Pairing Day until copulation (Day)	Group mean pairing Day until copulation (Day)
518	013							1	
519	014							2	
520	015							1	
521	016							1	
522	017							1	
523	018							1	1.6
524	019							3	
525	020							1	
526	021							2	
527	022							2	
528	023							1	
529	024							3	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V: Diestrus. + : Confirmed. - : Not confirmed.

Appendix 37-3 Individual estrous cycle of rats in mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(4 mg/kg/day)

Female number	Paired male number	Day of the mating period 1 Vaginal plug	1 Estrous cycle	1 Sperm	2 Vaginal plug	2 Estrous cycle	2 Sperm	3 Vaginal plug	3 Estrous cycle	3 Sperm	4 Vaginal plug	4 Estrous cycle	4 Sperm
530	025	-	IV	-	-	V	-	-	I	-	+	III	+
531	026	-	I	-	+	III	+						
532	027	-	I	-	+	III	+						
533	028	+	III	+									
534	029	+	III	+									
535	030	+	III	+									
536	031	-	V	-	-	I	-	+	III	+			
537	032	-	IV	-	-	V	-	-	V	-	-	V	-
538	033	-	IV	-	-	V	-	-	I	-	+	III	+
539	034	-	IV	-	-	V	-	-	I	-	+	III	+
540	035	+	III	+									
541	036	-	IV	-	-	V	-	-	I	-	+	III	+

Female number	Paired male number	Day of the mating period 5 Vaginal plug	5 Estrous cycle	5 Sperm	6 Vaginal plug	6 Estrous cycle	6 Sperm	7 Vaginal plug	7 Estrous cycle	7 Sperm	8 Vaginal plug	8 Estrous cycle	8 Sperm
530	025												
531	026												
532	027												
533	028												
534	029												
535	030												
536	031												
537	032	-	V	-	-	V	-	-	V	-	-	V	-
538	033												
539	034												
540	035												
541	036												

Female number	Paired male number	Day of the mating period 9 Vaginal plug	9 Estrous cycle	9 Sperm	10 Vaginal plug	10 Estrous cycle	10 Sperm	11 Vaginal plug	11 Estrous cycle	11 Sperm	12 Vaginal plug	12 Estrous cycle	12 Sperm
530	025												
531	026												
532	027												
533	028												
534	029												
535	030												
536	031												
537	032	-	V	-	-	V	-	-	V	-	-	V	-
538	033												
539	034												
540	035												
541	036												

Female number	Paired male number	Day of the mating period 13 Vaginal plug	13 Estrous cycle	13 Sperm	14 Vaginal plug	14 Estrous cycle	14 Sperm	Pairing Day until copulation (Day)	Group mean pairing Day until copulation (Day)
530	025							4	
531	026							2	
532	027							2	
533	028							1	
534	029							1	
535	030							1	3.4
536	031							3	
537	032	-	I	-	+	III	+	14	
538	033							4	
539	034							4	
540	035							1	
541	036							4	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V: Diestrus. + : Confirmed. - : Not confirmed.

Appendix 37-4 Individual estrous cycle of rats in mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(20 mg/kg/day)

Female number	Paired male number	Day of the mating period 1 Vaginal plug	1 Estrous cycle	1 Sperm	2 Vaginal plug	2 Estrous cycle	2 Sperm	3 Vaginal plug	3 Estrous cycle	3 Sperm	4 Vaginal plug	4 Estrous cycle	4 Sperm
542 NP	037	-	I	-	+	III	+						
543	038	-	I	-	+	III	+						
544	039	-	V	-	-	I	-	+	III	+			
545	040	-	IV	-	-	V	-	-	I	-	+	III	+
546	041	-	IV	-	-	V	-	-	V	-	+	III	+
547	042	-	V	-	-	V	-	-	V	-	-	V	-
548	043	-	IV	-	-	V	-	-	I	-	+	III	+
549	044	-	IV	-	-	V	-	-	I	-	+	III	+
550	045	-	I	-	+	III	+						
551	046	-	V	-	-	I	-	+	III	+			
552	047	-	V	-	-	I	-	+	III	+			
553	048	-	V	-	-	I	-	+	III	+			

Female number	Paired male number	Day of the mating period 5 Vaginal plug	5 Estrous cycle	5 Sperm	6 Vaginal plug	6 Estrous cycle	6 Sperm	7 Vaginal plug	7 Estrous cycle	7 Sperm	8 Vaginal plug	8 Estrous cycle	8 Sperm
542	037												
543	038												
544	039												
545	040												
546	041												
547	042	-	V	-	-	V	-	-	V	-	-	V	-
548	043												
549	044												
550	045												
551	046												
552	047												
553	048												

Female number	Paired male number	Day of the mating period 9 Vaginal plug	9 Estrous cycle	9 Sperm	10 Vaginal plug	10 Estrous cycle	10 Sperm	11 Vaginal plug	11 Estrous cycle	11 Sperm	12 Vaginal plug	12 Estrous cycle	12 Sperm
542	037												
543	038												
544	039												
545	040												
546	041												
547	042	-	V	-	-	V	-	-	V	-	-	V	-
548	043												
549	044												
550	045												
551	046												
552	047												
553	048												

Female number	Paired male number	Day of the mating period 13 Vaginal plug	13 Estrous cycle	13 Sperm	14 Vaginal plug	14 Estrous cycle	14 Sperm	Pairing Day until copulation (Day)	Group mean pairing Day until copulation (Day)
542	037							2	
543	038							2	
544	039							3	
545	040							4	
546	041							4	
547	042	-	I	-	+	III	+	14	4.0
548	043							4	
549	044							4	
550	045							2	
551	046							3	
552	047							3	
553	048							3	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V: Diestrus. + : Confirmed. - : Not confirmed.
NP : Non-pregnant.

Appendix 37-5 Individual estrous cycle of rats in mating period treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(100 mg/kg/day)

Female number	Paired male number	Day of the mating period 1 Vaginal plug	1 Estrous cycle	1 Sperm	2 Vaginal plug	2 Estrous cycle	2 Sperm	3 Vaginal plug	3 Estrous cycle	3 Sperm	4 Vaginal plug	4 Estrous cycle	4 Sperm
554	049	-	I	-	+	III	+						
555	050	+	III	+									
556	051	+	III	+									
557	052	+	III	+									
558	053	-	V	-	-	I	-	+	III	+			
559	054	-	I	-	+	III	+						
560	055	-	I	-	+	III	+						
561	056	+	III	+									
562	057	-	V	-	-	I	-	+	III	+			
563	058	-	V	-	-	V	-	-	I	-	+	III	+
564	059	-	IV	-	-	V	-	-	I	-	+	III	+
565	060	+	III	+									

Female number	Paired male number	Day of the mating period 5 Vaginal plug	5 Estrous cycle	5 Sperm	6 Vaginal plug	6 Estrous cycle	6 Sperm	7 Vaginal plug	7 Estrous cycle	7 Sperm	8 Vaginal plug	8 Estrous cycle	8 Sperm
554	049												
555	050												
556	051												
557	052												
558	053												
559	054												
560	055												
561	056												
562	057												
563	058												
564	059												
565	060												

Female number	Paired male number	Day of the mating period 9 Vaginal plug	9 Estrous cycle	9 Sperm	10 Vaginal plug	10 Estrous cycle	10 Sperm	11 Vaginal plug	11 Estrous cycle	11 Sperm	12 Vaginal plug	12 Estrous cycle	12 Sperm
554	049												
555	050												
556	051												
557	052												
558	053												
559	054												
560	055												
561	056												
562	057												
563	058												
564	059												
565	060												

Female number	Paired male number	Day of the mating period 13 Vaginal plug	13 Estrous cycle	13 Sperm	14 Vaginal plug	14 Estrous cycle	14 Sperm	Pairing Day until copulation (Day)	Group mean pairing Day until copulation (Day)
554	049							2	
555	050							1	
556	051							1	
557	052							1	
558	053							3	
559	054							2	2.1
560	055							2	
561	056							1	
562	057							3	
563	058							4	
564	059							4	
565	060							1	

I : Proestrus. III: Vaginal estrus. IV: Metaestrus. V: Diestrus. + : Confirmed. - : Not confirmed.

