最終報告書

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）の
ラット新生児における哺育期投与試験

（試験番号：98-094）

財団法人　畜産生物科学安全研究所

陳　述　書

試験の表題

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）のラット新生児における哺育期投与試験（試験番号：98-094）

本試験は，化審法のＧＬＰ「新規化学物質に係る試験および指定化学物質に係る有害性の調査の項目等を定める命令第４条に規定する試験施設について」（昭和59年３月31日付環保業第39号環境庁企画調整局長，薬発第229号厚生省薬務局長，59基局第85号通商産業省基礎産業局長，通達）に定める基準に準拠して実施した．

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　部長

[redacted]

平成 12 年 3 月 6 日

試験の表題

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）のラット新生児における哺育期投与試験（試験番号98-094）

試験委託者

名　　称	厚生省生活衛生局
所 在 地	東京都千代田区霞が関一丁目２番２号
委託責任者	局　　長 [redacted]

試験実施施設

名　　称	財団法人　畜産生物科学安全研究所
所 在 地	神奈川県相模原市橋本台三丁目７番11号
運営管理者	専務理事 [redacted]
	専務理事
試験責任者	安全性研究部長
信頼性保証	試験研究管理室
責任者	主任研究員

試験日程

試験開始	平成11年５月17日
母動物搬入	平成11年６月３日
分　　娩	平成11年６月10日
群 分 け	平成11年６月13日
投与開始	平成11年６月14日
投与終了・離乳	平成11年７月１日
投与終了時解剖	平成11年７月２日
観察終了	平成11年９月２日
観察終了時解剖	平成11年９月３日
試験終了	平成12年３月６日

試験成績の信頼性に影響を及ぼしたと思われる要因

本試験に関し，試験成績の信頼性に影響を及ぼしたと思われる要因はなかった．

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（一般状態，体重，摂餌量，感覚・反射機能検査，外形分化状態，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　部長

氏名 [redacted]　　平成12年 3月 6日

試験担当者およびその業務分担

投与液の調製

投与液の分析

動物飼育・投与・臨床観察

臨床検査

病理検査

[redacted]

信頼性保証証明書

試験表題　：　4,4'-イソプロピリデンビス(2,6-ジブロモフェノール)のラット新生児における哺育期投与試験

試験番号　：　９８－０９４

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．試験計画書記載事項変更審査		
（変－１） 平成11年07月01日	平成11年07月01日	平成11年07月01日
２．試験実施状況査察		
動物導入 平成11年06月03日	平成11年06月03日	平成11年06月03日
検　疫 平成11年06月04日	平成11年06月04日	平成11年06月04日
分娩の確認 平成11年06月10日	平成11年06月10日	平成11年06月10日
哺育状態の観察・被験物質調製 平成11年06月11日	平成11年06月11日	平成11年06月11日
群分け・個体識別 平成11年06月13日	平成11年06月14日	平成11年06月14日
体重測定・投与・症状観察 平成11年06月14日	平成11年06月14日	平成11年06月14日
被験物質調製 平成11年06月24日	平成11年06月24日	平成11年06月24日
餌測定(残餌量)・症状観察 平成11年06月29日	平成11年06月29日	平成11年06月29日
投与・感覚，反射機能検査・離乳 平成11年07月01日	平成11年07月01日	平成11年07月01日
解剖・病理組織標本作製（臓器・組織の固定）・血液検査 平成11年07月02日	平成11年07月02日	平成11年07月02日
病理組織標本作製の外部委託（病理検体の引き渡し） 平成11年07月07日	平成11年07月07日	平成11年07月07日
死亡動物の解剖 平成11年07月08日	平成11年07月08日	平成11年07月08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
餌測定(給餌量) 平成11年08月11日	平成11年08月11日	平成11年08月11日
体重測定 平成11年08月12日	平成11年08月12日	平成11年08月12日
投与液の濃度確認（標準溶液の調製，分析試料の調製，測定） 平成11年08月16日	平成11年08月16日	平成11年08月16日
尿検査 平成11年08月27日	平成11年08月27日	平成11年08月27日
解　剖 平成11年09月03日	平成11年09月03日	平成11年09月03日
病理組織標本作製の外部委託（病理組織標本の受け取り） 平成11年09月08日	平成11年09月08日	平成11年09月08日
血液学的検査 平成11年09月09日	平成11年09月09日	平成11年09月09日
3．生データ査察 平成12年01月11日 ～ 同年01月12日	平成12年01月12日	平成12年01月12日
4．報告書（草案）審査 平成12年01月13日 ～ 同年01月14日	平成12年01月14日	平成12年01月14日
5．報告書審査 平成12年03月06日	平成12年03月06日	平成12年03月06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 12 年 3 月 6 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]

目　次

添付資料Ｂ　個体別表等

要約

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）のラット新生児哺育期投与による反復投与毒性並びにその後の成長，機能及び形態に及ぼす影響について検討するため，SD系[Crj:CD(SD)IGS] ラットの新生児を1群雌雄各12匹とし，本物質を0，40，200及び600mg/kg/dayで，4日齢から21日齢までの18日間反復経口投与し，22日齢で各群の半数を解剖した．残りの半数は21日齢で離乳させ，84日齢まで観察し，85日齢で解剖した．

投与期間中及び投与終了時の観察・検査において，200及び600mg/kg群で雌雄に下痢が認められ，600mg/kg群の雌では体重増加の抑制が一過性に認められた．感覚・反射機能には，有意な変化は認められなかった．血液学検査では，600mg/kg群で雄に血色素量，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及び活性化部分トロンボプラスチン時間，雌に平均赤血球容積及び平均赤血球血色素量の，いずれもの有意な減少が認められた．血液生化学検査では，600mg/kg群で雌雄に，総ビリルビンの有意な増加が認められた．器官重量では，600mg/kg群で雌雄に腎臓の絶対及び相対重量，雄に肝臓の相対重量の有意な増加が認められ，雌の肝臓相対重量も増加傾向を示した．病理学検査では，600mg/kg群の雌雄及び200mg/kg群の雄に腎臓の多発性嚢胞形成，600mg/kg群の雄に肝臓の肝細胞肥大が認められ，600mg/kg群の雌雄の腎臓は肉眼的にも腫大していた．また，600mg/kg群で雌雄に盲腸の軽度な拡張が認められたが，病理組織学的には変化は認められなかった．

なお，投与後の観察期間の初期において，600mg/kg群の雄の2匹及び雌の1匹の一般状態が急激に悪化し，死亡あるいは切迫屠殺した．病理組織学検査で，腎臓に嚢胞形成を含む重篤な変化が認められた．

生存動物の投与後の観察及び観察期間終了時の検査では，一般状態，外形分化状態，摂餌量，尿検査，血液学検査及び血液生化学検査で，被験物質の投与に起因する変化は，認められなかった．器官重量では，600mg/kg群の雌雄の腎臓重量の変化は回復傾向を示したものの，絶対重量の有意な増加あるいは増加傾向が認められた．病理組織学検査では，腎臓の多発性嚢胞が200mg/kg群の雌及び600mg/kg群の雌雄に残存して認められたほか，600mg/kg群の雌雄では線維化を伴っており，肉眼的には腎臓の陥凹部あるいは変形が認められた．

以上の結果から，4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）のラット新生児に対する反復投与毒性は，腎臓，肝臓及び盲腸の拡張を伴う消化管機能に対する影響で，特に腎臓の形態的変化は特徴的であった．また，哺育期の投与により発現した変化は可逆的であるものの，腎臓の変化は観察期間終了時の検査においても残存してい

た．投与終了後のラットの成長，機能及び形態に対する遅発的な毒性影響は認められなかった．無影響量は，雌雄とも40mg/kg/dayと推定された．

緒言

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）は別名テトラブロモビスフェノールAと称し，プラスチック，紙，織物等の難燃剤として用いられている化学物質である．

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）の毒性について，*in vitro*でミトコンドリアの脱共役作用及び溶血作用を有することが知られている[1]．ラットにおける急性経口LD_{50}値は5000mg/kg以上で，最高0.1%濃度（体重当たりの摂取量50mg/kg/day）の28日間混餌投与において，ラットの一般状態，体重及び摂餌量に変化は認められず，またラットを用いた90日間飼料添加による反復投与毒性試験においても，最高100mg/kg/dayに相当する濃度の投与で毒性は認められていない[2]．マウスを用いた3か月間飼料添加による反復投与毒性試験においては，体重増加の抑制，赤血球数，血色素量，ヘマトクリット値，血清トリグリセライド及び総タンパクの減少，脾臓の重量増加及び髄外造血が認められ，無毒性量は0.49%（700mg/kg/day）と推定されている[2]．ラットを用いた催奇形性試験では，催奇形性は認められていない[3]．

一方，医薬品等のヒトに対する感受性は，新生児，小児，成人等で異なる場合のあることが知られており，一般化学物質に対する感受性も，異なる可能性が考えられる．しかしながら，化学物質の毒性学的影響は，離乳後の動物を用いて試験されており，新生児に投与した場合の影響については，ほとんど知られていない．

試験目的

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）をラットの新生児に哺育期間中反復経口投与し，新生児に対する反復投与毒性並びにその後のラットの成長，機能及び形態に及ぼす影響を検討する．

試験材料及び方法

1．被験物質

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）[CAS No.79-94-7]は，分子量543.88，融点182℃，沸点316℃，水に不溶，アセトン，メタノール，エーテルに可溶な白色・無臭の固体で，試験には東ソー株式会社（山口県新南陽市開成町4560番）から提供されたロット番号8Y291G，純度99.5%（不純物としてトリブロモビスフェノールAを含む）のものを冷暗所（4℃）で密栓して保管し，使用した．被験物質の詳細は，Appendix 1 に示した．用いた被験物質を東ソー株式会社に委託して試験終了後に分析し，試験期間中安定であったことを確認した（Appendix 2）．被験物質投与液について，

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）は油溶性であるが，食物油には投与に必要は高濃度に溶解できないことから，溶媒として0.1%Tween80添加0.5%カルボキシメチルセルロースナトリウム水溶液（Tween80：Difco Laboratories，ロット番号101911401；カルボキシメチルセルロースナトリウム：関東化学株式会社，ロット番号007G1484；局方精製水：共栄製薬株式会社，ロット番号181178）を用い，所定の投与用量になるような濃度の懸濁液に調製した．投与液は少なくとも８日間は安定であることが確認されている[5]ので週１回調製し，１日の使用量ごとに小分けして使用時まで冷暗所（４℃）・密栓下で保管し，調製後７日以内に使用した．また，初回に調製し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．供試動物及び飼育条件

動物はSD系［Crj:CD(SD)IGS］SPFラット（９週齢）の妊娠雌（妊娠15日）を，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番地）から20匹搬入し，分娩後新生児が３日齢に達するまでの10日間検疫・馴化飼育し，その間に体重測定及び臨床観察を行い，健康状態，分娩状態，哺育状態等を確認した．試験に用いる母動物は，妊娠21日の午後５時以降に分娩を開始し，妊娠22日の午前中に分娩を終了して正常な哺育状態を示す母動物の内，新生児数が中央値に近い個体から順に12匹を選別した．新生児の群分けは３日齢（出産日を０日齢とする）時に行い，選択した母動物の新生児を親から離して雌雄別にプールした後体重を測定し，体重の中央値に近い個体から順に雌雄各48匹の新生児を選別し，１群雌雄各12匹として体重に基づく層化無作為抽出法により４群に振り分けた．振り分けた各群の新生児の雌雄各１匹を，無作為抽出法により12匹の母動物（里親）に振り分け，母動物当たり群の異なる雌雄各１匹の計８匹が割り当てられるようにした(Appendix 4)．新生児の群分日平均体重（体重範囲）は雄 10.4 (9.8－11.2)g，雌 10.0(9.4－10.5)g，その翌日の投与開始日平均体重（体重範囲）は雄12.6(11.0－13.5)g，雌 12.1(10.7－13.0)gであった．各個体は，ラック及びケージへの標識並びに親動物及び離乳後の児動物は耳パンチ法，離乳前の新生児は雌雄別に左右前後肢の足掌に入れ墨することにより識別した．ラットは，温度21－23℃，湿度55－62%，換気回数10回以上／時（オールフレッシュエアー方式，温度・湿度の測定結果：Appendix 5），照明時間12時間／日（午前６時点灯，午後６時消灯）に制御されたバリアーシステム動物室（第４室）で，親動物及び離乳後（生後21日に離乳）の児動物は個体別に，離乳前は親動物と児動物と同居させて飼育した．飼育ケージは，導入時から分娩を経て離乳まではポリカーボネート製ケージ〔265W×426D×200H(mm)，床敷としてホワイトフレーク（日本チャールス・リバー株式会社）〕，離乳後はステンレス

製ケージ〔260 w×380D×180H(mm)〕を用い，これをステンレス製5段のラックに配置した．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99.03.73, 99.06.53, 99.07.55）と飲料水（1 μm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）は自由に摂取させた．飼料，床敷及び飲料水中の汚染物質についての分析の結果（Appendices 6−8）はいずれも許容濃度の範囲内で，動物室の温度・湿度の測定結果からも，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された．なお，児動物の離乳後は親動物を試験から除外した．

3．投与量の設定，試験群の構成及び投与方法

投与量は，本試験に先立ち実施した投与量設定試験の結果に基づいて設定した．投与量設定試験は1群雌雄各5匹の新生児ラットに4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）を0，40，200及び1000mg/kg/dayで，生後4日から21日までの18日間経口投与した．1000mg/kg群で雌雄に肛門周囲の汚れ，体重増加の抑制傾向，血小板数，血清LDH，GOT，総ビリルビン，尿素窒素，クレアチニン，肝臓及び腎臓重量のいずれも高値，血色素量，プロトロンビン時間，胸腺重量のいずれも低値，盲腸の拡張，200 mg/kg群で雌にプロトロンビン時間の低値が認められ，得に1000mg/kg群の腎臓重量の変化は，対照群の約6倍に達する顕著なものであった．

以上の結果から，本試験における投与量は，確実に毒性影響が発現すると予測される600mg/kg/dayを高用量，毒性影響が発現しないと予測される40mg/kg/dayを低用量とし，これらの用量の間に200mg/kg/dayの計3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40mg/kg/day投与群（40mg/kg群），(3) 同 200 mg/kg/day投与群（200mg/kg群），(4) 同 600mg/kg/day投与群（600mg/kg群）の4群とし，各群雌雄各12匹のうち，雌雄各6匹は投与終了の翌日（22日齢）に解剖に供する投与終了時解剖動物，残りの雌雄は観察終了翌日（85日齢）に解剖に供する観察終了時解剖動物とした．

投与方法は，投与液量を体重1kg当たり3mLとし，外径0.96mmのポリエチレン製チューブあるいはテフロン製マウス用経口ゾンデを装着した注射筒を用いて，生後4日から21日（離乳）までの18日間，毎日1回（午前中），胃内に投与した．各個体の投与液量は，至近日の測定体重をもとに算出した．対照群には，被験物質を投与液に調製するために用いた溶媒を同様に投与した．

4．観察及び検査

観察期間を，投与開始から親動物は児動物の離乳まで，児動物は生後84日までとし，

児動物については生後22日に投与終了時の解剖，85日に観察終了時の解剖を行った．その間に，次の観察及び検査を実施した．

1）親動物

(1) 一般状態観察

観察期間中毎日，哺育行動を含む一般状態について観察した．

(2) 体重

哺育4（分娩終了の確認日を哺育0日とする），10，16及び21日に測定した．

(3) 摂餌量

哺育6～7，12～13及び18～19日の間の24時間飼料消費量を，児動物を含めた母動物単位で測定した．

2）児動物

(1) 一般状態観察

毎日，少なくとも1回は動物の一般状態について観察した．投与期間中，毎日2回は動物の死亡や瀕死動物の有無を確認した．離乳前の観察では，親動物を離した状態での観察も行った．