Appendix 38-1 Individual reproduction results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0 mg/kg/day)

Female number	Paired male number	Date of copulation	Pairing days until copulation (days)	Pregnancy (+:a, -:b)	Parturition (+:a, -:b)	Date of delivery	Gestation length (days)	Fate of pregnant	No. of corpora lutea	No. of implantation sites	Implantation index (%)
501	001	'09.3.6	1	+	+	'09.3.28	22	TK	16	15	93.8
502	002	'09.3.6	1	+	+	'09.3.29	23	TK	16	16	100.0
503	003	'09.3.6	1	+	+	'09.3.28	22	TK	16	16	100.0
504	004	'09.3.9	4	+	+	'09.3.31	22	TK	19	19	100.0
505	005	'09.3.6	1	+	+	'09.3.28	22	TK	15	15	100.0
506	006	'09.3.6	1	+	+	'09.3.29	23	TK	15	12	80.0
507	007	'09.3.9	4	+	+	'09.4.1	23	TK	18	18	100.0
508	008	'09.3.9	4	+	+	'09.3.31	22	TK	15	15	100.0
509	009	'09.3.9	4	+	+	'09.3.31	22	TK	14	14	100.0
510	010	'09.3.9	4	+	+	'09.3.31	22	TK	15	15	100.0
511	011	'09.3.9	4	+	+	'09.4.1	23	TK	14	11	78.6
512	012	'09.3.7	2	+	+	'09.3.30	23	TK	17	16	94.1

	Copulation index (%)	No. Mean S.D.	Fertility index (%)	Gestation index (%)	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.
		12			12	12	12	12
	12/12	2.6	12/12	12/12	22.4	15.8	15.2	95.5
	(100)	1.5	(100)	(100)	0.5	1.5	2.2	7.9

Copulation index = (No. of pairs with successful copulation/No. of pairs mated)×100.
Fertility index = (No. of pregnant females/No. of pairs with successful copulation)×100.
Gestation index = (No. of females with live pups /No. of pregnant females)×100.
TK : Terminal kill on day 5 after parturition.
a : Confirmed. b : Not confirmed.

Appendix 38-2 Individual reproduction results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(0.8 mg/kg/day)

Female number	Paired male number	Date of copulation	Pairing days until copulation (days)	Pregnancy (+:a, -:b)	Parturition (+:a, -:b)	Date of delivery	Gestation length (days)	Fate of pregnant	No. of corpora lutea	No. of implantation sites	Implantation index (%)
518	013	'09.3.6	1	+	+	'09.3.28	22	TK	16	15	93.8
519	014	'09.3.7	2	+	+	'09.3.29	22	TK	16	15	93.8
520	015	'09.3.6	1	+	+	'09.3.29	23	TK	17	17	100.0
521	016	'09.3.6	1	+	+	'09.3.29	23	TK	16	14	87.5
522	017	'09.3.6	1	+	+	'09.3.28	22	TK	17	17	100.0
523	018	'09.3.6	1	+	+	'09.3.28	22	TK	16	16	100.0
524	019	'09.3.8	3	+	+	'09.3.30	22	TK	16	16	100.0
525	020	'09.3.6	1	+	+	'09.3.28	22	TK	16	16	100.0
526	021	'09.3.7	2	+	+	'09.3.30	23	TK	18	17	94.4
527	022	'09.3.7	2	+	+	'09.3.30	23	TK	16	15	93.8
528	023	'09.3.6	1	+	+	'09.3.28	22	TK	18	17	94.4
529	024	'09.3.8	3	+	+	'09.3.30	22	TK	18	17	94.4

Copulation index (%)	No. Mean S.D.	Fertility index (%)	Gestation index (%)	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.
	12			12	12	12	12
12/12	1.6	12/12	12/12	22.3	16.7	16.0	96.0
(100)	0.8	(100)	(100)	0.5	0.9	1.0	4.0

Copulation index = (No. of pairs with successful copulation/No. of pairs mated)×100.
Fertility index = (No. of pregnant females/No. of pairs with successful copulation)×100.
Gestation index = (No. of females with live pups /No. of pregnant females)×100.
TK : Terminal kill on day 5 after parturition.
a : Confirmed. b : Not confirmed.

Appendix 38-3 Individual reproduction results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(4 mg/kg/day)

Female number	Paired male number	Date of copulation	Pairing days until copulation (days)	Pregnancy (+:a, -:b)	Parturition (+:a, -:b)	Date of delivery	Gestation length (days)	Fate of pregnant	No. of corpora lutea	No. of implantation sites	Implantation index (%)
530	025	'09.3.9	4	+	+	'09.3.31	22	TK	16	16	100.0
531	026	'09.3.7	2	+	+	'09.3.29	22	TK	16	14	87.5
532	027	'09.3.7	2	+	+	'09.3.30	23	TK	19	18	94.7
533	028	'09.3.6	1	+	+	'09.3.29	23	TK	14	14	100.0
534	029	'09.3.6	1	+	+	'09.3.29	23	TK	14	14	100.0
535	030	'09.3.6	1	+	+	'09.3.28	22	TK	16	14	87.5
536	031	'09.3.8	3	+	+	'09.3.31	23	TK	15	15	100.0
537	032	'09.3.19	14	+	+	'09.4.10	22	TK	17	17	100.0
538	033	'09.3.9	4	+	+	'09.3.31	22	TK	15	15	100.0
539	034	'09.3.9	4	+	+	'09.4.1	23	TK	15	12	80.0
540	035	'09.3.6	1	+	+	'09.3.29	23	TK	16	14	87.5
541	036	'09.3.9	4	+	+	'09.3.31	22	TK	16	15	93.8

	Copulation index (%)	No. Mean S.D.	Fertility index (%)	Gestation index (%)	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.
		12			12	12	12	12
	12/12	3.4	12/12	12/12	22.5	15.8	14.8	94.3
	(100)	3.6	(100)	(100)	0.5	1.4	1.6	7.0

Copulation index = (No. of pairs with successful copulation/No. of pairs mated)×100.
Fertility index = (No. of pregnant females/No. of pairs with successful copulation)×100.
Gestation index = (No. of females with live pups /No. of pregnant females)×100.
TK : Terminal kill on day 5 after parturition.
a : Confirmed. b : Not confirmed.

Appendix 38-4 Individual reproduction results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(20 mg/kg/day)

Female number	Paired male number	Date of copulation	Pairing days until copulation (days)	Pregnancy (+:a, -:b)	Parturition (+:a, -:b)	Date of delivery	Gestation length (days)	Fate of pregnant	No. of corpora lutea	No. of implantation sites	Implantation index (%)
542 NP	037	'09.3.7	2	-	-	-	-	-	-	-	-
543	038	'09.3.7	2	+	+	'09.3.29	22	TK	15	15	100.0
544	039	'09.3.8	3	+	+	'09.3.31	23	TK	14	14	100.0
545	040	'09.3.9	4	+	+	'09.4.1	23	TK	14	14	100.0
546	041	'09.3.9	4	+	+	'09.4.1	23	TK	13	13	100.0
547	042	'09.3.19	14	+	+	'09.4.11	23	TK	17	17	100.0
548	043	'09.3.9	4	+	+	'09.4.1	23	TK	15	15	100.0
549	044	'09.3.9	4	+	+	'09.4.1	23	TK	18	18	100.0
550	045	'09.3.7	2	+	+	'09.3.29	22	TK	13	10	76.9
551	046	'09.3.8	3	+	+	'09.3.31	23	TK	17	17	100.0
552	047	'09.3.8	3	+	+	'09.3.30	22	TK	15	15	100.0
553	048	'09.3.8	3	+	+	'09.3.30	22	TK	15	15	100.0
		Copulation index (%)	No. Mean S.D.	Fertility index (%)	Gestation index (%)		No. Mean S.D.		No. Mean S.D.	No. Mean S.D.	No. Mean S.D.
			12				11		11	11	11
		12/12	4.0	11/12	11/11		22.6		15.1	14.8	97.9
		(100)	3.2	(91.7)	(100)		0.5		1.6	2.2	7.0

Copulation index = (No. of pairs with successful copulation/No. of pairs mated)×100.
Fertility index = (No. of pregnant females/No. of pairs with successful copulation)×100.
Gestation index = (No. of females with live pups /No. of pregnant females)×100.
TK : Terminal kill on day 5 after parturition.
NP : Non-pregnant.
a : Confirmed. b : Not confirmed.

Appendix 38-5 Individual reproduction results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

(100 mg/kg/day)

Female number	Paired male number	Date of copulation	Pairing days until copulation (days)	Pregnancy (+:a, -:b)	Parturition (+:a, -:b)	Date of delivery	Gestation length (days)	Fate of pregnant	No. of corpora lutea	No. of implantation sites	Implantation index (%)
554	049	'09.3.7	2	+	+	'09.3.30	23	TK	15	14	93.3
555	050	'09.3.6	1	+	+	'09.3.28	22	TK	13	12	92.3
556	051	'09.3.6	1	+	+	'09.3.28	22	TK	17	16	94.1
557	052	'09.3.6	1	+	+	'09.3.29	23	TK	16	16	100.0
558	053	'09.3.8	3	+	+	'09.3.31	23	TK	16	15	93.8
559	054	'09.3.7	2	+	+	'09.3.29	22	TK	16	16	100.0
560 KL	055	'09.3.7	2	+	+	'09.3.30	23	TK	19	18	94.7
561	056	'09.3.6	1	+	+	'09.3.29	23	TK	14	7	50.0
562	057	'09.3.8	3	+	+	'09.3.30	22	TK	18	18	100.0
563	058	'09.3.9	4	+	+	'09.4.1	23	TK	17	16	94.1
564	059	'09.3.9	4	+	+	'09.3.31	22	TK	16	16	100.0
565	060	'09.3.6	1	+	+	'09.3.28	22	TK	16	16	100.0

	Copulation index (%)	No. Mean S.D.	Fertility index (%)	Gestation index (%)	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.	No. Mean S.D.
		12			12	12	12	12
	12/12	2.1	12/12	12/12	22.5	16.1	15.0	92.7
	(100)	1.2	(100)	(100)	0.5	1.6	3.0	13.8

Copulation index = (No. of pairs with successful copulation/No. of pairs mated)×100.
Fertility index = (No. of pregnant females/No. of pairs with successful copulation)×100.
Gestation index = (No. of females with live pups /No. of pregnant females)×100.
TK : Terminal kill on day 5 after parturition.
a : Confirmed. b : Not confirmed.
KL : Killed because all pups died after delivery.

Appendix 39-1 Individual litter results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[0 mg/kg/day]

Perental female number	No. of implan-tation sites	No. of pups born	Delivery index (%)	No. of pups on day 0 of lactation							Live birth index (%)	No. of live pups on day 4 of lactation			Viability index (%)	Mean body weight of live pups (g)			
				Live pups			Dead pups									On day 0		On day 4	
				T	M	F	T	M	F	SI		T	M	F		M	F	M	F
501	15	14	93.3	14	9	5	0	0	0	0	100.0	14	9	5	100.0	6.8	6.9	11.3	11.1
502	16	13	81.3	13	8	5	0	0	0	0	100.0	13	8	5	100.0	7.7	7.1	12.5	11.9
503	16	16	100.0	16	11	5	0	0	0	0	100.0	15	10	5	93.8	6.7	6.2	11.3	10.6
504	19	16	84.2	15	10	5	1	1	0	0	93.8	13	8	5	86.7	6.8	6.2	11.5	10.2
505	15	15	100.0	15	6	9	0	0	0	0	100.0	15	6	9	100.0	6.4	6.0	9.5	9.2
506	12	12	100.0	12	5	7	0	0	0	0	100.0	11	5	6	91.7	7.5	7.4	12.1	11.5
507	18	17	94.4	17	10	7	0	0	0	0	100.0	17	10	7	100.0	7.4	6.9	11.8	11.0
508	15	15	100.0	15	9	6	0	0	0	0	100.0	14	9	5	93.3	6.6	6.3	10.7	10.4
509	14	13	92.9	13	4	9	0	0	0	0	100.0	12	3	9	92.3	6.5	6.4	12.0	11.6
510	15	14	93.3	14	7	7	0	0	0	0	100.0	14	7	7	100.0	6.9	6.7	11.3	10.9
511	11	11	100.0	11	6	5	0	0	0	0	100.0	11	6	5	100.0	8.1	7.7	14.0	13.3
512	16	14	87.5	14	9	5	0	0	0	0	100.0	14	9	5	100.0	7.6	7.1	11.8	11.4
No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	15.2	14.2	93.9	14.1	7.8	6.3	0.1	0.1	0.0	0.0	99.5	13.6	7.5	6.1	96.5	7.1	6.7	11.7	11.1
S.D.	2.2	1.7	6.6	1.7	2.2	1.5	0.3	0.3	0.0	0.0	1.8	1.7	2.2	1.6	4.7	0.6	0.5	1.1	1.0

Sex ratio : 1.27 (Total number of male pups on day 0 of lactation / Total number of female pups on day 0 of lactation = 95 / 75).
T : Total. M : Male. F : Female. SI : Sex was indistinction.
Delivery index = (No. of pups born/No. of implantation sites)×100.
Live birth index = (No. of live pups on day 0/No. of pups born)×100.
Viability index = (No. of live pups on day 4/No. of live pups on day 0)×100.
Sex ratio = Total number of male pups/Total number of female pups.
NP : Non-pregnant. ND : Non-delivery.