(2) 感覚・反射機能検査

雄は生後20日，雌は21日にスコアリングシステムにより歩行状態（1：不動，2：正常，3：よろめく，4：後肢伸展／引きずり，5：肢が外側を向く，6：前肢の引きずり／体重が支えきれない，7：つま先立で歩行，8：体を引きずる／平伏），瞳孔反射（1：直ちに反応，2：反応なし），耳介反射（Preyer反射）及び角膜反射（1：正常，2：やや反応遅い，3：反応遅い，4：反応なし），視覚性踏み直り反射（1：直ちにつかむ，2：つかもうと繰り返した後つかむ，3：つかもうとするが方向を間違える，4：つかもうとしない），面上正向反射（1：素早く復帰／正常，2：やや遅い／1秒以上，3：遅い／2秒以上，4：仰向けのまま），空中正向反射（1：正常に着地，2：側位，3：背位）並びに同側屈筋反射（1：直ちに同側に反応，2：反対側に反応，3：反応なし）について検査した．

(3) 外形分化状態観察

全例について，投与終了日を限度として生後7日から毛生，9日から切歯萌出，11日から眼瞼開裂の状態を陽性になるまで，また観察期間終了時屠殺動物についてのみ，雄は生後17日から精巣下降，雌は29日から膣開口の状態を陽性になるまで毎日観察した．

(4) 体重

生後4，7，10，13，16，19，21日，その後は7日間隔で測定し，投与期間中及びその後の観察期間中の体重増加量を算出した．また屠殺日にも測定した．

(5) 摂餌量

離乳後，体重の測定日に合わせて前日からの24時間飼料消費量を測定した．

(6) 尿検査

生後78～82日の間に検査を行った．すなわち，新鮮尿を採取し試験紙法（マルティスティックス，バイエル・三共株式会社）による潜血，pH，タンパク，糖，ケトン体，ビリルビン，ウロビリノーゲンの定性的検査，またラットを代謝ケージに短時間（約3時間）収容して得た蓄尿について，色調の観察，比重の測定（屈折計，エルマ光学株式会社）及び沈渣の検査（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時間の尿量を測定した．

(7) 血液学検査

採血は，投与期間終了翌日及び観察期間終了翌日にエーテル麻酔下で開腹して腹大動脈より行った．動物は前日の午後5時より除餌し，水のみを与えた．採取した血液は3分割し，その一部は EDTA-2K で凝固防止処理し，多項目自動血球計数装置（E-4000，東亜医用電子株式会社）により，赤血球数（電気抵抗検出方式），血色素量（ラウリル硫酸ナトリウムーヘモグロビン法），ヘマトクリット値（パルス検出方式），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），白血球数及び血小板数（以上，電気抵抗検出方式）を，また塗抹標本を作製して網状赤血球数（Brilliant cresyl blue染色標本の鏡検）及び白血球百分率（May-Giemsa染色標本の鏡検）を測定した．さらに，一部は3.8%クエン酸ナトリウム液で処理後血漿を分離し，血液凝固自動測定装置（KC-10A，米国アメルング社）によりプロトロンビン時間（Quick 一段法）及び活性化部分トロンボプラスチン時間（エラジン酸活性化法）を測定した．

(8) 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-BM 8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（Glck[1)]-G-6-PHD[2)]法），総コレステロール（酵素法，CES[3)]-CO[4)]-POD[5)]系），トリグリセライド（酵素法，LPL[6)]-GK[7)]-GPO[8)]-POD[5)]系），リン脂質（PLD[9)]-COD[10)]-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），GOT，GPT，ALP，γ-GTP（以上，JSCC[11)] 法），LDH（SFBC[12)]法），コリンエステラーゼ（BTC[13)]-DTNB[14)]法），カルシウム（OCPC法）

及び無機リン（酵素法，PNP[15]-XOD[16]-POD[5]系）を，また電解質自動分析装置(NAKL-132，東亜電波工業株式会社）によりナトリウム，カリウム及び塩素（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]：ホスフォリパーゼ，[10]：コリンオキシダーゼ，[11]：日本臨床化学会，[12]：フランス臨床生物学会，[13]：ブチリルチオコリン，[14]：5,5-ジチオビス-2-ニトロ安息香酸，[15]：プリンヌクレオシドホスフォリラーゼ，[16]：キサンチンオキシダーゼ

(9) 剖検

死亡動物は発見後速やかに，瀕死状態にある動物はエーテル麻酔下で，及び生存動物は最終投与日の翌日あるいは観察終了日の翌日の採血に続いていずれも放血屠殺し，体表，開口部粘膜及び内部諸器官を肉眼的に観察した．

(10) 器官重量

脳，下垂体，胸腺，甲状腺，心臓，肺（気管を含めて秤量），肝臓，脾臓，腎臓，副腎，雄ではさらに精巣，精巣上体，前立腺，精嚢（投与終了時解剖動物では前立腺を含めて秤量），雌では卵巣，子宮を秤量（絶対重量）し，解剖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，甲状腺は固定後に秤量した．

(11)病理組織学検査

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）で固定して保存した．

脳，下垂体、眼球，胸腺，甲状腺（上皮小体を含む），肺（気管支を含む），気管，心臓，舌，食道，胃，腸（十二指腸，空腸，回腸，盲腸，結腸，直腸），肝臓，膵臓，脾臓，腎臓，副腎，リンパ節（頸部リンパ節，腸間膜リンパ節），膀胱，脊髄の頸，胸，腰部），骨髄（大腿骨，胸骨），坐骨神経，大動脈，下腿三頭筋，その他肉眼的異常部位，さらに雄では精巣，精巣上体，前立腺，精嚢，雌では卵巣，子宮

病理組織学検査は，対照群と600mg/kg群の全動物の脳，下垂体，胸腺，甲状腺，

肺，気管，心臓，胃，腸，肝臓，膵臓，脾臓，腎臓，副腎，リンパ節，膀胱，脊髄，骨髄，坐骨神経，精巣，精巣上体，前立腺，精嚢，卵巣及び子宮について実施した．40及び200mg/kg群については，投与期間終了時解剖動物では600mg/kg群の検査で雌雄の腎臓及び雄の肝臓に変化が認められたので雌雄の腎臓及び雄の肝臓について検査した．また，また，投与後観察期間終了時解剖動物では，雌雄の腎臓に変化が認められたので雌雄の腎臓について実施した．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．組織標本は，株式会社組織科学研究所（東京都青梅市黒沢二丁目984-1番）に委託して作製した．

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．すなわち，パラメトリックデータ（体重・体重増加量・摂餌量・外形分化状態観察データ・尿量及び尿比重・血液学検査データ・血液生化学検査データ・器官重量）は，Bartrett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，その結果有意差が認められた場合，Dunnett 法あるいはScheffe 法（群間で標本数が異なる場合）により，被験物質投与各群と対照群との比較検定を行った．分散が一様でない場合及びノンパラメトリックデータ（白血球百分率・尿検査における定性的データ）は，Kruskal-Wallisの順位検定を行い，その結果有意差が認められた場合，Dunnett 型あるいはScheffe 型（群間で標本数が異なる場合）の検定により，被験物質投与各群と対照群を比較した．カテゴリカルデータ（一般状態の観察・感覚反射機能検査・剖検・病理組織学検査の各データ）には，Fisherの直接確率法を用いた．

試験結果

1．児動物

1）一般状態及び死亡（Tables 1, 2, Appendices 9, 10）

投与期間中の観察において，下痢及びそれによる肛門周囲の汚れが，雌雄各12匹中，200mg/kg群で雄の8匹，雌の9匹及び600mg/kg群で雌雄の全例に認められた．死亡は，認められなかった．

投与終了後の観察期間中の観察においては，600mg/kg群で雄の2匹及び雌の1匹に削痩，自発運動低下，蒼白，立毛あるいは腹部膨満等の症状が投与終了後4日以降に発現し，投与終了後7日に雌雄各1匹が死後発見された．また，雄の他の1匹も瀕死状態となったので，同日に切迫屠殺した．その他の動物には，変化は認められなかった．

2）感覚・反射機能（Table 3, Appendices 11, 12）

投与期間中の検査において，歩行状態並びに空中正向反射，視覚性踏み直り反射，角膜反射，同側屈筋反射，耳介反射及び瞳孔反射の各機能については，検査した全ての例で正常であった．面上正向反射については，各12匹中200mg/kg群の雄1匹並びに600mg/kg群の雄1匹及び雌1匹に軽度な遅延が認められたが，統計学的に有意な変化でなかった．

3）外形分化状態（Table 4, Appendices 13, 14）

雌雄の腹部毛生，切歯萌出，眼瞼開裂，雄の精巣下降及び雌の膣開口の時期において，有意な変化は認められなかった．

4）体重（Figures 1, 2, Tables 5, 6, Appendices 15, 16）

投与期間において，600mg/kg群で雌の投与7日の体重が対照群に比べて有意に少なかった．しかしながら，投与期間中の体重増加量には有意な変化は認められなかった．投与終了後の観察期間では，雌雄とも体重に有意な変化は認められなかった．

5）摂餌量（Tables 7, 8, Appendices 17, 18）

投与終了後の観察期間において，摂餌量に有意な変化は認められなかった．

6）尿検査（Tables 9, 10, Appendices 19, 20）

観察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．

7）血液学検査（Tables 11－14, Appendices 21－24, 背景データ：Appendices 43, 44）

投与期間終了時の検査において，600mg/kg群の雌雄の血色素量及びヘマトクリット値は対照群に比べてやや低値を示し，雌の血色素量には有意差が認められた．また，同群で雌雄に平均赤血球容積及び平均赤血球血色素量，さらに雌に平均赤血球血色素濃度のいずれも有意な減少が認められた．また，600mg/kg群で雄に活性化部分トロンボプラスチン時間の有意な短縮が認められ，雌においても同様の傾向が認められた．なお，40mg/kg群の雌の活性化部分トロンボプラスチン時間は対照群に比べて有意な高値を示したが，変化に用量相関性は認められず，また背景データにおける正常範囲内での変動であった．

観察期間終了時の検査においては，各検査項目に有意な変化は認められなかった．

8）血液生化学検査（Tables 15－18, Appendices 25－28, 背景データ：Appendices 43, 44）

投与期間終了時の検査において，600mg/kg群で雌雄に総ビリルビンの有意な増加が認められた．

観察期間終了時の検査においては，各検査項目に有意な変化は認められなかった．

なお，３匹の死亡動物のうち，瀕死期に採血し得た雄の１匹では，尿素窒素の異常高値およびGOT, ALP, γ-GTP, ChEの高値が認められた．

9）剖検（Tables 19－20, Appendices 29－32）

投与期間終了時の解剖動物において，600mg/kg群で雌雄各６匹中全例に，腎臓の中等度ないし重度の腫大が認められ，雌の１匹には赤色・暗赤色・灰白色の変色点／域も認められた．また，同群で雄の２匹及び雌の４匹に，盲腸の軽度な拡張が認められた．

死亡あるいは切迫屠殺した600mg/kg群の雄の２匹及び雌の１匹においても，腎臓の重度な腫大及び中等度な赤色点／域が共通して認められた．

観察期間終了時の解剖動物において，600mg/kg群で腎臓の軽度ないし中等度な陥凹部が，雄の４匹中３匹及び雌の５匹中５匹に認められ，雌の２匹には腎臓の変形が認められた．

なお，被験物質の投与とは無関係と思われる変化として，観察期間終了時の解剖動物の対照群の雄の１匹に肺の黒色点，600mg/kg群の雄の１匹に水腎症が認められた．

10) 器官重量 (Tables 21－24, Appendices 33－40)

投与期間終了時の解剖において，600mg/kg群で雌雄に腎臓の絶対重量及び相対重量の有意，かつ，顕著な増加が認められた．さらに，同群で雄に甲状腺の絶対重量の有意な減少並びに肝臓の相対重量の有意な増加が認められた．肝臓の相対重量の増加傾向は，600mg/kg群の雌にも認められた．

観察期間終了時の解剖においては，600mg/kg群で雌に腎臓の絶対重量の有意な増加が認められ，同群の雄においても増加傾向が認められた．しかしながら，投与期間終了時に比べて，変化の程度は明らかに軽減していた．

11) 病理組織学検査 (Tables 25－28, Appendices 29－32)

投与期間終了時解剖動物において，腎臓及び肝臓に被験物質の投与による変化が認められた．すなわち，単発性の嚢胞は対照群においても認められたが，皮髄境界部から皮質内帯にかけての集合管及び遠位尿細管の拡張によると思われる多発性の嚢胞が，200 mg/kg 群で雄の 6 匹中 2 匹，600mg/kg群で雌雄各 6 匹中全例に認められ，600mg/kg群の変化は肉眼的にも組織標本がスポンジ様を呈する重度なもので，健常な部分の皮質はやや萎縮していた．また，皮髄境界部における集合管上皮細胞の変性及び過形成が，多発性の嚢胞が認められた200mg/kg群の雄の 2 匹及び600mg/kg群の雄の 6 匹，雌の 4 匹に認められた．さらに，600mg/kg群では，雌雄に尿細管の硝子円柱及び好塩基性尿細管がめだつ例，雌に感染を伺わせる化膿性の炎症を随伴する例も認められた．肝臓については，小葉中心性の軽度な肝細胞肥大が600mg/kg群で雄の 3 匹に認められた．

600mg/kg群で認められた雄 2 匹，雌 1 匹の死亡動物では，腎臓に投与期間終了時解剖動物で認められた変化が認められたほか，尿細管あるいは尿細管上皮の壊死及び顆粒円柱が共通して，雄 2 匹には好塩基性尿細管の増加が認められ，2 匹とも生存動物に比べて変化が重篤であった．腎臓以外の変化としては，雌に子宮の萎縮が認められたほか，肝臓の巣状壊死，腺胃のびらん，肺のうっ血水腫，胸腺の皮質萎縮，脾臓の白脾髄萎縮等の変化が認められたが，死亡動物に共通した変化ではなかった．

観察期間終了時解剖動物においても腎臓に変化が認められ，多発性の嚢胞が200mg/kg群で雌の 6 匹中 1 匹，600mg/kg群で雄 4 匹，雌 5 匹の全例に認められたほか，600mg/kg群では雌雄とも 4 匹に線維化が認められ，硝子円柱，皮質のリンパ球浸潤，好塩基性尿細管の増加例も比較的高率に認められた．そのほかに，比較的低い発現率で顆粒円柱，皮質萎縮，尿細管壊死，褐色色素沈着，集合管上皮細胞の変性及び過形成等の変化が認められた．

なお，投与期間終了時解剖動物，観察期間終了時解剖動物及び死亡動物において，以

上の変化以外にも検査した各器官に変化が認められたが，被験物質の投与との関連性は認められなかった．

2．親動物の健康状態（Appendices 41，42）

一般状態，児動物の哺育状態，体重及び摂餌量に異常は認められなかった．

考察

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）をラットの新生児に哺育期間中経口投与し，新生児に対する反復投与毒性並びにその後のラットの成長，機能及び形態に及ぼす影響について検討した．

新生児に対する反復投与毒性について，200及び600mg/kg群で，雌雄に下痢が認められた．体重では，一過性の増加抑制が，600mg/kg群で雌に認められた．血液学及び血液生化学検査では，600mg/kg群で雌に血色素量の有意な減少が認められ，雌雄の平均赤血球容積及び平均赤血球血色素量並びに雌の平均赤血球血色素濃度は，有意な低値を示した．また，600mg/kg群で雌雄に総ビリルビンの有意な増加，及び雄に活性化部分トロンボプラスチン時間の有意な短縮が認められた．病理学検査では，600mg/kg群で雌雄に腎臓の肉眼的腫大，絶対及び相対重量の有意，かつ，顕著な増加，盲腸の拡張，雄に肝臓の相対重量の有意な増加及び雌に増加傾向が認められた．病理組織学的には，200mg/kgの雄及び600mg/kg群の雌雄に腎臓の多発性嚢胞，雄に肝臓の肝細胞肥大が認められ，盲腸には変化は認められなかった．また，投与期間終了後の観察期間の初期に，600mg/kg群の雄2匹及び雌1匹が死亡し，死亡例に共通して腎臓に嚢胞形成死を伴う重度な病理組織学的変化が認められた．さらに，観察期間終了時の解剖動物においても，投与期間中の変化によると思われる腎臓の多発性嚢胞が，200mg/kgの雌及び600mg/kg群の雌雄に認められた．投与期間中の体重及び感覚・反射機能には，有意な変化は認められなかった．