Appendix 39-2 Individual litter results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[0.8 mg/kg/day]

Perental female number	No. of implan-tation sites	No. of pups born	Delivery index (%)	No. of pups on day 0 of lactation							Live birth index (%)	No. of live pups on day 4 of lactation			Viability index (%)	Mean body weight of live pups (g)			
				Live pups			Dead pups									On day 0		On day 4	
				T	M	F	T	M	F	SI		T	M	F		M	F	M	F
518	15	15	100.0	15	7	8	0	0	0	0	100.0	15	7	8	100.0	7.0	6.5	10.3	10.1
519	15	14	93.3	14	7	7	0	0	0	0	100.0	14	7	7	100.0	7.0	6.6	10.5	10.1
520	17	16	94.1	16	9	7	0	0	0	0	100.0	16	9	7	100.0	6.9	6.5	11.0	10.3
521	14	13	92.9	13	8	5	0	0	0	0	100.0	12	8	4	92.3	8.0	7.8	13.5	13.5
522	17	16	94.1	16	8	8	0	0	0	0	100.0	16	8	8	100.0	6.9	6.7	11.3	10.8
523	16	16	100.0	16	6	10	0	0	0	0	100.0	16	6	10	100.0	6.7	6.2	10.8	10.0
524	16	15	93.8	15	7	8	0	0	0	0	100.0	15	7	8	100.0	6.9	6.3	10.7	9.9
525	16	15	93.8	15	6	9	0	0	0	0	100.0	15	6	9	100.0	6.8	6.4	10.7	10.5
526	17	10	58.8	10	3	7	0	0	0	0	100.0	10	3	7	100.0	8.9	7.5	15.9	14.1
527	15	15	100.0	15	6	9	0	0	0	0	100.0	15	6	9	100.0	8.0	7.7	13.0	12.5
528	17	17	100.0	17	6	11	0	0	0	0	100.0	17	6	11	100.0	6.0	6.2	10.0	10.2
529	17	16	94.1	16	7	9	0	0	0	0	100.0	15	7	8	93.8	6.7	6.2	11.0	10.5
No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	16.0	14.8	92.9	14.8	6.7	8.2	0.0	0.0	0.0	0.0	100.0	14.7	6.7	8.0	98.8	7.2	6.7	11.6	11.0
S.D.	1.0	1.9	11.2	1.9	1.5	1.6	0.0	0.0	0.0	0.0	0.0	1.9	1.5	1.8	2.7	0.8	0.6	1.7	1.5

Sex ratio : 0.82 (Total number of male pups on day 0 of lactation / Total number of female pups on day 0 of lactation = 80 / 98).
T : Total. M : Male. F : Female. SI : Sex was indistinction.
Delivery index = (No. of pups born/No. of implantation sites)×100.
Live birth index = (No. of live pups on day 0/No. of pups born)×100.
Viability index = (No. of live pups on day 4/No. of live pups on day 0)×100.
Sex ratio = Total number of male pups/Total number of female pups.

Appendix 39-3 Individual litter results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[4 mg/kg/day]

Perental female number	No. of implan-tation sites	No. of pups born	Delivery index (%)	No. of pups on day 0 of lactation							Live birth index (%)	No. of live pups on day 4 of lactation			Viability index (%)	Mean body weight of live pups (g)			
				Live pups			Dead pups									On day 0		On day 4	
				T	M	F	T	M	F	SI		T	M	F		M	F	M	F
530	16	14	87.5	14	6	8	0	0	0	0	100.0	14	6	8	100.0	7.2	6.9	11.8	11.2
531	14	12	85.7	12	3	9	0	0	0	0	100.0	12	3	9	100.0	6.8	6.6	10.8	10.7
532	18	18	100.0	18	10	8	0	0	0	0	100.0	18	10	8	100.0	6.9	6.4	10.4	9.7
533	14	13	92.9	13	6	7	0	0	0	0	100.0	13	6	7	100.0	8.5	7.9	13.9	13.2
534	14	14	100.0	14	5	9	0	0	0	0	100.0	14	5	9	100.0	7.5	7.3	12.2	12.2
535	14	12	85.7	12	5	7	0	0	0	0	100.0	12	5	7	100.0	6.6	5.9	12.0	10.8
536	15	15	100.0	15	10	5	0	0	0	0	100.0	15	10	5	100.0	7.7	7.5	12.0	12.1
537	17	15	88.2	15	10	5	0	0	0	0	100.0	15	10	5	100.0	6.6	6.1	10.9	10.8
538	15	14	93.3	14	8	6	0	0	0	0	100.0	14	8	6	100.0	7.4	6.9	12.2	11.7
539	12	11	91.7	11	6	5	0	0	0	0	100.0	11	6	5	100.0	8.7	8.3	13.7	13.8
540	14	13	92.9	13	6	7	0	0	0	0	100.0	13	6	7	100.0	7.5	7.1	12.7	12.6
541	15	14	93.3	14	6	8	0	0	0	0	100.0	14	6	8	100.0	6.6	6.1	10.6	10.6
No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	14.8	13.8	92.6	13.8	6.8	7.0	0.0	0.0	0.0	0.0	100.0	13.8	6.8	7.0	100.0	7.3	6.9	11.9	11.6
S.D.	1.6	1.8	5.3	1.8	2.3	1.5	0.0	0.0	0.0	0.0	0.0	1.8	2.3	1.5	0.0	0.7	0.7	1.1	1.2

Sex ratio : 0.96 (Total number of male pups on day 0 of lactation / Total number of female pups on day 0 of lactation = 81 / 84).
T : Total. M : Male. F : Female. SI : Sex was indistinction.
Delivery index = (No. of pups born/No. of implantation sites)×100.
Live birth index = (No. of live pups on day 0/No. of pups born)×100.
Viability index = (No. of live pups on day 4/No. of live pups on day 0)×100.
Sex ratio = Total number of male pups/Total number of female pups.