腎臓の多発性嚢胞形成について，皮髄境界部の集合管及び遠位尿細管の拡張によるもので，また皮髄境界部の集合管には上皮細胞の変性を伴った過形成を示す部位が認められた．

多発性嚢胞腎については，diphenylamine[4]，nordihydroguaiaretic acid[5]，diphenylthiazole[6]，alloxan，ferric-nitrilotriacetate,streptozocin[7]，2-amino-4,5-diphenylthiazole[8]等の化学物質の投与により発現することが知られている．化学物質の種類によりネフロンに対する作用や最初に拡張する部位は異なるものの，嚢胞形成の発現機序についは，尿細管上皮あるいは基底膜の代謝を変化させ，その結果上皮の変性脱落，過形成，異常な細胞外マトリックスの産生等により尿細管が閉塞し，管腔圧の上昇により嚢胞が形成されると考えられている[9,10]．

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）の投与により認められた嚢胞の発現機序は不明であるが，皮髄境界部の集合管の上皮に変性や過形成が認められたことから，集合管に閉塞が起こり内圧が高まったため，集合管および遠位尿細管が拡張し，嚢胞が形成されたものと推測される．

化学物質による多発性嚢胞腎の予後について，diphenylthiazoleの投与による変化は可逆的で，正常な組織構造に回復することが知られている[11]．

4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）投与後の観察期間終了時解剖動物の腎臓においては，嚢胞の数は投与期間終了時解剖動物に比べて少なく，腎臓重量の変化の程度も軽減していたが，線維化及び線維化と関連すると考えられる腎臓の陥凹部あるいは変形が認められ，diphenylthiazoleの投与による変化とは異なる経過を示した．

なお，投与期間終了時解剖動物及び投与後の観察期間終了時解剖動物とも，血液生化学検査等で腎機能と関連する変化は認められず，障害を受けていないネフロンは正常な機能を維持していることが示唆された．ただし，死亡例で瀕死期に採血して検査し得た1匹では，尿素窒素の異常高値が認められ，腎不全が主な死因であることが血液生化学検査においても確認された．

今回，新生児ラットへの4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）の投与により多発性嚢胞腎が認められ，従来の成熟ラットに投与して行われた反復投与毒性試験に関する報告[2]とは異なる結果が得られた．この違いについて，片側の尿管を閉塞して惹起させる腎臓の変化は成熟ラットに比べて幼弱ラットで強いことが知られており[12]，幼弱ラットは成熟ラットに比べて尿路系の閉塞性変化が発現し易いものと推測される．

肝臓に対する影響について，雌雄に肝臓相対重量の増加あるいは増加傾向，雄に肝細胞の肥大が認められた．また，雌雄に認められた総ビリルビンの増加も，肝臓に対する影響と関連した変化と考えられる．

下痢について，脱水状態を示唆する血液学的及び血液生化学的変化は認めらず，体重に対する影響も軽度なものであった．剖検で認められた盲腸の拡張は下痢と関連する変化と考えられが，病理組織学的変化を伴わない単純な拡張であった．

貧血所見について，同様の変化は4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）のマウスを用いた反復投与毒性試験においても認められており[2]，本物質の溶血作用[1]によるものと考えられる．しかしながら，脾臓等に溶血を示唆するヘモジデリンの沈着や骨髄，脾臓，末梢血に貧血に対する造血細胞の反応を示唆する変化が認められず，また血液像も正常範囲（Appendices 43, 44参照）内の軽度な変化であった．

雄に認められた活性化部分トロンボプラスチン時間の短縮について，雌においても同様の傾向が認められることから，被験物質の投与による影響と考えられるが，変化の程度は概ね正常範囲内の軽度な変化であった．

なお，600mg/kg群で雄に甲状腺の絶対重量のみの有意な減少が認められたが，病理組

織学的変化は認められず，また雌にはこのような傾向は認められなかったことから，被験物質の投与による影響ではなく，偶発的な所見と判断された．

投与終了後のラットの成長，機能及び形態に及ぼす影響については，投与後の観察期間の初期に死亡例が認められ，また腎臓には投与期間終了時に認められた変化が残存していたが，一般状態，摂餌量，外形分化状態，尿検査，血液学検査，血液生化学検査，剖検，器官重量，病理組織学検査において，遅発的な毒性影響を示唆する変化は認められなかった．

以上の結果から，4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）のラット新生児に対する主な反復投与毒性は腎臓に対する影響で，肝臓，血液及び消化管機能の変化を伴う盲腸に対する影響も認められた．腎臓に対する影響は投与後の観察期間終了時においても残存していたが，遅発的な毒性影響は認められなかった．無毒性量は，雌雄とも40mg/kg/dayと推定された．

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4,4'-イソプロピリデンビス（2,6-ジブロモフェノール）の

ラット新生児における哺育期投与試験

（試験番号：98-094）

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

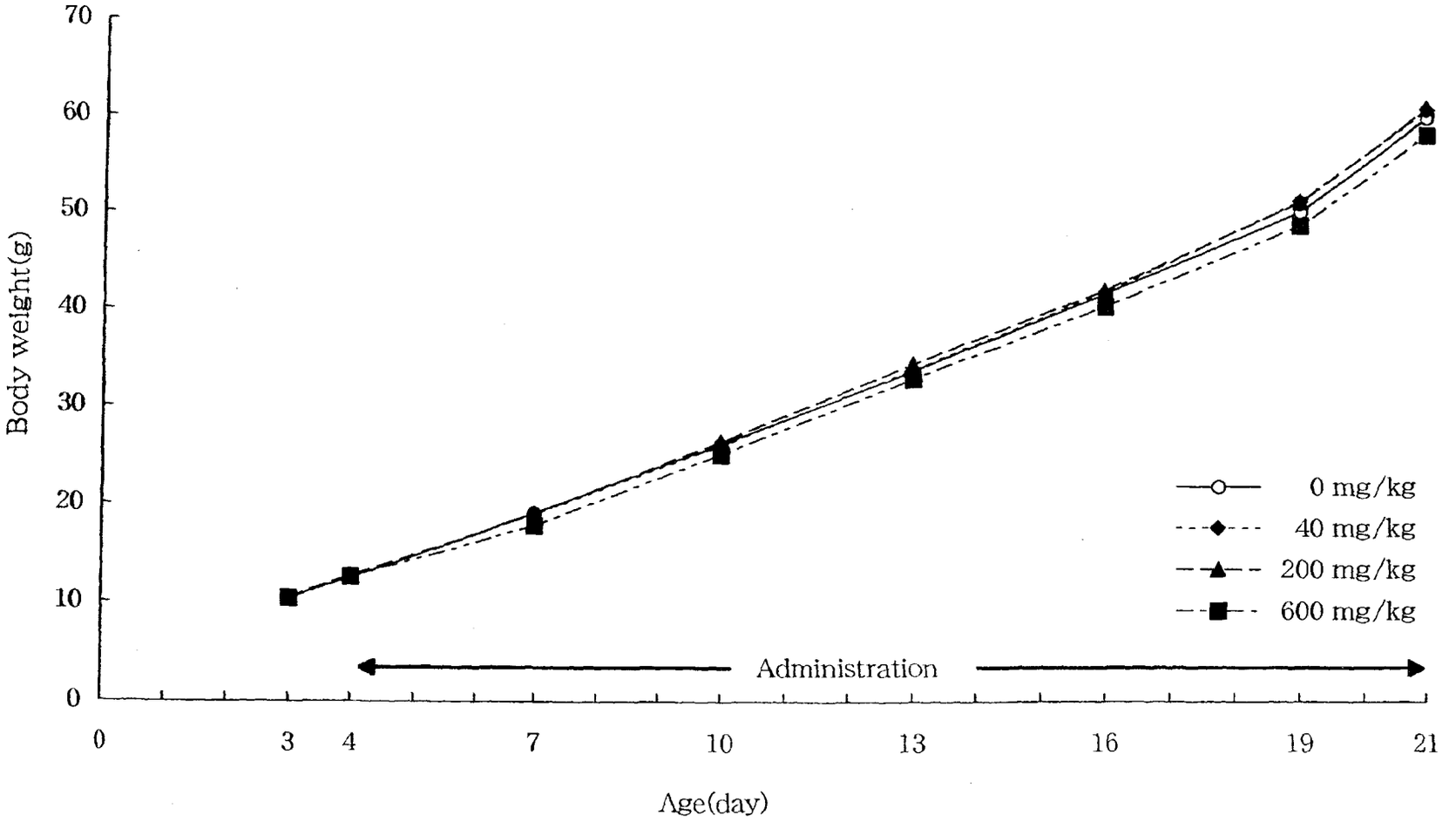


Fig.1-1 Body weight changes of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

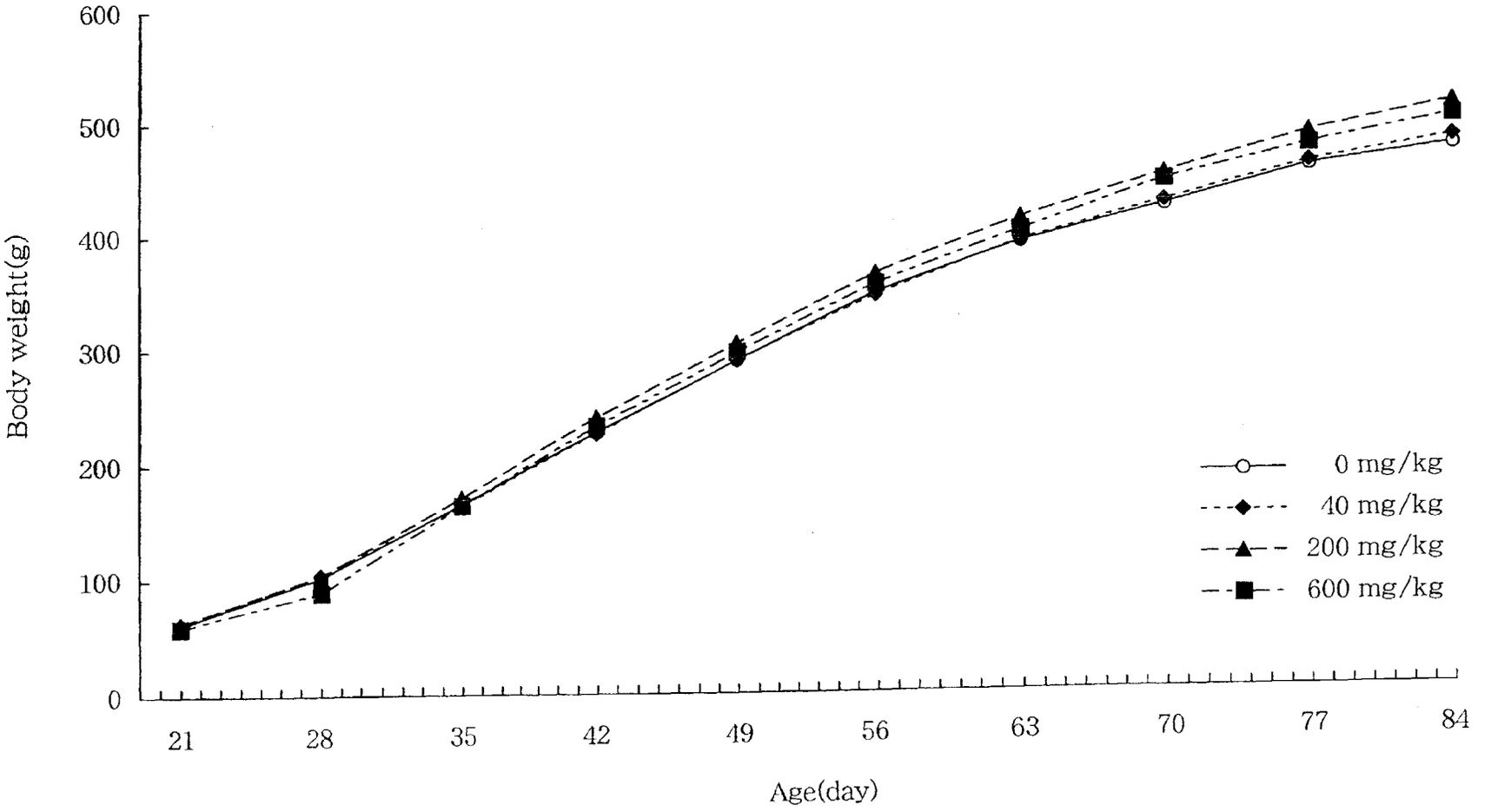


Fig.1-2 Body weight changes of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

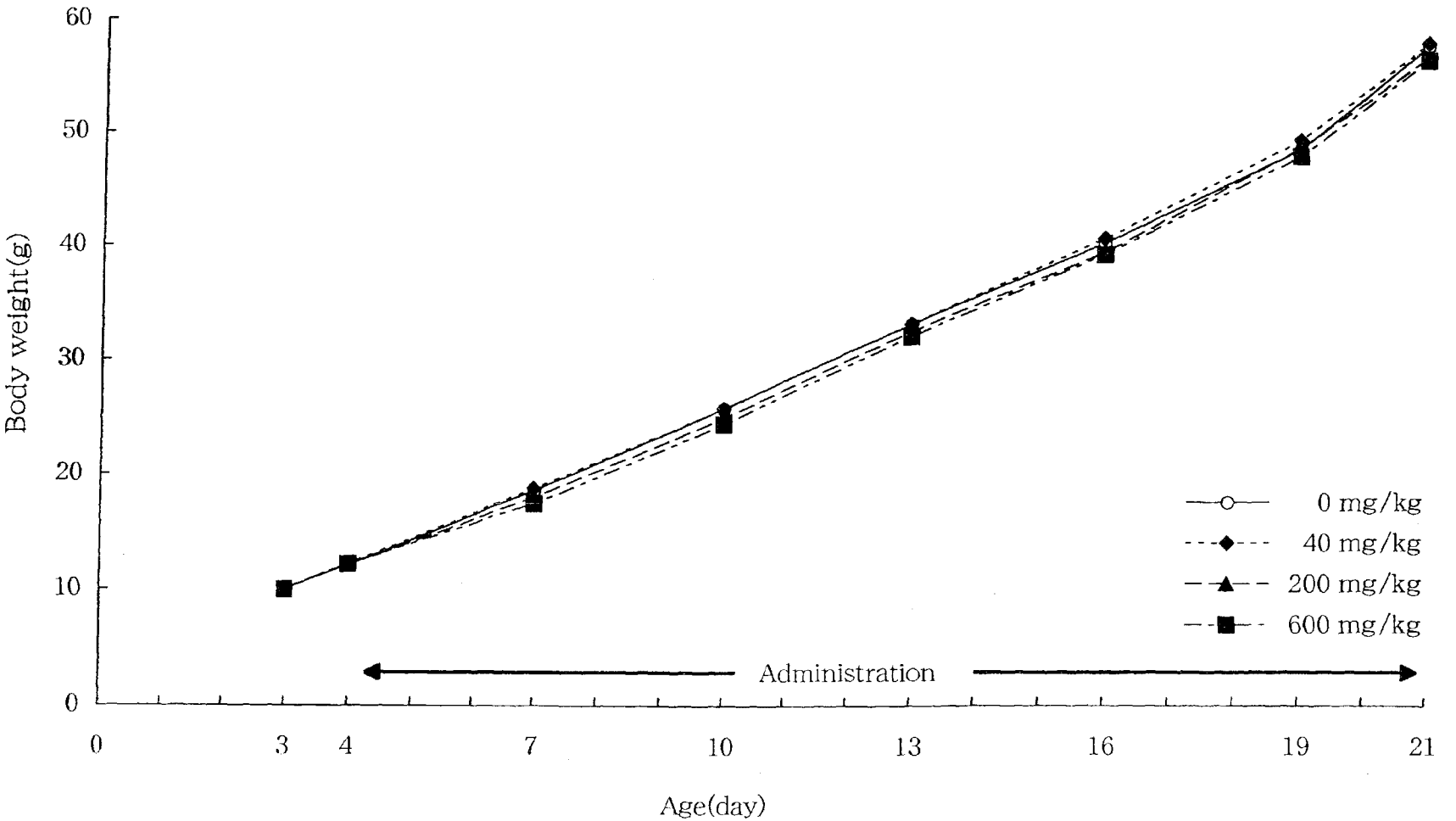


Fig.2-1 Body weight changes of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