Appendix 39-4 Individual litter results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[20 mg/kg/day]

Perental female number	No. of implan-tation sites	No. of pups born	Delivery index (%)	No. of pups on day 0 of lactation							Live birth index (%)	No. of live pups on day 4 of lactation			Viability index (%)	Mean body weight of live pups (g)			
				Live pups			Dead pups									On day 0		On day 4	
				T	M	F	T	M	F	SI		T	M	F		M	F	M	F
542 NP	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
543	15	14	93.3	14	10	4	0	0	0	0	100.0	14	10	4	100.0	6.7	6.6	9.9	10.0
544	14	12	85.7	12	8	4	0	0	0	0	100.0	12	8	4	100.0	7.7	7.4	11.6	11.3
545	14	13	92.9	13	8	5	0	0	0	0	100.0	13	8	5	100.0	7.4	7.5	11.2	11.3
546	13	12	92.3	12	5	7	0	0	0	0	100.0	12	5	7	100.0	7.6	7.5	13.5	13.1
547	17	17	100.0	14	9	5	3	3	0	0	82.4	14	9	5	100.0	6.8	6.8	11.3	11.5
548	15	15	100.0	15	11	4	0	0	0	0	100.0	15	11	4	100.0	7.6	7.2	12.5	11.9
549	18	15	83.3	15	7	8	0	0	0	0	100.0	15	7	8	100.0	7.4	6.6	12.1	11.3
550	10	9	90.0	8	5	3	1	0	1	0	88.9	8	5	3	100.0	6.5	6.1	12.0	10.9
551	17	16	94.1	16	9	7	0	0	0	0	100.0	16	9	7	100.0	7.2	6.7	11.1	10.5
552	15	14	93.3	14	8	6	0	0	0	0	100.0	14	8	6	100.0	6.9	6.6	10.8	10.4
553	15	13	86.7	13	7	6	0	0	0	0	100.0	13	7	6	100.0	7.3	7.4	12.3	12.7
No.	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	14.8	13.6	92.0	13.3	7.9	5.4	0.4	0.3	0.1	0.0	97.4	13.3	7.9	5.4	100.0	7.2	6.9	11.7	11.4
S.D.	1.6	2.2	5.3	2.1	1.9	1.6	0.9	0.9	0.3	0.0	6.0	2.1	1.9	1.6	0.0	0.4	0.5	1.0	0.9

Sex ratio : 1.50 (Total number of male pups on day 0 of lactation / Total number of female pups on day 0 of lactation = 90 / 60).
T : Total. M : Male. F : Female. SI : Sex was indistinction.
Delivery index = (No. of pups born/No. of implantation sites)×100.
Live birth index = (No. of live pups on day 0/No. of pups born)×100.
Viability index = (No. of live pups on day 4/No. of live pups on day 0)×100.
Sex ratio = Total number of male pups/Total number of female pups.
NP : Non-pregnant.

Appendix 39-5 Individual litter results of rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[100 mg/kg/day]

Perental female number		No. of implan-tation sites	No. of pups born	Delivery index (%)	No. of pups on day 0 of lactation							Live birth index (%)	No. of live pups on day 4 of lactation			Viability index (%)	Mean body weight of live pups (g)			
					Live pups			Dead pups									On day 0		On day 4	
					T	M	F	T	M	F	SI		T	M	F		M	F	M	F
554		14	14	100.0	14	5	9	0	0	0	0	100.0	13	5	8	92.9	8.0	7.4	13.0	12.1
555		12	11	91.7	11	6	5	0	0	0	0	100.0	11	6	5	100.0	7.5	7.1	12.5	12.3
556		16	16	100.0	16	7	9	0	0	0	0	100.0	16	7	9	100.0	6.4	6.0	10.3	10.0
557		16	15	93.8	15	8	7	0	0	0	0	100.0	15	8	7	100.0	6.9	6.8	10.8	10.2
558		15	13	86.7	13	5	8	0	0	0	0	100.0	13	5	8	100.0	7.9	7.4	12.3	11.7
559		16	14	87.5	14	8	6	0	0	0	0	100.0	13	7	6	92.9	6.7	6.1	11.5	10.5
560	KL	18	17	94.4	15	6	9	2	1	1	0	88.2	0	0	0	0.0	7.5	6.0	-	-
561		7	5	71.4	5	4	1	0	0	0	0	100.0	5	4	1	100.0	8.3	8.2	16.2	16.2
562		18	17	94.4	17	6	11	0	0	0	0	100.0	16	5	11	94.1	6.7	6.0	9.8	8.8
563		16	15	93.8	15	6	9	0	0	0	0	100.0	15	6	9	100.0	7.9	6.9	11.9	10.7
564		16	14	87.5	14	9	5	0	0	0	0	100.0	14	9	5	100.0	6.9	6.9	11.0	10.8
565		16	15	93.8	14	8	6	1	0	1	0	93.3	13	8	5	92.9	6.9	6.7	10.8	10.3
No.		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11
Mean		15.0	13.8	91.3	13.6	6.5	7.1	0.3	0.1	0.2	0.0	98.5	12.0	5.8	6.2	89.4	7.3	6.8	11.8	11.2
S.D.		3.0	3.2	7.6	3.1	1.5	2.7	0.6	0.3	0.4	0.0	3.8	4.8	2.4	3.2	28.3	0.6	0.7	1.7	1.9

Sex ratio : 0.91 (Total number of male pups on day 0 of lactation / Total number of female pups on day 0 of lactation = 79 / 87).
T : Total. M : Male. F : Female. SI : Sex was indistinction.
Delivery index = (No. of pups born/No. of implantation sites)×100.
Live birth index = (No. of live pups on day 0/No. of pups born)×100.
Viability index = (No. of live pups on day 4/No. of live pups on day 0)×100.
Sex ratio = Total number of male pups/Total number of female pups.
NP : Non-pregnant.
KL : Killed because all pups died after delivery.

Appendix 40-1 Individual external findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[0 mg/kg/day]

Parental female number	501	502	503	504	505	506	507	508	509	510	511	512	Total	No.	Mean	S.D.
No. of pups born	14	13	16	16	15	12	17	15	13	14	11	14	170	12	–	–
No. of pups examined																
Total	14	13	16	16	15	12	17	15	13	14	11	14	170	12	–	–
Live	14	13	16	15	15	12	17	15	13	14	11	14	169	–	–	–
Dead	0	0	0	1	0	0	0	0	0	0	0	0	1	–	–	–
No. of pups with external malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	–	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–

Appendix 40-2 Individual external findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[0.8 mg/kg/day]

Parental female number	518	519	520	521	522	523	524	525	526	527	528	529	Total	No.	Mean	S.D.
No. of pups born	15	14	16	13	16	16	15	15	10	15	17	16	178	12	–	–
No. of pups examined																
Total	15	14	16	13	16	16	15	15	10	15	17	16	178	12	–	–
Live	15	14	16	13	16	16	15	15	10	15	17	16	178	–	–	–
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
No. of pups with external malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–

Appendix 40-3 Individual external findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[4 mg/kg/day]

Parental female number	530	531	532	533	534	535	536	537	538	539	540	541	Total	No.	Mean	S.D.
No. of pups born	14	12	18	13	14	12	15	15	14	11	13	14	165	12	—	—
No. of pups examined																
Total	14	12	18	13	14	12	15	15	14	11	13	14	165	12	—	—
Live	14	12	18	13	14	12	15	15	14	11	13	14	165	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with external malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—

Appendix 40-4 Individual external findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[20 mg/kg/day]

Parental female number	542	543	544	545	546	547	548	549	550	551	552	553	Total	No.	Mean	S.D.
	NP															
No. of pups born	—	14	12	13	12	17	15	15	9	16	14	13	150	11	—	—
No. of pups examined																
Total	—	14	12	13	12	17	15	15	9	16	14	13	150	11	—	—
Live	—	14	12	13	12	14	15	15	8	16	14	13	146	—	—	—
Dead	—	0	0	0	0	3	0	0	1	0	0	0	4	—	—	—
No. of pups with external malformations																
Total	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	—	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	11	(0)	(0)
Live	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—

NP : Non-pregnant.