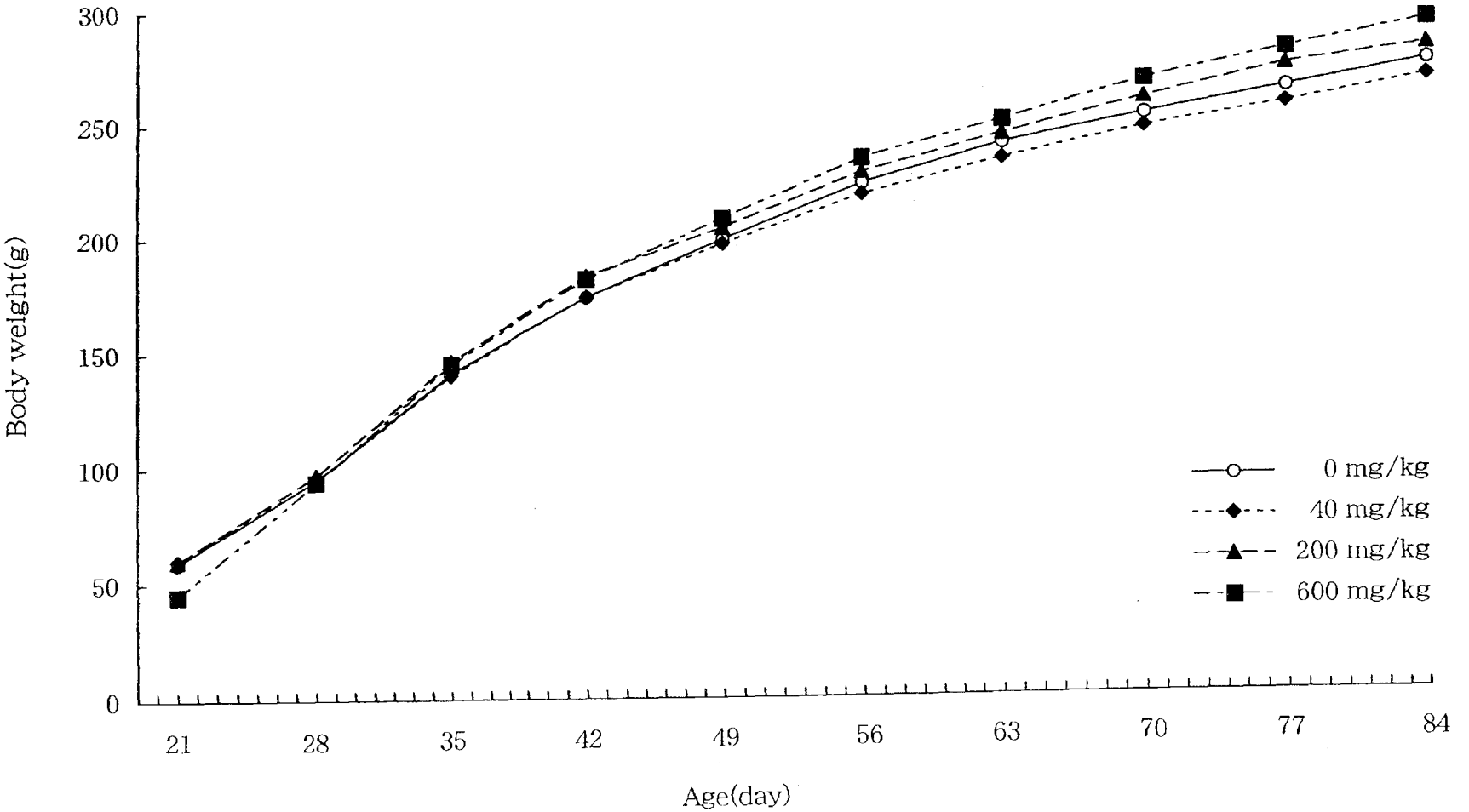


Fig.2-2 Body weight changes of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Table 1 Mortality rate and incidence of clinical signs of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

		Administration period				Post-administration period					
Dose (mg/kg/day)		0	40	200	600	0	40	200	600		
Fate		TK	TK	TK	TK	TK	TK	TK	TK	KE/FD	Total
No. of animals examined		12	12	12	12	6	6	6	4	2	(6)
Mortality (%)	Grade	0	0	0	0	0	0	0	33		
Clinical signs											
No abnormalities detected		12	12	5	0	6	6	6	4	0	(4)
Diarrhea	+	0	0	7 **	12 **	0	0	0	0	0	(0)
Decrease in locomotor activity	+	0	0	0	0	0	0	0	0	2	(2)
Piloerection	+	0	0	0	0	0	0	0	0	2	(2)
Emaciation	+～+++	0	0	0	0	0	0	0	0	2	(2)
Pale skin	+	0	0	0	0	0	0	0	0	2	(2)
Abdominal distension	+	0	0	0	0	0	0	0	0	1	(1)

TK : Terminal kill; KE : Killed in extremis; FD: Found dead; + : Slight; +++: Severe
Significantly different from control (**: $p<0.01$)

Table 2 Mortality rate and incidence of clinical signs of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

		Administration period				Post-administration period			
Dose (mg/kg/day)		0	40	200	600	0	40	200	600
Fate		TK	TK	TK	TK	TK	TK	TK	TK FD Total
No. of animals examined		12	12	12	12	6	6	6	5 1 (6)
Mortality (%)	Grade	0	0	0	0	0	0	0	17
Clinical signs									
No abnormalities detected		12	12	4	0	6	6	6	5 0 (5)
Diarrhea	+	0	0	8 **	12 **	0	0	0	0 0 (0)
Decrease in locomotor activity	+	0	0	0	0	0	0	0	0 1 (1)
Piloerection	+	0	0	0	0	0	0	0	0 1 (1)
Emaciation	+～+++	0	0	0	0	0	0	0	0 1 (1)
Pale skin	+	0	0	0	0	0	0	0	0 1 (1)
Abdominal distension	+	0	0	0	0	0	0	0	0 1 (1)

TK : Terminal kill; FD : Found dead; + : Slight; +++: Severe
Significantly different from control (**: $p<0.01$)

Table 3 Sensory functions of rats treated orally with 4.4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Sex	Contents	Dose(mg/kg)	0	40	200	600
Male		No. of animals examined	12	12	12	12
	State of gait	Normal	12	12	12	12
	Pupil reflex	Normal	12	12	12	12
	Pinna reflex	Normal	12	12	12	12
	Corneal reflex	Normal	12	12	12	12
	Visiual stepping reflex	Normal	12	12	12	12
	Righting reflex	Normal Slightly slow	12	12	11 1	11 1
	Air righting reflex	Normal	12	12	12	12
	Ispilateral flexor reflex	Normal	12	12	12	12
Female		No. of animals examined	12	12	12	12
	State of gait	Normal	12	12	12	12
	Pupil reflex	Normal	12	12	12	12
	Pinna reflex	Normal	12	12	12	12
	Corneal reflex	Normal	12	12	12	12
	Visiual stepping reflex	Normal	12	12	12	12
	Righting reflex	Normal Slightly slow	12	12	12	11 1
	Air righting reflex	Normal	12	12	12	12
	Ispilateral flexor reflex	Normal	12	12	12	12

Table 4 External differentiation and estrous cycle of rats treated orally with 4,4'-isopropylidene bis(dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	0	40	200	400
Male				
Appearance of hair (days of age)	7.0 ± 0.0 (12)	7.0 ± 0.0 (12)	7.0 ± 0.0 (12)	7.0 ± 0.0 (12)
Eruption of lower incisor (days of age)	9.7 ± 0.8 (12)	9.3 ± 0.7 (12)	9.4 ± 0.7 (12)	9.5 ± 0.9 (12)
Separation of eyelieds (days of age)	14.1 ± 0.3 (12)	14.1 ± 0.5 (12)	14.0 ± 0.4 (12)	14.3 ± 1.0 (12)
Descent of testes (days of age)	18.0 ± 0.0 (6)	18.2 ± 0.4 (6)	18.0 ± 0.0 (6)	18.0 ± 0.0 (6)
Female				
Appearance of hair (days of age)	7.0 ± 0.0 (12)	7.0 ± 0.0 (12)	7.0 ± 0.0 (12)	7.0 ± 0.0 (12)
Eruption of lower incisor (days of age)	9.3 ± 0.5 (12)	9.6 ± 0.8 (12)	9.3 ± 0.6 (12)	9.6 ± 0.9 (12)
Separation of eyelieds (days of age)	14.0 ± 0.0 (12)	13.9 ± 0.5 (12)	13.8 ± 0.7 (12)	13.6 ± 0.5 (12)
Opening of vagina (days of age)	33.3 + 1.4 (6)	33.8 ± 3.1 (6)	31.7 ± 1.0 (6)	34.0 ± 2.3 (5)

Each value is expressed mean ± S.D. (No. of rats observed)

Table 5-1 Body weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< Administration period >

(g)

Dose (mg/kg/day)	Days of age 3	4	7	10	13	16	19	21	Gain 4-21
0	10.4 ± 0.4 (12)	12.5 ± 0.6 (12)	19.1 ± 1.1 (12)	26.1 ± 1.7 (12)	33.6 ± 1.9 (12)	41.5 ± 2.2 (12)	50.0 ± 2.5 (12)	59.8 ± 2.7 (12)	47.3 ± 2.4 (12)
40	10.4 ± 0.5 (12)	12.5 ± 0.6 (12)	19.0 ± 1.0 (12)	26.0 ± 1.6 (12)	33.7 ± 2.1 (12)	41.7 ± 2.8 (12)	51.1 ± 3.6 (12)	60.6 ± 3.4 (12)	48.1 ± 3.4 (12)
200	10.5 ± 0.4 (12)	12.7 ± 0.4 (12)	19.0 ± 0.8 (12)	26.4 ± 1.2 (12)	34.3 ± 1.8 (12)	41.9 ± 2.4 (12)	51.0 ± 3.2 (12)	60.8 ± 3.4 (12)	48.1 ± 3.2 (12)
600	10.4 ± 0.4 (12)	12.6 ± 0.5 (12)	17.8 ± 0.8 (12)	25.1 ± 1.3 (12)	32.8 ± 1.8 (12)	40.2 ± 2.5 (12)	48.6 ± 3.2 (12)	58.0 ± 4.1 (12)	45.4 ± 3.9 (12)

Each value is mean and SD. (n): Number of animals weighed.

Table 5-2 Body weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< Post-administration period >

(g)

Dose (mg/kg/day)	Days of age 21	28	35	42	49	56	63	70	77	84	Gain 21-84
0	61 ± 1 (6)	102 ± 4 (6)	165 ± 6 (6)	227 ± 7 (6)	289 ± 9 (6)	347 ± 11 (6)	390 ± 16 (6)	421 ± 20 (6)	454 ± 27 (6)	471 ± 30 (6)	410 ± 29 (6)
40	62 ± 3 (6)	104 ± 6 (6)	164 ± 13 (6)	226 ± 20 (6)	289 ± 25 (6)	345 ± 29 (6)	391 ± 29 (6)	424 ± 31 (6)	457 ± 34 (6)	478 ± 34 (6)	416 ± 33 (6)
200	63 ± 4 (6)	104 ± 5 (6)	171 ± 9 (6)	240 ± 14 (6)	304 ± 18 (6)	364 ± 25 (6)	411 ± 28 (6)	449 ± 36 (6)	484 ± 37 (6)	509 ± 41 (6)	447 ± 40 (6)
600	59 ± 5 (4)	89 ± 23 (4)	164 ± 20 (4)	232 ± 24 (4)	296 ± 25 (4)	355 ± 25 (4)	400 ± 28 (4)	443 ± 32 (4)	473 ± 39 (4)	497 ± 41 (4)	435 ± 42 (4)

Each value is mean and SD. (n): Number of animals weighed.

Table 6-1 Body weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< Administration period >

(g)

Dose (mg/kg/day)	Days of age 3	4	7	10	13	16	19	21	Gain 4-21
0	10.0 ± 0.3 (12)	12.1 ± 0.5 (12)	18.6 ± 1.2 (12)	25.8 ± 1.6 (12)	33.2 ± 2.0 (12)	40.3 ± 2.8 (12)	48.6 ± 3.5 (12)	57.8 ± 4.4 (12)	45.6 ± 4.1 (12)
40	10.0 ± 0.3 (12)	12.2 ± 0.5 (12)	18.8 ± 0.9 (12)	25.8 ± 1.4 (12)	33.2 ± 1.5 (12)	40.7 ± 2.3 (12)	49.4 ± 2.8 (12)	58.0 ± 3.5 (12)	45.8 ± 3.3 (12)
200	10.0 ± 0.3 (12)	12.1 ± 0.6 (12)	18.0 ± 1.0 (12)	25.0 ± 1.6 (12)	32.5 ± 2.0 (12)	39.5 ± 2.6 (12)	48.7 ± 3.0 (12)	56.8 ± 3.5 (12)	44.8 ± 3.2 (12)
600	10.0 ± 0.3 (12)	12.2 ± 0.4 (12)	17.5 ± 0.7 (12)	24.4 ± 1.4 (12)	32.1 ± 1.5 (12)	39.3 ± 2.5 (12)	48.0 ± 2.8 (12)	56.5 ± 4.4 (12)	44.3 ± 4.2 (12)

Each value is mean and SD. (n): Number of animals weighed.

Table 6-2 Body weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< Post-administration period >

(g)

Dose (mg/kg/day)	Days of age 21	28	35	42	49	56	63	70	77	84	Gain 21-84
0	60 ± 4 (6)	95 ± 4 (6)	141 ± 8 (6)	174 ± 9 (6)	199 ± 10 (6)	223 ± 13 (6)	240 ± 14 (6)	252 ± 16 (6)	263 ± 17 (6)	274 ± 19 (6)	214 ± 17 (6)
40	60 ± 4 (6)	95 ± 7 (6)	140 ± 10 (6)	174 ± 10 (6)	197 ± 9 (6)	218 ± 10 (6)	233 ± 10 (6)	246 ± 11 (6)	256 ± 10 (6)	267 ± 11 (6)	208 ± 10 (6)
200	59 ± 4 (6)	97 ± 8 (6)	146 ± 12 (6)	183 ± 12 (6)	204 ± 12 (6)	228 ± 14 (6)	244 ± 12 (6)	259 ± 12 (6)	273 ± 15 (6)	281 ± 18 (6)	223 ± 14 (6)
600	58 ± 1 (5)	94 ± 6 (5)	145 ± 9 (5)	182 ± 9 (5)	208 ± 9 (5)	234 ± 12 (5)	250 ± 9 (5)	267 ± 11 (5)	280 ± 9 (5)	292 ± 11 (5)	234 ± 10 (5)

Each value is mean and SD. (n): Number of animals weighed.

Table 7 Food consumption of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< Post-administration period >

(g)

Dose (mg/kg/day)	Days of age 28	35	42	49	56	63	70	77	84
0	20 ± 5 (6)	25 ± 1 (6)	30 ± 1 (6)	34 ± 3 (6)	36 ± 4 (6)	35 ± 3 (6)	36 ± 4 (6)	39 ± 4 (6)	33 ± 4 (6)
40	19 ± 1 (6)	26 ± 2 (6)	30 ± 3 (6)	34 ± 2 (6)	37 ± 4 (6)	37 ± 3 (6)	36 ± 5 (6)	37 ± 5 (6)	33 ± 4 (6)
200	19 ± 1 (6)	26 ± 3 (6)	33 ± 1 (6)	31 ± 10 (6)	39 ± 6 (6)	39 ± 6 (6)	39 ± 5 (6)	40 ± 5 (6)	38 ± 4 (6)
600	18 ± 3 (4)	26 ± 4 (4)	34 ± 3 (4)	37 ± 4 (4)	40 ± 4 (4)	36 ± 3 (4)	43 ± 5 (4)	39 ± 5 (4)	37 ± 4 (4)

Each value is mean and SD. (n): Number of animals weighed.