Appendix 40-5 Individual external findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[100 mg/kg/day]

Parental female number	554	555	556	557	558	559	560	561	562	563	564	565	Total	No.	Mean	S.D.
							KL									
No. of pups born	14	11	16	15	13	14	17	5	17	15	14	15	166	12	–	–
No. of pups examined																
Total	14	11	16	15	13	14	17	5	17	15	14	15	166	12	–	–
Live	14	11	16	15	13	14	15	5	17	15	14	14	163	–	–	–
Dead	0	0	0	0	0	0	2	0	0	0	0	1	3	–	–	–
No. of pups with external malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	–	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	–	–	–

KL : Killed because all pups died after delivery.

Appendix 41-1 Individual visceral findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[0 mg/kg/day]

Parental female number	501	502	503	504	505	506	507	508	509	510	511	512	Total	No.	Mean	S.D.
No. of pups born	14	13	16	16	15	12	17	15	13	14	11	14	170	12	—	—
No. of pups examined																
Total	14	13	15	16	15	12	17	15	13	14	11	14	169	12	—	—
Live	14	13	15	13	15	11	17	14	12	14	11	14	163	—	—	—
Dead	0	0	0	3	0	1	0	1	1	0	0	0	6	—	—	—
No. of pups with visceral malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with visceral variations																
Total	0	0	0	0	0	1	0	0	0	0	1	0	2	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(8.3)	(0)	(0)	(0)	(0)	(9.1)	(0)	—	12	(2.0)	(3.7)
Live	0	0	0	0	0	0	0	0	0	0	1	0	1	—	—	—
Dead	0	0	0	0	0	1	0	0	0	0	0	0	1	—	—	—
visceral variations																
Thymic remnant in neck																
Total	0	0	0	0	0	0	0	0	0	0	1	0	1	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(9.1)	(0)	—	12	(0.8)	(2.6)
Live	0	0	0	0	0	0	0	0	0	0	1	0	1	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dilatation of renal pelvis																
Total	0	0	0	0	0	1	0	0	0	0	0	0	1	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(8.3)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(1.3)	(2.9)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	1	0	0	0	0	0	0	1	—	—	—

Appendix 41-2 Individual visceral findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-te
butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening t
[0.8 mg/kg/day]

Parental female number	518	519	520	521	522	523	524	525	526	527	528	529	Total	No.	Mean	S.D.
												a				
No. of pups born	15	14	16	13	16	16	15	15	10	15	17	16	178	12	—	—
No. of pups examined																
Total	15	14	16	13	16	16	15	15	10	15	17	15	177	12	—	—
Live	15	14	16	12	16	16	15	15	10	15	17	15	176	—	—	—
Dead	0	0	0	1	0	0	0	0	0	0	0	0	1	—	—	—
No. of pups with visceral malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with visceral variations																
Total	0	0	0	1	0	0	0	0	0	0	0	1	2	—	—	—
(%)	(0)	(0)	(0)	(7.7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6.3)	—	12	(1.2)	(2.8)
Live	0	0	0	1	0	0	0	0	0	0	0	1	2	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
visceral variations																
Persistent left umbilical artery																
Total	0	0	0	1	0	0	0	0	0	0	0	1	2	—	—	—
(%)	(0)	(0)	(0)	(7.7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6.3)	—	12	(1.2)	(2.8)
Live	0	0	0	1	0	0	0	0	0	0	0	1	2	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—

a : One pup was cannibalized.

Appendix 41-3 Individual visceral findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-tert-butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test

[4 mg/kg/day]

Parental female number	530	531	532	533	534	535	536	537	538	539	540	541	Total	No.	Mean	S.D.
No. of pups born	14	12	18	13	14	12	15	15	14	11	13	14	165	12	—	—
No. of pups examined																
Total	14	12	18	13	14	12	15	15	14	11	13	14	165	12	—	—
Live	14	12	18	13	14	12	15	15	14	11	13	14	165	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with visceral malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with visceral variations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—

Appendix 41-4 Individual visceral findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-te
butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening t

[20 mg/kg/day]

Parental female number	542	543	544	545	546	547	548	549	550	551	552	553	Total	No.	Mean	S.D.
	NP					b										
No. of pups born	—	14	12	13	12	17	15	15	9	16	14	13	150	11	—	—
No. of pups examined																
Total	—	14	12	13	12	15	15	15	9	16	14	13	148	11	—	—
Live	—	14	12	13	12	14	15	15	8	16	14	13	146	—	—	—
Dead	—	0	0	0	0	1	0	0	1	0	0	0	2	—	—	—
No. of pups with visceral malformations																
Total	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	—	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	11	(0)	(0)
Live	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with visceral variations																
Total	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	—	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	11	(0)	(0)
Live	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	—	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—

NP : Non-pregnant.
b : Two pup was cannibalized.

Appendix 41-5 Individual visceral findings of pups from pregnant rats treated orally with 2-(2H-benzotriazol-2-yl)6-sec-butyl-4-te
butylphenol in the combined repeated dose toxicity study with the reproduction/developmental toxicity screening t
[100 mg/kg/day]

Parental female number	554	555	556	557	558	559	560	561	562	563	564	565	Total	No.	Mean	S.D.
						a	KL, b									
No. of pups born	14	11	16	15	13	14	17	5	17	15	14	15	166	12	—	—
No. of pups examined																
Total	14	11	16	15	13	13	15	5	17	15	14	15	163	12	—	—
Live	13	11	16	15	13	13	0	5	16	15	14	13	144	—	—	—
Dead	1	0	0	0	0	0	15	0	1	0	0	2	19	—	—	—
No. of pups with visceral malformations																
Total	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	—	12	(0)	(0)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
No. of pups with visceral variations																
Total	0	0	0	0	0	0	1	0	0	1	0	0	2	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(6.7)	(0)	(0)	(6.7)	(0)	(0)	—	12	(1.1)	(2.6)
Live	0	0	0	0	0	0	0	0	0	1	0	0	1	—	—	—
Dead	0	0	0	0	0	0	1	0	0	0	0	0	1	—	—	—
visceral variations																
Thymic remnant in neck																
Total	0	0	0	0	0	0	0	0	0	1	0	0	1	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6.7)	(0)	(0)	—	12	(0.6)	(1.9)
Live	0	0	0	0	0	0	0	0	0	1	0	0	1	—	—	—
Dead	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dilatation of renal pelvis																
Total	0	0	0	0	0	0	1	0	0	0	0	0	1	—	—	—
(%)	(0)	(0)	(0)	(0)	(0)	(0)	(6.7)	(0)	(0)	(0)	(0)	(0)	—	12	(0.6)	(1.9)
Live	0	0	0	0	0	0	0	0	0	0	0	0	0	—	—	—
Dead	0	0	0	0	0	0	1	0	0	0	0	0	1	—	—	—

KL : Killed because all pups died after delivery.
a : One pup was cannibalized.
b : Two pup was cannibalized.