Table 8 Food consumption of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< Post-administration period >

(g)

Dose (mg/kg/day)	Days of age 28	35	42	49	56	63	70	77	84
0	17 ± 1 (6)	22 ± 2 (6)	23 ± 2 (6)	23 ± 2 (6)	25 ± 2 (6)	25 ± 1 (6)	25 ± 3 (6)	23 ± 2 (6)	25 ± 2 (6)
40	17 ± 2 (6)	22 ± 2 (6)	22 ± 2 (6)	23 ± 2 (6)	25 ± 2 (6)	24 ± 4 (6)	24 ± 2 (6)	24 ± 3 (6)	24 ± 3 (6)
200	18 ± 2 (6)	23 ± 2 (6)	24 ± 3 (6)	25 ± 3 (6)	26 ± 3 (6)	25 ± 2 (6)	27 ± 2 (6)	27 ± 3 (6)	25 ± 4 (6)
600	17 ± 2 (5)	23 ± 3 (5)	25 ± 1 (5)	26 ± 3 (5)	28 ± 2 (5)	26 ± 2 (5)	27 ± 4 (5)	26 ± 4 (5)	27 ± 2 (5)

Each value is mean and SD. (n): Number of animals weighed.

Table 9 - 1 Urinary findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	No. of animals	Color	Cloudy		Volume (mL/18hrs)	Specific gravity	pH							Protein				
		PY	−	+			5.0	6.0	6.5	7.0	7.5	8.0	8.5	−	±	+	++	+++
0	6	6	4	2	10.9 ± 1.9	1.054 ± 0.018				1		4	1			5	1	
40	6	6	6		10.9 ± 2.6	1.042 ± 0.018						4	2		1	5		
200	6	6	4	2	13.6 ± 7.4	1.048 ± 0.015					1	2	3		2	3	1	
600	4	4	4		16.7 ± 4.8	1.034 ± 0.009							4		1	2	1	

Dose (mg/kg)	No. of animals	Glucose					Ketone body					Occult blood					Urobilinogen				Bilirubin			
		−	±	+	++	+++	−	±	+	++	+++	−	±	+	++	+++	0.1	1	2	4	−	+	++	+++
0	6	6					3	3				5	1				6				6			
40	6	6					3	2	1			6					6				6			
200	6	6					2	3	1			6					6				6			
600	4	4					3	1				2		1	1		4				4			

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

Table 9 - 2 Urinary findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	No. of animals	Erythrocytes				Leukocytes				Crystals											
										Mg				Ca				Ams			
		−	+	++	+++	−	+	++	+++	−	+	++	+++	−	+	++	+++	−	+	++	+++
0	6	6				6				1	3	1	1	6				6			
40	6	6				6				1	1	4		5		1		6			
200	6	6				6					3	3		6				6			
600	4	4				4					2	2		4				4			

Dose (mg/kg)	No. of animals	Epithelial cells									Casts						Fat globules		
		Sq				R			S			G		H		W			
		−	+	++	+++	−	+	++	−	+	++	−	+	−	+	−	+	−	+	++
0	6		5	1		6			6			6		6		6		6		
40	6		6			6			6			6		6		6		6		
200	6		6			6			6			6		6		6		6		
600	4		4			4			4			4		4		4		4		

− : Not observed; + : A few in some fields; ++ : A few in all fields; +++ : Many in all fields

Crystals
- Mg(ammonium magnesium phosphate)
- Ca(calcium phosphate)
- Ams(amorphous)

Epithelial cells
- Sq(squamous)
- R(round)
- S(spindle)

Casts
- G(granule)
- H(hyaline)
- W(waxy)

Table 10 - 1 Urinary findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	No. of animals	Color	Cloudy		Volume (mL/18hrs)	Specific gravity	pH							Protein				
		PY	−	+			5.0	6.0	6.5	7.0	7.5	8.0	8.5	−	±	+	++	+++
0	6	6	4	2	12.5 ± 9.3	1.062 ± 0.012			1		1	1	3		4	2		
40	6	6	5	1	11.6 ± 5.8	1.053 ± 0.020			1		1	3	1		5	1		
200	6	6	5	1	9.5 ± 3.0	1.052 ± 0.025						3	3		5	1		
600	5	5	3	2	17.3 ± 9.7	1.046 ± 0.016				1	1	1	2		2	3		

Dose (mg/kg)	No. of animals	Glucose					Ketone body					Occult blood					Urobilinogen				Bilirubin			
		−	±	+	++	+++	−	±	+	++	+++	−	±	+	++	+++	0.1	1	2	4	−	+	++	+++
0	6	6					6					6					6				6			
40	6	6					5	1				6					6				6			
200	6	6					5	1				6					6				6			
600	5	5					5					5					5				5			

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

Table 10 - 2 Urinary findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	No. of animals	Erythrocytes				Leukocytes				Crystals											
										Mg				Ca				Ams			
		−	+	++	+++	−	+	++	+++	−	+	++	+++	−	+	++	+++	−	+	++	+++
0	6	6				6				3	1	2		6				6			
40	6	6				6				6				6				6			
200	6	6				6				2	2	2		6				6			
600	5	5				5				4	1			5				5			

Dose (mg/kg)	No. of animals	Epithelial cells									Casts						Fat globules		
		Sq				R			S			G		H		W			
		−	+	++	+++	−	+	++	−	+	++	−	+	−	+	−	+	−	+	++
0	6		5	1		6			6			6		6		6		6		
40	6		6			6			6			6		6		6		6		
200	6	1	4	1		6			6			6		6		6		6		
600	5		5			5			5			5		5		5		5		

− : Not observed; + : A few in some fields; ++ : A few in all fields; +++ : Many in all fields

Crystals
- Mg(ammonium magnesium phosphate)
- Ca(calcium phosphate)
- Ams(amorphous)

Epithelial cells
- Sq(squamous)
- R(round)
- S(spindle)

Casts
- G(granule)
- H(hyaline)
- W(waxy)

Table 11 Hematological findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	No. of animals	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	6	480 ± 9	9.7 ± 0.4	30.9 ± 1.2	65 ± 2	20.1 ± 0.7	31.3 ± 0.8	227 ± 44	13.6 ± 0.3	15.2 ± 0.4
40	6	479 ± 14	9.6 ± 0.5	30.7 ± 1.7	64 ± 2	20.1 ± 0.6	31.4 ± 0.4	230 ± 44	13.7 ± 0.3	14.4 ± 0.7
200	6	483 ± 24	9.3 ± 0.9	30.4 ± 2.3	63 ± 3	19.3 ± 1.4	30.6 ± 0.8	221 ± 30	13.7 ± 0.3	14.4 ± 0.8
600	6	483 ± 19	8.9 ± 0.7	29.1 ± 1.6	60 * ± 2	18.5 * ± 1.0	30.5 ± 0.7	240 ± 26	13.3 ± 0.4	14.2 * ± 0.3

Dose (mg/kg)	No. of animals	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)						Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	6	16 ± 5	0 ± 0	1 ± 1	0 ± 0	18 ± 6	78 ± 5	4 ± 1	0 ± 0	145 ± 14
40	6	18 ± 5	0 ± 0	0 ± 0	0 ± 0	13 ± 5	84 ± 4	3 ± 1	0 ± 0	139 ± 11
200	6	16 ± 7	0 ± 0	0 ± 0	0 ± 1	15 ± 5	82 ± 5	2 ± 2	0 ± 0	141 ± 9
600	6	18 ± 7	0 ± 0	0 ± 0	0 ± 0	15 ± 6	83 ± 5	2 ± 1	0 ± 0	153 ± 15

Each value is expressed as mean±S.D.
Significantly different from control(*:P<0.05)

Table 12 Hematological findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	No. of animals	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	6	507 ± 26	10.0 ± 0.8	31.5 ± 2.0	62 ± 2	19.8 ± 0.7	31.8 ± 0.4	197 ± 28	13.9 ± 0.2	14.4 ± 0.7
40	6	512 ± 12	10.2 ± 0.4	32.7 ± 1.3	64 ± 2	20.0 ± 0.6	31.3 ± 0.4	207 ± 21	14.0 ± 0.6	15.6 * ± 0.9
200	6	507 ± 23	9.9 ± 0.5	32.0 ± 1.8	63 ± 2	19.6 ± 0.8	31.1 ± 0.8	215 ± 18	13.6 ± 0.4	14.2 ± 0.6
600	6	503 ± 12	9.0 ** ± 0.4	29.5 ± 1.0	59 ** ± 2	17.9 ** ± 0.7	30.5 ** ± 0.7	210 ± 25	13.6 ± 0.4	13.5 ± 0.9

Dose (mg/kg)	No. of animals	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)						Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	6	23 ± 7	0 ± 0	0 ± 0	0 ± 0	14 ± 3	85 ± 3	1 ± 1	0 ± 0	142 ± 17
40	6	23 ± 6	0 ± 0	0 ± 0	0 ± 0	19 ± 3	80 ± 3	2 ± 1	0 ± 0	155 ± 15
200	6	26 ± 14	0 ± 0	1 ± 1	0 ± 1	13 ± 8	84 ± 10	2 ± 2	0 ± 0	152 ± 22
600	6	25 ± 4	0 ± 0	1 ± 1	0 ± 1	12 ± 3	86 ± 4	2 ± 1	0 ± 0	160 ± 23

Each value is expressed as mean±S.D.
Significantly different from control(*:P<0.05, **:P<0.01)

Table 13 Hematological findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	No. of animals	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	6	838 ± 27	15.8 ± 0.4	44.5 ± 1.2	53 ± 1	18.9 ± 0.2	35.6 ± 0.3	32 ± 9	12.7 ± 0.3	18.7 ± 0.3
40	6	853 ± 26	15.7 ± 0.7	44.6 ± 1.6	52 ± 2	18.4 ± 0.7	35.2 ± 0.4	31 ± 8	12.9 ± 0.4	17.9 ± 1.1
200	6	831 ± 37	15.3 ± 0.7	43.7 ± 1.7	53 ± 2	18.4 ± 0.5	35.0 ± 0.3	38 ± 15	12.5 ± 0.2	17.3 ± 0.9
600	4	817 ± 41	15.6 ± 0.6	44.6 ± 1.5	55 ± 2	19.1 ± 0.5	34.9 ± 0.3	42 ± 7	12.5 ± 0.3	17.6 ± 1.0

Dose (mg/kg)	No. of animals	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)						Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	6	67 ± 13	0 ± 0	0 ± 0	0 ± 0	12 ± 5	88 ± 6	1 ± 1	0 ± 0	125 ± 10
40	6	62 ± 11	0 ± 0	1 ± 0	0 ± 0	12 ± 5	86 ± 6	1 ± 1	0 ± 0	129 ± 12
200	6	66 ± 15	0 ± 0	1 ± 1	0 ± 0	16 ± 4	82 ± 5	2 ± 1	0 ± 0	129 ± 7
600	4	64 ± 5	0 ± 0	1 ± 1	0 ± 0	19 ± 8	79 ± 8	2 ± 1	0 ± 0	132 ± 10

Each value is expressed as mean±S.D.

Table 14 Hematological findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	No. of animals	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	6	803 ± 28	15.5 ± 0.7	43.6 ± 1.6	54 ± 1	19.3 ± 0.8	35.5 ± 0.6	27 ± 10	12.7 ± 0.3	16.7 ± 1.6
40	5	803 ± 54	15.2 ± 0.9	43.0 ± 2.2	54 ± 1	19.0 ± 0.4	35.4 ± 0.3	24 ± 8	12.9 ± 0.6	15.8 ± 0.9
200	6	792 ± 17	15.0 ± 0.6	42.7 ± 1.2	54 ± 1	19.0 ± 0.7	35.2 ± 0.9	25 ± 5	12.4 ± 0.2	16.2 ± 0.6
600	5	795 ± 43	15.4 ± 1.0	43.2 ± 2.5	54 ± 2	19.3 ± 0.7	35.6 ± 0.5	34 ± 12	12.2 ± 0.5	15.9 ± 0.8

Dose (mg/kg)	No. of animals	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)						Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	6	40 ± 9	0 ± 0	1 ± 1	0 ± 0	9 ± 4	88 ± 4	2 ± 2	0 ± 0	125 ± 10
40	5	44 ± 8	0 ± 0	0 ± 0	0 ± 0	10 ± 4	89 ± 4	1 ± 2	0 ± 0	127 ± 24
200	6	39 ± 10	0 ± 0	1 ± 1	0 ± 0	12 ± 4	86 ± 4	1 ± 1	0 ± 0	137 ± 16
600	5	37 ± 14	0 ± 0	1 ± 1	0 ± 0	13 ± 2	86 ± 3	1 ± 1	0 ± 0	131 ± 23

Each value is expressed as mean±S.D.

Table 15 Blood biochemical findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	No. of animals	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	6	521 ± 120	127 ± 12	25 ± 1	995 ± 184	1.09 ± 0.17	94 ± 24	4.93 ± 0.12	3.13 ± 0.07	1.76 ± 0.17	80 ± 15	29 ± 6
40	6	462 ± 198	129 ± 11	28 ± 5	1079 ± 138	1.08 ± 0.13	98 ± 12	4.71 ± 0.24	2.98 ± 0.21	1.76 ± 0.32	82 ± 7	24 ± 3
200	6	557 ± 143	132 ± 10	28 ± 4	1075 ± 96	0.84 ± 0.19	83 ± 11	4.69 ± 0.23	2.95 ± 0.18	1.71 ± 0.14	74 ± 13	25 ± 4
600	6	536 ± 143	139 ± 17	31 ± 5	1224 ± 146	0.95 ± 0.17	89 ± 14	4.70 ± 0.16	2.99 ± 0.14	1.75 ± 0.13	80 ± 12	24 ± 6

Dose (mg/kg)	No. of animals	PL (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	6	121 ± 17	140 ± 9	15.2 ± 3.4	0.45 ± 0.03	0.41 ± 0.02	9.9 ± 0.3	9.4 ± 0.4	143 ± 1	6.93 ± 0.65	107 ± 2
40	6	121 ± 11	140 ± 7	15.4 ± 3.0	0.43 ± 0.05	0.40 ± 0.03	9.8 ± 0.3	9.1 ± 0.2	142 ± 1	7.07 ± 0.31	108 ± 1
200	6	115 ± 14	144 ± 7	16.0 ± 4.0	0.45 ± 0.02	0.43 ± 0.03	9.8 ± 0.4	8.7 ± 0.2	142 ± 1	7.19 ± 0.60	107 ± 1
600	6	121 ± 13	142 ± 9	14.8 ± 4.2	0.45 ± 0.02	0.50** ± 0.05	9.9 ± 0.2	9.1 ± 0.6	142 ± 1	6.80 ± 0.54	106 ± 2

Each value is expressed as mean±S.D.
Significantly different from control(**:P<0.01)

Table 16 Blood biochemical findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	No. of animals	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	6	598 ± 249	135 ± 18	19 ± 2	925 ± 189	0.95 ± 0.24	83 ± 10	5.01 ± 0.25	3.25 ± 0.20	1.85 ± 0.17	69 ± 13	25 ± 5
40	6	613 ± 48	137 ± 16	21 ± 4	1007 ± 99	1.10 ± 0.27	85 ± 10	4.94 ± 0.07	3.15 ± 0.11	1.77 ± 0.16	74 ± 23	27 ± 7
200	6	479 ± 88	119 ± 11	20 ± 4	983 ± 150	0.75 ± 0.12	83 ± 13	4.77 ± 0.17	3.03 ± 0.18	1.75 ± 0.21	72 ± 11	26 ± 8
600	6	615 ± 158	148 ± 23	23 ± 4	1109 ± 94	2.85 ± 4.83	88 ± 20	4.82 ± 0.39	3.03 ± 0.08	1.73 ± 0.26	93 ± 31	33 ± 18

Dose (mg/kg)	No. of animals	PL (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	6	108 ± 16	135 ± 20	18.5 ± 4.1	0.46 ± 0.04	0.38 ± 0.03	9.8 ± 0.4	9.0 ± 0.7	142 ± 1	7.18 ± 0.69	108 ± 2
40	6	115 ± 27	139 ± 6	16.6 ± 2.6	0.47 ± 0.03	0.39 ± 0.03	9.7 ± 0.2	9.1 ± 0.4	142 ± 1	7.29 ± 0.43	108 ± 1
200	6	112 ± 11	133 ± 9	14.6 ± 2.0	0.43 ± 0.03	0.41 ± 0.02	10.0 ± 0.2	9.5 ± 0.2	142 ± 1	7.24 ± 0.20	107 ± 1
600	6	133 ± 37	136 ± 10	21.6 ± 13.4	0.48 ± 0.11	0.50** ± 0.13	9.8 ± 0.3	9.3 ± 0.5	142 ± 1	7.01 ± 0.53	106 ± 3

Each value is expressed as mean±S.D.
Significantly different from control(**:P<0.01)

Table 17 Blood biochemical findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	No. of animals	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	6	382 ± 229	80 ± 10	41 ± 8	492 ± 70	0.87 ± 0.23	45 ± 12	6.29 ± 0.13	3.28 ± 0.11	1.09 ± 0.08	65 ± 10	62 ± 24
40	6	490 ± 500	77 ± 10	38 ± 3	489 ± 115	0.92 ± 0.16	41 ± 3	6.24 ± 0.29	3.30 ± 0.10	1.13 ± 0.11	77 ± 17	86 ± 38
200	6	265 ± 84	79 ± 8	41 ± 4	556 ± 87	0.71 ± 0.09	55 ± 13	6.14 ± 0.11	3.09 ± 0.14	1.02 ± 0.09	77 ± 8	89 ± 22
600	4	310 ± 119	87 ± 13	41 ± 6	627 ± 135	0.92 ± 0.42	43 ± 6	6.07 ± 0.16	3.12 ± 0.12	1.06 ± 0.04	77 ± 5	64 ± 23

Dose (mg/kg)	No. of animals	PL (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	6	104 ± 14	153 ± 10	14.6 ± 2.1	0.57 ± 0.04	0.35 ± 0.02	9.9 ± 0.3	7.4 ± 0.2	144 ± 1	5.08 ± 0.17	103 ± 2
40	6	121 ± 21	161 ± 12	16.0 ± 1.7	0.59 ± 0.03	0.31 ± 0.03	10.0 ± 0.4	7.3 ± 0.4	145 ± 1	5.18 ± 0.27	103 ± 1
200	6	124 ± 8	158 ± 22	14.9 ± 2.3	0.59 ± 0.07	0.34 ± 0.02	10.2 ± 0.2	7.5 ± 0.8	144 ± 1	4.88 ± 0.21	102 ± 1
600	4	117 ± 9	153 ± 25	17.8 ± 2.7	0.60 ± 0.04	0.36 ± 0.03	10.0 ± 0.2	7.7 ± 0.5	146 ± 1	4.91 ± 0.26	102 ± 2

Each value is expressed as mean±S.D.