Appendix 42 Historical background data of the Crl:CD(SD) strain male rats on the hematological and biochemical parameters

Parameters	Mean		Normal range[a)]	
	A	B	A	B
Hematological parameters				
① Erythrocyte count (10^4/μL)	850 (55)	878 (55)	767 ~ 932	801 ~ 956
② Hemoglobin concentration (g/dL)	15.4 (55)	15.6 (55)	14.0 ~ 16.7	14.2 ~ 16.9
③ Hematocrit value (%)	45.5 (55)	45.9 (55)	41.1 ~ 49.9	41.9 ~ 49.9
④ Mean corpuscular volume (fL)	54 (55)	52 (55)	48 ~ 59	49 ~ 56
⑤ Mean corpuscular hemoglobin (pg)	18.1 (55)	17.7 (55)	17.0 ~ 19.2	16.6 ~ 18.8
⑥ Mean corpuscular hemoglobin concentration (%)	33.8 (55)	33.9 (55)	31.3 ~ 36.4	31.9 ~ 35.9
⑦ Reticulocyte count (‰)	23.8* (55)	24.3* (55)	11.9 ~ 35.6	10.2 ~ 38.3
⑧ Prothrombin time (sec)	14.8 (25)	15.2 (25)	12.4 ~ 17.3	12 ~ 18.3
⑨ Activated partial thromboplastin time (sec)	19.1 (25)	18.4 (25)	16.9 ~ 21.3	14.4 ~ 22.3
⑩ Total leukocyte count (10^2/μL)	75 (55)	83 (55)	40 ~ 111	39 ~ 128
⑪ Platelet count (10^4/μL)	124 (55)	124 (55)	98 ~ 150	92 ~ 157
⑫ Baso	0.0 (55)	0.0 (55)		
⑬ Eosin	1.1 (55)	1.2 (55)	0.2 ~ 2.0	0.0 ~ 2.6
⑭ Seg	18.5 (55)	18.5 (55)	8.1 ~ 29	8.2 ~ 28.8
⑮ Lymph	77.0 (55)	76.6 (55)	65.2 ~ 88.7	65.4 ~ 87.8
⑯ Mono	3.4 (55)	3.6 (55)	0.3 ~ 6.4	0.8 ~ 6.5
Biochemical parameters				
① Lactate dehydrogenase (IU/L)	350* (75)	316* (75)	59 ~ 641	47 ~ 585
② Aspartate aminotransferase (IU/L)	72* (75)	76* (75)	52 ~ 92	49 ~ 103
③ Alanine aminotransferase (IU/L)	37* (75)	40* (75)	26 ~ 47	21 ~ 59
④ Alkaline phosphatase (IU/L)	450* (75)	352* (75)	213 ~ 686	226 ~ 478
⑤ γ-Glutamyl transpeptidase (IU/L)	0.65* (75)	0.64* (75)	0.14 ~ 1.15	0.16 ~ 1.13
⑥ Cholinesterase (IU/L)	46 (75)	44 (75)	15 ~ 76	12 ~ 76
⑦ Total protein (g/dL)	5.97 (75)	6.01 (75)	5.46 ~ 6.48	5.4 ~ 6.61
⑧ Albumin (g/dL)	2.90 (75)	2.86 (75)	2.51 ~ 3.3	2.47 ~ 3.25
⑨ A/G ratio	0.95 (75)	0.91 (75)	0.78 ~ 1.12	0.75 ~ 1.07
⑩ Total cholesterol (mg/dL)	63 (75)	69 (75)	37 ~ 89	38 ~ 99
⑪ Triglyceride (mg/dL)	52 (75)	49 (75)	9 ~ 94	6 ~ 92
⑫ Glucose (mg/dL)	155 (75)	157 (75)	126 ~ 184	131 ~ 182
⑬ Urea nitrogen (mg/dL)	13.6* (75)	15.8* (75)	10.5 ~ 16.7	8.6 ~ 23
⑭ Creatinine (mg/dL)	0.42 (75)	0.44 (75)	0.30 ~ 0.54	0.31 ~ 56
⑮ Total bilirubin (mg/dL)	0.31 (75)	0.30 (75)	0.21 ~ 0.42	0.16 ~ 0.44
⑯ Calcium (mg/dL)	9.9 (75)	9.9 (75)	8.9 ~ 10.8	9.1 ~ 10.8
⑰ Inorganic phosphorus (mg/dL)	7.0 (75)	6.8 (75)	5.8 ~ 8.1	5.6 ~ 8.0
⑱ Sodium (mEq/L)	145 (75)	145 (75)	141 ~ 149	140 ~ 150
⑲ Potassium (mEq/L)	4.74 (75)	4.81 (75)	3.88 ~ 5.60	3.92 ~ 5.70
⑳ Chloride (mEq/L)	106 (75)	106 (75)	101 ~ 110	101 ~ 110

a) : (mean−2S.D.) ~ (mean+2S.D.) .

( ) : Number of animals.

* : Calculated from log-transformed data.

A : 15~16-week-old rat.

B : 17~18-week-old rat.

Appendix 43 Historical background data of the Crl:CD(SD) strain female rats on the hematological and biochemical parameters