Table 18 Blood biochemical findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	No. of animals	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	6	328 ± 136	79 ± 16	37 ± 18	383 ± 117	1.57 ± 0.36	412 ± 110	6.39 ± 0.39	3.55 ± 0.17	1.26 ± 0.08	89 ± 15	25 ± 11
40	5	335 ± 65	73 ± 13	30 ± 6	311 ± 104	2.28 ± 1.32	375 ± 201	6.16 ± 0.38	3.49 ± 0.25	1.31 ± 0.12	90 ± 17	20 ± 7
200	6	410 ± 145	72 ± 10	30 ± 7	326 ± 85	1.52 ± 0.82	456 ± 105	6.65 ± 0.22	3.78 ± 0.17	1.32 ± 0.09	98 ± 14	23 ± 12
600	5	300 ± 57	70 ± 4	25 ± 2	317 ± 42	1.41 ± 0.28	424 ± 117	6.36 ± 0.19	3.56 ± 0.17	1.27 ± 0.08	95 ± 10	22 ± 6

Dose (mg/kg)	No. of animals	PL (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	6	147 ± 18	131 ± 10	13.4 ± 1.4	0.60 ± 0.05	0.31 ± 0.02	10.2 ± 0.4	7.1 ± 0.4	145 ± 1	4.53 ± 0.19	105 ± 1
40	5	140 ± 21	131 ± 14	12.9 ± 1.0	0.60 ± 0.04	0.33 ± 0.04	10.1 ± 0.3	6.9 ± 0.3	144 ± 0	4.72 ± 0.30	104 ± 1
200	6	155 ± 16	133 ± 12	15.2 ± 3.1	0.60 ± 0.04	0.32 ± 0.03	10.1 ± 0.4	6.7 ± 0.4	145 ± 1	4.84 ± 0.14	104 ± 2
600	5	149 ± 10	134 ± 6	14.7 ± 2.5	0.62 ± 0.04	0.31 ± 0.04	10.1 ± 0.3	6.9 ± 0.7	145 ± 2	4.60 ± 0.20	106 ± 2

Each value is expressed as mean±S.D.

Table 19 Incidence of necropsy findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

			Scheduled scrificed								FD/KE
			<22 days of age>				<85 days of age>				
		Dose(mg/kg)	0	40	200	600	0	40	200	600	600
Organ	: Findings	Grade No. of animals	6	6	6	6	6	6	6	4	2
Lung	: Black spot	−	6	6	6	6	5	6	6	4	2
		+	0	0	0	0	1	0	0	0	0
Cecum	: Dilatation	−	6	6	6	4	6	6	6	4	2
		+	0	0	0	2	0	0	0	0	0
Kidney	: Enlargement	−	6	6	6	0	6	6	6	4	0
		++	0 (0)	0 (0)	0 (0)	4 (6)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (2)
		+++	0	0	0	2	0	0	0	0	2
	Dark red spots	−	6	6	6	6	6	6	6	4	0
		++	0	0	0	0	0	0	0	0	2
	Hydronephrosis	−	6	6	6	6	6	6	6	3	2
		+	0	0	0	0	0	0	0	1	0
	Recessed area	−	6	6	6	6	6	6	6	1	2
		+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (3)*	0 (0)
		++	0	0	0	0	0	0	0	1	0

FD/KE : Found dead or killed in extremis
− : Negative; + : Slight
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)

Table 20 Incidence of necropsy findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

				Scheduled scrificed								FD
				<22 days of age>				<85 days of age>				
			Dose(mg/kg)	0	40	200	600	0	40	200	600	600
Organ	: Findings	Grade	No. of animals	6	6	6	6	6	6	6	5	1
Cecum	: Dilatation	−		6	6	6	2	6	6	6	5	1
		+		0	0	0	4 *	0	0	0	0	0
Kidney	: Enlargement	−		6	6	6	0	6	6	6	5	0
		++		0 (0)	0 (0)	0 (0)	3 (6)**	0 (0)	0 (0)	0 (0)	0 (0)	0 (1)
		+++		0	0	0	3	0	0	0	0	1
	Red/dark red /grayish white spots/areas	−		6	6	6	5	6	6	6	5	0
		++		0	0	0	1	0	0	0	0	1
	Deformity	−		6	6	6	6	6	6	6	3	1
		+		0	0	0	0	0	0	0	2	0
	Recessed area	−		6	6	6	6	6	6	6	0	1
		+		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (5)**	0 (0)
		++		0	0	0	0	0	0	0	1	0

FD : Found dead
− : Negative; + : Slight
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)

Table 21 Absolute and relative organ weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
〈22 days of age〉

	Dose (mg/kg)	No.of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (mg)	Heart (mg)	Lung (mg)	Thymus (mg)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Testis (mg)	Prost.† (mg)	Epidid. (mg)
Absolute	0	6	51.4 ±3.0	1.50 ±0.05	1.67 ±0.12	0.65 ±0.04	187 ±17	284 ±23	413 ±23	230 ±30	9.1 ±0.8	3.0 ±0.1	25.5 ±1.6	290 ±29	92.6 ±11.6	53.4 ±3.5
	40	6	52.2 ±3.4	1.54 ±0.04	1.71 ±0.14	0.67 ±0.04	203 ±25	299 ±16	430 ±29	247 ±26	9.7 ±0.8	3.1 ±0.2	25.7 ±2.2	311 ±13	86.0 ±13.9	57.9 ±4.0
	200	6	51.7 ±2.7	1.55 ±0.06	1.74 ±0.06	0.63 ±0.02	183 ±21	286 ±14	433 ±20	236 ±18	9.5 ±0.5	3.2 ±0.2	24.0 ±3.7	309 ±11	85.3 ±14.7	56.4 ±5.7
	600	6	50.7 ±2.3	1.53 ±0.05	1.83 ±0.16	1.81 * ±0.43	179 ±34	304 ±20	415 ±21	203 ±28	7.8 * ±0.9	2.9 ±0.1	21.7 ±3.3	295 ±18	82.5 ±18.6	50.6 ±5.1
Relative @	0	6	51.4 ±3.0	2.93 ±0.23	3.25 ±0.14	1.26 ±0.04	365 ±40	552 ±33	806 ±56	450 ±76	17.7 ±1.9	5.9 ±0.3	49.6 ±3.2	566 ±65	180.1 ±18.8	104.1 ±8.2
	40	6	52.2 ±3.4	2.97 ±0.14	3.27 ±0.11	1.28 ±0.04	389 ±37	575 ±57	824 ±27	472 ±29	18.6 ±1.5	6.0 ±0.3	49.2 ±1.6	599 ±41	165.0 ±26.7	111.1 ±8.4
	200	6	51.7 ±2.7	3.01 ±0.13	3.37 ±0.09	1.22 ±0.03	354 ±32	554 ±28	840 ±46	456 ±22	18.4 ±1.7	6.2 ±0.5	46.5 ±6.7	600 ±39	165.0 ±26.4	109.3 ±11.7
	600	6	50.7 ±2.3	3.02 ±0.14	3.60 ** ±0.17	3.57 * ±0.77	352 ±55	599 ±24	820 ±47	399 ±42	15.5 ±1.9	5.8 ±0.3	42.8 ±5.4	583 ±35	163.0 ±38.0	100.2 ±11.6

† : Total weights of the prostate and seminal vesicle
Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)

Table 22 Absolute and relative organ weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

	Dose (mg/kg)	No.of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (mg)	Heart (mg)	Lung (mg)	Thymus (mg)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Ovary (mg)	Uterus (mg)
Absolute	0	6	47.6 ±4.1	1.51 ±0.05	1.52 ±0.12	0.64 ±0.07	148 ±49	277 ±15	403 ±32	229 ±56	9.3 ±0.8	2.9 ±0.2	23.7 ±2.7	13.4 ±2.2	42.9 ±3.7
	40	6	48.4 ±2.2	1.47 ±0.04	1.57 ±0.07	0.65 ±0.05	142 ±42	273 ±20	421 ±39	238 ±42	9.5 ±0.9	3.0 ±0.3	22.4 ±2.7	16.1 ±3.7	41.5 ±6.6
	200	6	48.2 ±2.4	1.47 ±0.06	1.60 ±0.12	0.66 ±0.05	165 ±30	279 ±26	421 ±26	246 ±34	8.8 ±1.1	3.1 ±0.2	21.9 ±2.6	14.7 ±4.0	43.6 ±7.7
	600	6	48.3 ±4.2	1.45 ±0.05	1.66 ±0.14	2.23 ** ±1.75	145 ±27	291 ±26	393 ±41	202 ±40	8.8 ±0.6	2.9 ±0.2	22.1 ±4.2	13.9 ±3.8	44.9 ±4.4
Relative @	0	6	47.6 ±4.1	3.18 ±0.21	3.21 ±0.21	1.33 ±0.07	308 ±81	584 ±51	848 ±26	477 ±87	19.8 ±3.2	6.2 ±0.6	49.8 ±4.4	28.2 ±3.8	90.3 ±6.7
	40	6	48.4 ±2.2	3.04 ±0.10	3.24 ±0.05	1.33 ±0.06	293 ±46	565 ±33	870 ±58	491 ±82	19.5 ±1.5	6.2 ±0.7	46.4 ±5.8	33.4 ±8.4	86.0 ±14.1
	200	6	48.2 ±2.4	3.06 ±0.17	3.32 ±0.11	1.37 ±0.10	342 ±58	580 ±55	874 ±64	508 ±54	18.3 ±2.3	6.4 ±0.4	45.3 ±3.8	30.5 ±8.0	90.7 ±17.6
	600	6	48.3 ±4.2	3.01 ±0.22	3.44 ±0.26	4.86 * ±4.47	299 ±40	607 ±82	812 ±26	417 ±80	18.2 ±1.6	6.0 ±0.3	45.7 ±7.6	28.5 ±7.1	94.0 ±16.1

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)

Table 23 Absolute and relative organ weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

	Dose (mg/kg)	No.of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Testis (g)	Prost. (g)	Semi.v (g)	Epidid. (g)
Absolute	0	6	437 ±25	2.05 ±0.05	12.58 ±1.79	3.16 ±0.28	0.83 ±0.09	1.41 ±0.16	1.46 ±0.11	0.52 ±0.13	33.7 ±3.5	14.0 ±1.2	70.4 ±4.4	3.36 ±0.11	0.70 ±0.09	1.98 ±0.12	1.21 ±0.06
	40	6	445 ±33	2.06 ±0.08	13.51 ±1.62	3.04 ±0.24	0.83 ±0.12	1.38 ±0.09	1.40 ±0.12	0.48 ±0.08	33.4 ±5.3	13.8 ±1.4	63.4 ±11.3	3.44 ±0.44	0.59 ±0.18	1.71 ±0.38	1.26 ±0.11
	200	6	471 ±39	2.17 ±0.08	13.91 ±1.21	3.19 ±0.20	0.89 ±0.08	1.48 ±0.11	1.53 ±0.13	0.52 ±0.07	35.7 ±2.8	14.9 ±1.2	74.4 ±14.0	3.70 ±0.38	0.62 ±0.15	1.94 ±0.24	1.31 ±0.11
	600	4	459 ±40	2.13 ±0.07	13.67 ±2.01	4.18 ±0.84	0.92 ±0.05	1.53 ±0.06	1.56 ±0.11	0.50 ±0.10	32.3 ±2.1	14.5 ±2.2	68.0 ±17.4	3.51 ±0.09	0.68 ±0.13	1.85 ±0.11	1.23 ±0.09
Relative @	0	6	437 ±25	0.47 ±0.02	2.88 ±0.34	0.72 ±0.05	0.19 ±0.02	0.32 ±0.03	0.34 ±0.02	0.12 ±0.02	7.7 ±0.4	3.2 ±0.2	16.2 ±1.3	0.77 ±0.06	0.16 ±0.02	0.45 ±0.04	0.28 ±0.02
	40	6	445 ±33	0.46 ±0.03	3.03 ±0.20	0.68 ±0.04	0.19 ±0.02	0.31 ±0.01	0.32 ±0.02	0.11 ±0.02	7.5 ±1.2	3.1 ±0.3	14.3 ±2.3	0.78 ±0.11	0.14 ±0.05	0.39 ±0.09	0.28 ±0.02
	200	6	471 ±39	0.46 ±0.03	2.96 ±0.16	0.68 ±0.05	0.19 ±0.02	0.32 ±0.02	0.33 ±0.01	0.11 ±0.01	7.6 ±0.9	3.2 ±0.3	15.8 ±2.7	0.79 ±0.07	0.13 ±0.03	0.41 ±0.04	0.28 ±0.02
	600	4	459 ±40	0.47 ±0.03	2.97 ±0.20	0.91 ±0.18	0.20 ±0.02	0.33 ±0.02	0.34 ±0.02	0.11 ±0.03	7.1 ±0.2	3.1 ±0.2	14.7 ±3.0	0.77 ±0.07	0.15 ±0.02	0.41 ±0.06	0.27 ±0.03

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight

Table 24 Absolute and relative organ weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

	Dose (mg/kg)	No.of Animals	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Ovary (mg)	Uterus (g)
Absolute	0	6	252 ±16	1.91 ±0.08	6.78 ±0.61	1.94 ±0.18	0.51 ±0.09	0.90 ±0.04	1.10 ±0.10	0.43 ±0.09	24.2 ±3.1	16.3 ±3.1	76.2 ±7.1	84.2 ±20.9	0.59 ±0.22
	40	6	246 ±11	1.97 ±0.08	6.56 ±1.08	1.95 ±0.17	0.54 ±0.03	0.90 ±0.10	1.08 ±0.08	0.40 ±0.05	23.8 ±2.6	14.1 ±2.9	69.9 ±8.7	77.5 ±27.6	0.53 ±0.06
	200	6	262 ±14	1.99 ±0.10	7.27 ±0.40	2.07 ±0.16	0.55 ±0.05	0.89 ±0.09	1.12 ±0.06	0.46 ±0.07	25.5 ±4.4	16.5 ±1.7	72.8 ±10.0	88.9 ±18.9	0.57 ±0.20
	600	5	270 ±11	1.94 ±0.07	7.61 ±0.61	2.48 ** ±0.30	0.61 ±0.12	0.98 ±0.09	1.17 ±0.08	0.48 ±0.05	23.4 ±0.9	16.5 ±1.9	66.3 ±5.3	84.6 ±4.0	0.69 ±0.17
Relative @	0	6	252 ±16	0.76 ±0.03	2.70 ±0.22	0.77 ±0.05	0.20 ±0.04	0.36 ±0.02	0.44 ±0.04	0.17 ±0.03	9.7 ±1.1	6.5 ±1.2	30.4 ±3.2	33.7 ±9.6	0.23 ±0.08
	40	6	246 ±11	0.80 ±0.02	2.67 ±0.41	0.79 ±0.05	0.22 ±0.01	0.37 ±0.04	0.44 ±0.03	0.16 ±0.02	9.7 ±1.0	5.8 ±1.1	28.4 ±2.6	31.4 ±10.4	0.22 ±0.02
	200	6	262 ±14	0.76 ±0.04	2.78 ±0.07	0.79 ±0.03	0.21 ±0.02	0.34 ±0.03	0.43 ±0.01	0.18 ±0.03	9.8 ±1.9	6.3 ±0.5	27.9 ±4.4	33.9 ±6.4	0.22 ±0.06
	600	5	270 ±11	0.72 ±0.02	2.82 ±0.23	0.92 ±0.13	0.23 ±0.04	0.36 ±0.03	0.43 ±0.03	0.18 ±0.02	8.7 ±0.4	6.1 ±0.8	24.6 ±2.0	31.4 ±1.0	0.25 ±0.06

Each value is expressed as mean ± S.D.
@ : Relative organ weight per 100g body weight
Significantly different from control (** : $p<0.01$)

Table 25 Incidence of histopathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

Organ	: Findings	Dose(mg/kg) / Grade / No. of animals	0 6	40 6	200 6	600 6
Heart	: Degeneration, myocardial	-	5	—	—	6
		+	1	—	—	0
Lung	: Metaplasia, osseous	-	5	—	—	6
		+	1	—	—	0
Liver	: Hematopoiesis, extra-medullary	-	0	0	0	0
		+	6	6	6	6
	Hypertrophy, hepatocyte, centrilobular	-	6	6	6	3
		+	0	0	0	3
Kidney	: Cyst, solitary	-	4	4	2	6
		+	2	2	4	0
	Cyst, multiple	-	6	6	4	0
		+	0 (0)	0 (0)	2 (2)	0 (6)**
		+++	0	0	0	6
	Cast, hyaline	-	6	6	6	4
		+	0	0	0	2
	Atrophy, cortical	-	6	6	6	0
		+	0 (0)	0 (0)	0 (0)	5 (6)**
		++	0	0	0	1
	Basophilic tubules	-	2 (6)	1 (6)	1 (6)	0 (4)
		+	4	5	5	4
		++	0	0	0	2
	Cellular infiltration, lymphocyte, cortex	-	6	5	6	6
		+	0	1	0	0
	Degeneration/hyperplasia, collecting tubular epithelium	-	6	6	4	0
		+	0	0	2	6 **
	Dilatation, renal pelvis	-	5	6	5	6
		+	1	0	1	0
Pancreas	: Proliferation, ductule, focal	-	5	—	—	6
		+	1	—	—	0
Spleen	: Hematopoiesis, extra-medullary	-	0	—	—	0
		++	6	—	—	6

- : Negative; + : Slight; ++ : Moderate; +++ : Severe; — : Not examined
Significantly different from control (** : $p<0.01$)
No abnormalities were detected in the organs of the brain, pituitary, thymus, thyroid, parathyroid, trachea, stomach, intestine, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis, prostate and seminal vesicle from control and 600mg/kg groups.

Table 26 Incidence of histopathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

Organ	: Findings	Dose(mg/kg) / Grade / No. of animals	0 / 6	40 / 6	200 / 6	600 / 6
Lung	: Accumulation, foam cell	−	4	—	—	6
		+	2	—	—	0
Liver	: Hematopoiesis, extra-medullary	−	0	—	—	0
		+	6	—	—	6
Pancreas	: Atrophy, acinar cell, focal	−	5	—	—	6
		+	1	—	—	0
Kidney	: Cyst, solitary	−	5	3	4	6
		+	1	3	2	0
	Cyst, multiple	−	6	6	6	0
		++	0	0	0	6 **
	Cast, hyaline	−	6	6	6	3
		+	0	0	0	3
	Atrophy, cortical	−	6	6	6	0
		+	0 (0)	0 (0)	0 (0)	5 (6)**
		++	0	0	0	1
	Basophilic tubules	−	0 (6)	1 (6)	1 (6)	1 (5)
		+	6	5	5	4
		++	0	0	0	1
	Degeneration/hyperplasia, collecting tubular epithelium	−	6	6	6	2
		+	0 (0)	0 (0)	0 (0)	3 (4)*
		++	0	0	0	1
	Degeneration, vacuolar, proximal tubular epithelium	−	6	5	6	6
		+	0	1	0	0
	Fibrosis	−	6	5	6	6
		+	0	1	0	0
	Hyperplasia, pelvic epithelium	−	6	6	5	6
		+	0	0	1	0
	Inflammation, suppurative	−	6	6	6	5
		+++	0	0	0	1
Spleen	: Hematopoiesis, extra-medullary	−	0	—	—	0
		+	4	—	—	4
		++	2	—	—	2

− : Negative; + : Slight; ++ : Moderate; +++ : Severe; — : Not examined
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)
No abnormalities were detected in the organs of the brain, pituitary, thyroid, parathyroid, trachea, heart, stomach, intestine, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus from control and 600mg/kg groups.

Table 27-1 Incidence of histopathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Organ	: Findings	Grade	Scheduled scrificed				FD/KE
		Dose(mg/kg)	0	40	200	600	600
		No. of animals	6	6	6	4	2
Heart	: Myocardial degeneration /fibrosis	-	5	—	—	3	2
		+	1	—	—	1	0
Lung	: Hemorrhage/inflammation, focal	-	5	—	—	4	2
		+	1	—	—	0	0
	Mineralization, artery	-	4	—	—	2	2
		+	2	—	—	2	0
	Metaplasia, osseous	-	6	—	—	4	1
		+	0	—	—	0	1
Liver	: Microgranuloma	-	3	—	—	3	2
		+	3	—	—	1	0
	Necrosis, focal	-	6	—	—	4	1
		++	0	—	—	0	1
Pancreas	: Cellular infiltration, lymphocyte, focal	-	6	—	—	3	2
		+	0	—	—	1	0
Stomach	: Erosion, glandular stomach	-	6	—	—	4	1
		+	0	—	—	0	1
Kidney	: Cyst, multiple	-	6	6	5	0	0
		+	0 (0)	0 (0)	1 (1)	0 (4)**	0 (2)
		++	0	0	0	3	0
		+++	0	0	0	1	2
	Cast, hyaline	-	6	6	6	1	0
		+	0 (0)	0 (0)	0 (0)	1 (3)*	0 (2)
		++	0	0	0	2	1
		+++	0	0	0	0	1
	Cast, granular	-	6	6	6	3	0
		+	0	0	0	1	2
	Atrophy, cortical	-	6	6	6	3	0
		+	0 (0)	0 (0)	0 (0)	1 (1)	0 (2)
		++	0	0	0	0	1
		+++	0	0	0	0	1
	Basophilic tubules	-	4 (6)	3 (6)	3 (6)	1 (2)	0 (0)
		+	2	3	3	1	0
		++	0 (0)	0 (0)	0 (0)	2 (2)	1 (2)
		+++	0	0	0	0	1

- : Negative; + : Slight; ++ : Moderate; +++ : Severe; — : Not examined
FD : Found dead; KE : Killed in extremis
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)
No abnormalities were detected in the organs of the brain, pituitary, thyroid, parathyroid, trachea, intestine, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis and seminal vesicle from control and 600mg/kg groups.

Table 27-2 Incidence of histopathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Organ	: Findings	Grade	Scheduled scrificed				FD/KE
		Dose(mg/kg)	0	40	200	600	600
		No. of animals	6	6	6	4	2
Kidney	: Eosinophilic body, proximal	−	3	5	5	3	2
(Continued)	tubular epithelium	+	2 (3)	1 (1)	1 (1)	1 (1)	0 (0)
		++	1	0	0	0	0
		+++	0	0	0	0	0
	Hyaline droplet, proximal	−	0	0	0	0	1
	tubular epithelium	+	6	6	6	4	1
	Cellular infiltration,	−	6	5	5	0	2
	lymphocyte, cortex	+	0 (0)	1 (1)	1 (1)	2 (4)**	0 (0)
		++	0	0	0	2	0
	Degeneration/hyperplasia,	−	6	6	6	2	0
	collecting tubular	+	0 (0)	0 (0)	0 (0)	2 (2)	1 (2)
	epithelium	++	0	0	0	0	1
	Dilatation, renal pelvis	−	6	5	6	3	2
		+	0	1	0	1	0
	Fibrosis	−	6	6	6	0	2
		+	0 (0)	0 (0)	0 (0)	1 (4)**	0 (0)
		++	0	0	0	2	0
		+++	0	0	0	1	0
	Necrosis, tubular	−	6	6	6	4	0
	epithelium	++	0	0	0	0	2
Prostate	: Cellular infiltration,	−	4	—	—	4	1
	lymphocyte, interstitium	+	2	—	—	0	1
Thymus	: Atrophy, cortical	−	6	—	—	4	0
		+	0	—	—	0	2
Spleen	: Hematopoiesis, extra-	−	0 (6)	—	—	0 (4)	0 (0)
	medullary	+	6	—	—	4	0
		++	0	—	—	0	2
	Deposit, brown pigment	−	0	—	—	0	1
		+	6	—	—	4	1
	Atrophy, white pulp	−	6	—	—	4	1
		+	0	—	—	0	1

− : Negative; + : Slight; ++ : Moderate; +++ : Severe; — : Not examined
FD : Found dead; KE : Killed in extremis
Significantly different from control (** : $p<0.01$)
No abnormalities were detected in the organs of the brain, pituitary, thyroid, parathyroid, trachea, intestine, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis and seminal vesicle from control and 600mg/kg groups.

Table 28-1 Incidence of histopathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Organ	: Findings	Grade	Scheduled scrificed				FD
		Dose(mg/kg)	0	40	200	600	600
		No. of animals	6	6	6	5	1
Lung	: Mineralization, artery	-	4	—	—	2	1
		+	2	—	—	3	0
	Metaplasia, osseous	-	6	—	—	4	1
		+	0	—	—	1	0
	Congestive edema	-	6	—	—	5	0
		++	0	—	—	0	1
Liver	: Microgranuloma	-	5	—	—	4	1
		+	1	—	—	1	0
Pancreas	: Cellular infiltration,	-	5	—	—	4	1
	neutrophil, focal	+	1	—	—	1	0
Kidney	: Cyst, solitary	-	5	5	4	5	1
		+	1	1	2	0	0
	Cyst, multiple	-	6	6	5	0	0
		+	0 (0)	0 (0)	1 (1)	1 (5)**	0 (1)
		++	0	0	0	4	0
		+++	0	0	0	0	1
	Cast, hyaline	-	6	6	6	1	0
		+	0 (0)	0 (0)	0 (0)	2 (4)*	0 (1)
		++	0	0	0	2	1
	Cast, granular	-	6	6	6	5	0
		++	0	0	0	0	1
	Atrophy, cortical	-	6	6	6	5	0
		++	0	0	0	0	1
	Basophilic tubules	-	6	4	5	1	1
		+	0 (0)	2 (2)	1 (1)	3 (4)*	0 (0)
		++	0	0	0	1	0
	Cellular infiltration,	-	5	6	6	2	1
	lymphocyte, cortex	+	1 (1)	0 (0)	0 (0)	1 (3)	0 (0)
		++	0	0	0	2	0

- : Negative; + : Slight; ++ : Moderate; +++ : Severe; — : Not examined
FD : Found dead
Significantly different from control (* : $p<0.05$; ** : $p<0.01$)
No abnormalities were detected in the organs of the brain, pituitary, thyroid, parathyroid, trachea, heart, stomach, intestine, adrenal, lymph node, urinary bladder, spinal cord, bone marrow and sciatic nerve from control and 600mg/kg groups.

Table 28-2 Incidence of histopathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Organ	: Findings	Grade	Scheduled scrificed				FD
		Dose(mg/kg)	0	40	200	600	600
		No. of animals	6	6	6	5	1
Kidney (Continued)	Degeneration/hyperplasia, collecting tubular epithelium	-	6	6	6	3	0
		+	0 (0)	0 (0)	0 (0)	2 (2)	0 (1)
		++	0	0	0	0	1
	Deposit, brown pigment	-	6	6	6	3	1
		+	0	0	0	2	0
	Fibrosis	-	6	6	6	1	1
		+	0 (0)	0 (0)	0 (0)	1 (4)*	0 (0)
		++	0	0	0	3	0
	Necrosis, tubular	-	6	6	6	4	0
		+	0 (0)	0 (0)	0 (0)	1 (1)	0 (1)
		++	0	0	0	0	1
	Mineralization, cortico-medullary junction/cortex	-	5	6	6	4	1
		+	1	0	0	1	0
Ovary	: Atrophy	-	6	—	—	5	0
		++	0	—	—	0	1
Uterus	: Atrophy	-	6	—	—	5	0
		+-	0	—	—	0	1
Thymus	: Hemorrhage	-	6	—	—	4	1
		+	0	—	—	1	0
Spleen	: Hematopoiesis, extra-medullary	-	0	—	—	0	0
		+	6	—	—	5	0
		++	0	—	—	0	1
	Deposit, brown pigment	-	0	—	—	0	1
		+	6	—	—	5	0
	Atrophy, white pulp	-	6	—	—	5	0
		+	0	—	—	0	1

- : Negative; + : Slight; ++ : Moderate; +++ : Severe; — : Not examined
FD : Found dead
Significantly different from control (* : $p<0.05$)
No abnormalities were detected in the organs of the brain, pituitary, thyroid, parathyroid, trachea, heart, stomach, intestine, adrenal, lymph node, urinary bladder, spinal cord, bone marrow and sciatic nerve from control and 600mg/kg groups.