Parameters	Mean		Normal range[a)]	
	A	B	A	B
Hematological parameters				
① Erythrocyte count (10^4/μL)	690 (55)	814 (55)	613 ~ 767	738 ~ 890
② Hemoglobin concentration (g/dL)	13.2 (55)	14.9 (55)	12 ~ 14.5	13.7 ~ 16.2
③ Hematocrit value (%)	40.5 (55)	43.5 (55)	36 ~ 45.1	39.3 ~ 47.7
④ Mean corpuscular volume (fL)	59 (55)	54 (55)	52 ~ 66	50 ~ 57
⑤ Mean corpuscular hemoglobin (pg)	19.2 (55)	18.4 (55)	17.9 ~ 20.4	17.3 ~ 19.5
⑥ Mean corpuscular hemoglobin concentration (%)	32.6 (55)	34.4 (55)	30.1 ~ 35.1	32.5 ~ 36.4
⑦ Reticulocyte count (‰)	76.2* (55)	22.2* (55)	36 ~ 116.5	12.4 ~ 32.1
⑧ Prothrombin time (sec)	16.0 (25)	15.4 (25)	11.8 ~ 20.3	12.2 ~ 18.6
⑨ Activated partial thromboplastin time (sec)	16.7 (25)	16.4 (25)	13.8 ~ 19.6	13.8 ~ 18.9
⑩ Total leukocyte count (10^2/μL)	78 (55)	42 (55)	40 ~ 117	20 ~ 63
⑪ Platelet count (10^4/μL)	148 (55)	121 (55)	95 ~ 202	94 ~ 148
⑫ Baso	0.0 (55)	0.0 (55)		
⑬ Eosin	0.8 (55)	1.6 (55)	0.0 ~ 1.5	0.4 ~ 2.7
⑭ Seg	28.8 (55)	18.5 (55)	15.2 ~ 42.3	7.6 ~ 29.4
⑮ Lymph	67.3 (55)	77.8 (55)	53.6 ~ 80.9	66.5 ~ 89.1
⑯ Mono	3.2 (55)	2.1 (55)	0.8 ~ 5.6	0.5 ~ 3.7
Biochemical parameters				
① Lactate dehydrogenase (IU/L)	370* (75)	333* (75)	64 ~ 677	68 ~ 599
② Aspartate aminotransferase (IU/L)	88* (75)	81* (75)	40 ~ 135	14 ~ 176
③ Alanine aminotransferase (IU/L)	66* (75)	35* (75)	40 ~ 93	7 ~ 63
④ Alkaline phosphatase (IU/L)	404* (75)	165* (75)	84 ~ 723	72 ~ 257
⑤ γ-Glutamyl transpeptidase (IU/L)	0.75* (75)	0.90* (75)	0.13 ~ 1.36	0.03 ~ 1.78
⑥ Cholinesterase (IU/L)	276 (75)	560 (75)	100 ~ 452	190 ~ 930
⑦ Total protein (g/dL)	6.11 (75)	6.65 (75)	5.38 ~ 6.84	5.81 ~ 7.49
⑧ Albumin (g/dL)	3.13 (75)	3.64 (75)	2.52 ~ 3.74	2.85 ~ 4.43
⑨ A/G ratio	1.06 (75)	1.22 (75)	0.79 ~ 1.33	0.87 ~ 1.57
⑩ Total cholesterol (mg/dL)	76 (75)	85 (75)	46 ~ 106	51 ~ 118
⑪ Triglyceride (mg/dL)	119 (75)	28 (75)	13 ~ 226	1 ~ 57
⑫ Glucose (mg/dL)	144 (75)	136 (75)	116 ~ 172	108 ~ 164
⑬ Urea nitrogen (mg/dL)	22.9* (75)	17.2* (75)	14.5 ~ 31.3	11.6 ~ 22.7
⑭ Creatinine (mg/dL)	0.51 (75)	0.48 (75)	0.39 ~ 0.62	0.36 ~ 0.60
⑮ Total bilirubin (mg/dL)	0.28 (75)	0.26 (75)	0.20 ~ 0.36	0.18 ~ 0.35
⑯ Calcium (mg/dL)	10.7 (75)	10.2 (75)	9.5 ~ 12.0	9.3 ~ 11
⑰ Inorganic phosphorus (mg/dL)	8.6 (75)	5.7 (75)	6.7 ~ 10.5	3.8 ~ 7.5
⑱ Sodium (mEq/L)	144 (75)	145 (75)	138 ~ 150	141 ~ 150
⑲ Potassium (mEq/L)	4.77 (75)	4.62 (75)	3.92 ~ 5.63	3.79 ~ 5.44
⑳ Chloride (mEq/L)	102 (75)	107 (75)	96 ~ 108	102 ~ 112

a) : (mean−2S.D.) ~ (mean+2S.D.) .

( ) : Number of animals.

* : Calculated from log-transformed data.

A : 15~16-week-old rat.

B : 17~18-week-old rat.

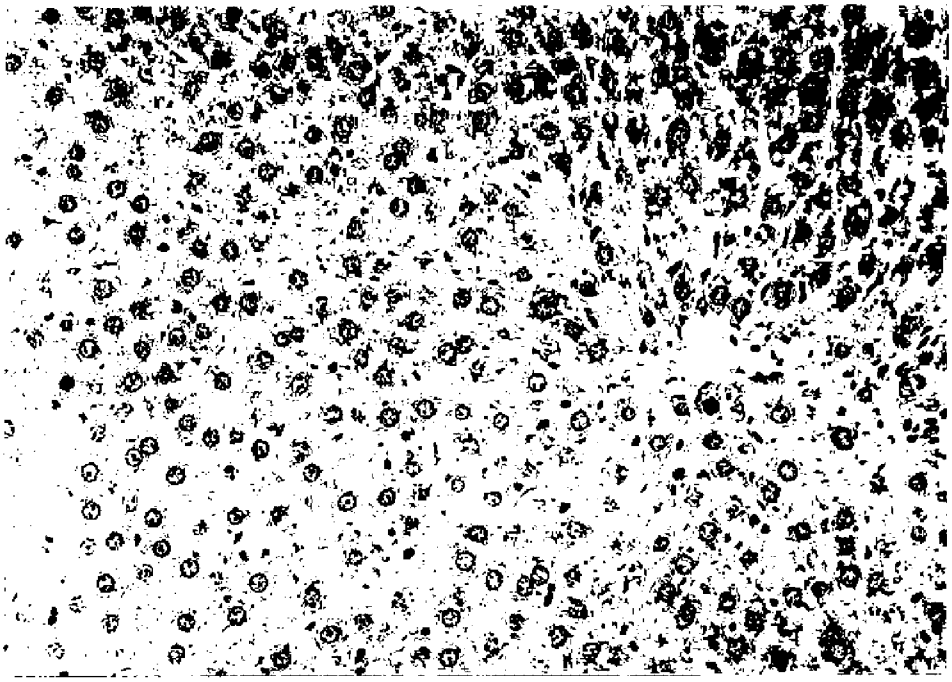

Photo 1. Liver (0 mg/kg group, male, No. 003, H·E stain, ×264)
No abnormalities

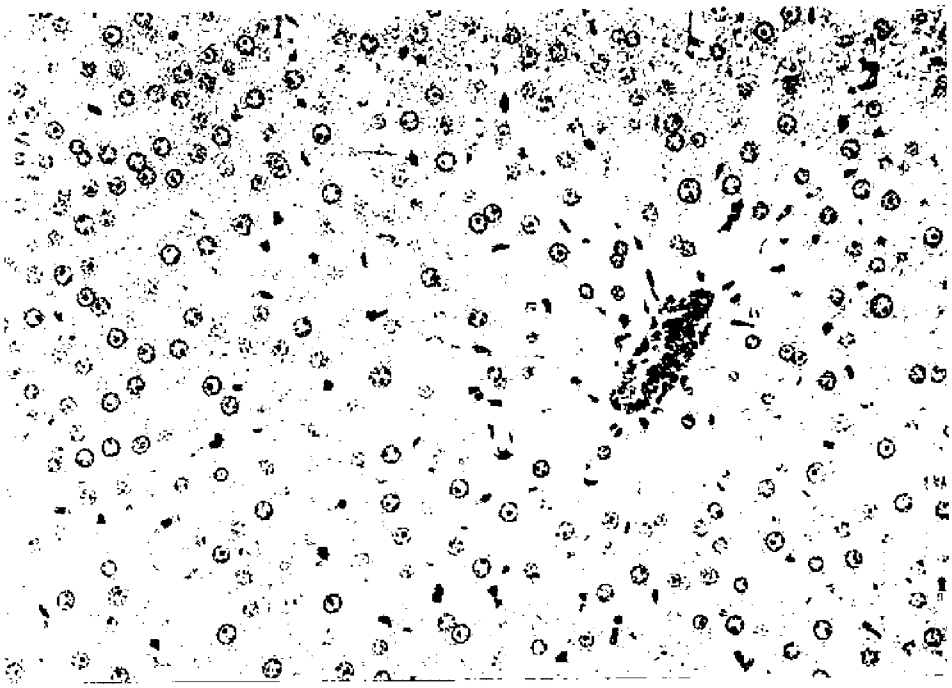

Photo 2. Liver (100 mg/kg group, male, No. 054, H·E stain, ×264)
Centrilobular hepatocellular hypertrophy