4,4′-イソプロピリデンビス（2,6-ジブロモフェノール）の
ラット新生児における哺育期投与試験

（試験番号：98-094）

報告書　添付資料B

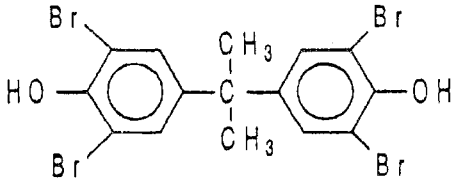
（個体別表等）

財団法人　畜産生物科学安全研究所

Appendix 1 Test article characterization

1. Chemical name (synonym) : 4,4'-Isopropylidene bis(2,6-dibromophenol) (tetrabromobisphenol A)
2. CAS Registry No. : 79-94-7
3. Lot No. : 8Y291G
4. Purity (impurity) : 99.5% (tribromobisphenol A)
5. Supplier : TOSOH Co., Ltd. (4560 Kaisei-machi, Shinnanyo-shi, Yamaguchi, Japan)
6. Day of reception : December 8, 1998
7. Amount : 2.0kg
8. Physico-chemical characterization

Structural formura :



Molecular formura : $C_{15}H_{12}Br_4O_2$

Molecular weight : 543.88

Appearance at ordinary temperature : Solid, white

Melting point : 182℃

Boilinng point : 316℃

Solubility : Oil-solubility

9. Preservation : 4℃, Dark place and sealed

Appendix 2 Test article stability

The purity of the test article was analysed after the termination of the study, and the datum obtained was compared with that obtained by analysis before the initiation of the study for stability. Analyses were made by the TOSOH Co., Ltd. (4560 Kaisei-machi, Shinnanyo-shi, Yamaguchi, Japan)

Test article : 4,4'-Isopropylidene bis(2,6-dibromophenol)

Lot number : 8Y291G

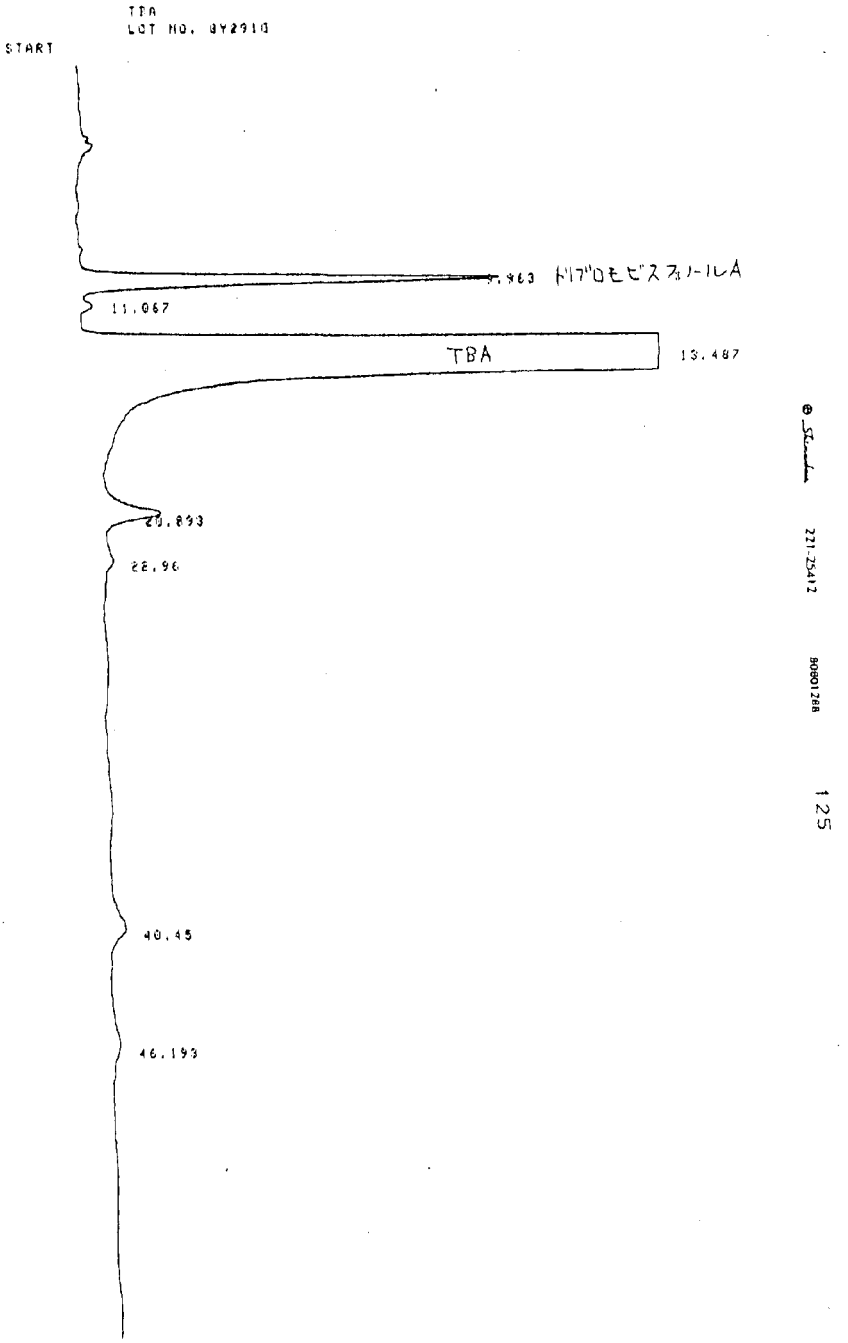
Method : LC method

Results :

	Date of analysis	Purity
Before the initiation of the study	December 2, 1998	99.5%
After the termination of the study	November 5, 1999	99.5%

Conclusion : The test article was concluded to be stable during the study period.

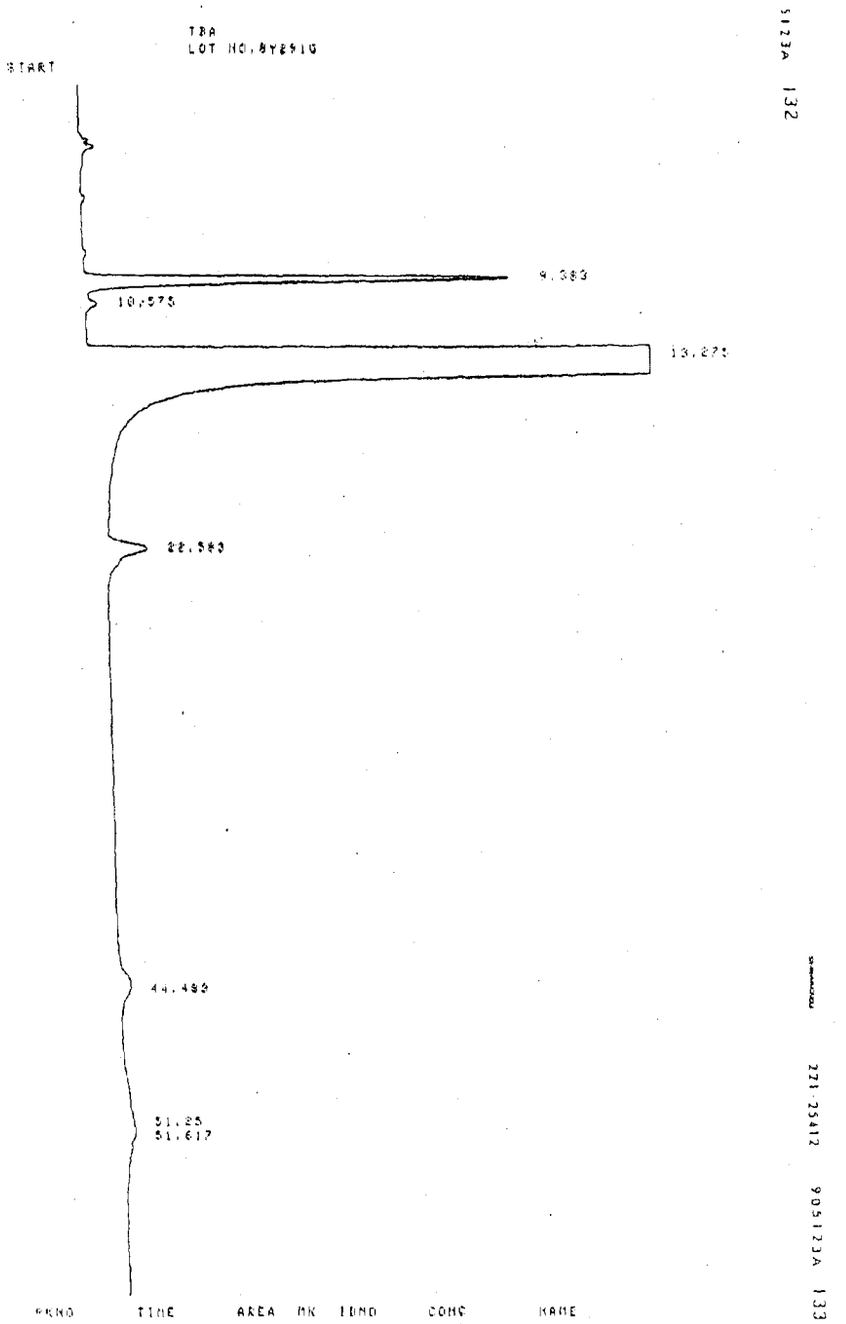
4,4'-イソプロピリデンビス(2,6- ジブロモフェノール) の液体クロマトグラム:
試験開始前 (平成10年12月 2日)



CHROMATOGRAM 1 MEMORIZED

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	9.963	39053			0.3859	トリブロモビスフェノールA
		27.1sec				
2	11.067	872			0.0086	不明
		22.5sec				
3	13.487	10068656			99.4547	テトラブロモビスフェノールA
		34.1sec				
4	20.893	8610			0.0851	不明
		44.8sec				
5	22.96	1262			0.0125	〃
		48.3sec				
6	40.45	3979			0.0393	〃
		80.8sec				
7	46.193	1428			0.0141	〃
		72.7sec				
	TOTAL	10123065			100	

4,4'-イソプロピリデンビス(2,6- ジブロモフェノール) の液体クロマトグラム:
投与終了後 (平成11年11月 5日)



PEAK NO	TIME	AREA	MK	IDNO	CONC	NAME
1	9.383	32813			0.3893	トリブロモビスフェノールA
2	10.575	21.9sec 1031	V		0.0122	不明
3	13.275	23.8sec 8384472			99.4882	テトラブロモビスフェノールA
4	22.583	28 sec 6573			0.078	不明
5	44.483	47.1sec 2411			0.0286	〃
6	51.25	73.9sec 134			0.0016	〃
7	51.617	22.5sec 641	V		0.0076	〃
	TOTAL	49.3sec 8429072			100	

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

Test article : 4,4'-Isopropylidene bis(2,6-dibromophenol)
(lot No. 8Y291G)

Nominal concentrations of the test article in the dose solutions
: 1.3, 6.7 and 20w/v%

Method : LC method

Results :

Date of preparation	Nominal concentrations (w/v%)		
	1.3	6.7	20
June 11, 1998 (Analytical value)	1.2%	6.3%	19%

Each value expressed as mean from 3 analyses

Appendix 4 Animal numbers of foster mother rats and those of pups reared by them

Foster mothers	Pups
No. 601	Males : Nos. 001, 013, 025, 037; Femals : Nos. 501, 513, 525, 537
No. 602	Males : Nos. 002, 014, 026, 038; Femals : Nos. 502, 514, 526, 538
No. 603	Males : Nos. 003, 015, 027, 039; Femals : Nos. 503, 515, 527, 539
No. 604	Males : Nos. 004, 016, 028, 040; Femals : Nos. 504, 516, 528, 540
No. 605	Males : Nos. 005, 017, 029, 041; Femals : Nos. 505, 517, 529, 541
No. 606	Males : Nos. 006, 018, 030, 042; Femals : Nos. 506, 518, 530, 542
No. 607	Males : Nos. 007, 019, 031, 043; Femals : Nos. 507, 519, 531, 543
No. 608	Males : Nos. 008, 020, 032, 044; Femals : Nos. 508, 520, 532, 544
No. 609	Males : Nos. 009, 021, 033, 045; Femals : Nos. 509, 521, 533, 545
No. 610	Males : Nos. 010, 022, 034, 046; Femals : Nos. 510, 522, 534, 546
No. 611	Males : Nos. 011, 023, 035, 047; Femals : Nos. 511, 523, 535, 547
No. 612	Males : Nos. 012, 024, 036, 048; Femals : Nos. 512, 524, 536, 548

Appendix 5-1 Environmental condition of animal room

Establishment : Temperature, 22±3℃ ; Relative humidity, 55±10%

	Date	Comment	Animal room No.4 Range of temperature(℃)	Range of humidity(%)
June	3, 1999	Arrival of animals	22.1 – 22.2	56 – 57
	4,		22.0 – 22.3	56 – 57
	5,		22.1 – 22.3	56 – 57
	6,		22.1 – 22.4	55 – 57
	7,		22.0	57
	8,		22.0 – 22.3	55 – 57
	9,		22.0 – 22.4	56 – 57
	10,		22.0	57
	11,		22.0 – 22.1	57 – 58
	12,		22.1	56 – 57
	13,	Grouping, beginning of administration	22.1 – 22.2	57 – 58
	14,		22.0 – 22.1	57 – 58
	15,		22.0	58
	16,		21.9 – 22.1	57 – 58
	17,		21.9 – 22.0	58
	18,		21.8 – 21.9	58
	19,		21.9 – 22.0	58
	20,		21.9 – 22.1	58 – 59
	21,		22.0	58 – 59
	22,		22.0 – 22.1	58 – 59
	23,		21.9 – 22.2	58 – 59
	24,		22.0 – 22.2	58 – 61
	25,		22.0 – 22.1	58 – 59
	26,		22.0 – 22.1	59 – 60
	27,		22.1	59 – 60
	28,		21.9 – 22.0	59 – 60
	29,		21.9 – 22.0	59 – 60
	30,		21.9 – 22.1	60 – 61
July	1,		21.9 – 22.2	59 – 61
	2,	Terminal kill after administration period	22.1 – 22.2	56 – 61
	3,		22.1 – 22.2	57 – 59
	4,		22.2 – 22.3	56 – 58

Appendix 5-2 Environmental condition of animal room

Establishment : Temperature, 22±3℃ ; Relative humidity, 55±10%

	Date	Comment	Animal room No.4 Range of temperature(℃)	Range of humidity(%)
July	5, 1999		21.9 – 22.1	57 – 58
	6,		21.9 – 22.0	58 – 59
	7,		21.9 – 22.1	57 – 59
	8,		21.9 – 22.2	57 – 59
	9,		22.0	58 – 59
	10,		22.0 – 22.2	57 – 58
	11,		22.1	58
	12,		21.9 – 22.1	59 – 61
	13,		21.8 – 22.1	58 – 60
	14,		21.9 – 22.0	58 – 59
	15,		21.9 – 22.1	58 – 59
	16,		22.0 – 22.1	58 – 59
	17,		22.1 – 22.2	58 – 60
	18,		22.1 – 22.2	58
	19,		22.0 – 22.1	57 – 59
	20,		22.1	58
	21,		22.0 – 22.1	59 – 60
	22,		21.9 – 22.1	58 – 59
	23,		22.0 – 22.2	59 – 62
	24,		22.1 – 22.2	58 – 59
	25,		22.1 – 22.2	58 – 59
	26,		21.9 – 22.3	59 – 62
	27,		22.0 – 22.1	60 – 62
	28,		22.0 – 22.2	59 – 61
	29,		21.9 – 22.1	60 – 61
	30,		21.9 – 22.1	60 – 62
	31,		22.1 – 22.2	58 – 59
August	1,		22.1	59
	2,		22.1	61
	3,		22.0 – 22.1	59 – 61
	4,		22.0 – 22.1	60 – 61
	5,		21.9 – 22.0	59 – 61
	6,		21.9 – 22.0	59 – 61
	7,		21.9 – 22.0	59 – 60

Appendix 5-3 Environmental condition of animal room

Establishment : Temperature, 22±3℃ ; Relative humidity, 55±10%

Date	Comment	Animal room No.4 Range of temperature(℃)	Range of humidity(%)
August 8, 1999		22.0 – 22.1	60
9,		21.9 – 22.0	59 – 60
10,		21.9	60
11,		21.9 – 22.1	59 – 60
12,		21.9 – 22.0	60 – 61
13,		21.9 – 22.0	60
14,		21.9	60
15,		21.9 – 22.0	60 – 62
16,		21.9	60 – 61
17,		21.9 – 22.0	61 – 62
18,		21.9 – 22.6	60 – 62
19,		22.5	58
20,		22.5	57 – 59
21,		22.6 – 22.7	57 – 60
22,		22.6 – 22.7	57
23,		22.4 – 22.5	56 – 58
24,		22.4 – 22.5	58 – 59
25,		22.4 – 22.5	57 – 58
26,		22.4	56 – 57
27,		22.4	57 – 59
28,		22.5 – 22.6	57 – 58
29,		22.5 – 22.6	58
30,		22.4 – 22.5	57 – 58
31,		22.3 – 22.5	57 – 59
September 1,		22.5	58 – 59
2,		22.3 – 22.5	58
3,	Terminal kill after recovery period	22.3 – 22.4	56 – 57

Appendix 6-1-1 Analysis of contaminants in animal feed

Authorized by the Ministry of Health & Welfare of Japan

TOKYO KENBIKYOIN FOUNDATION

CENTER FOR FOOD ENVIRONMENT HYGIENE

IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103, JAPAN
TEL:03(3663)9631 FAX:03(3663)9635

Date : April 28 , 1999

CERTIFICATE

Applicant : NIHON NOSAN KOGYO K. K
Samples : LABO MR-STOCK, Lot No. 990373
Date of Application : April 5, 1999
Date of Examination : April 5 ～ 28 , 1999
Examination No. : 3904801

As a result of tests carried out on the sample submitted under the above mentioned name on April 5, 1999. We herewith report as follows :

RESUTS

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)
N-Nitrosodimethylamine	not detected (detection limit 10 ppb)
N-Nitrosodiethylamine	not detected (detection limit 10 ppb)
Arsenic (As)	0.03 ppm
Lead (Pb)	0.2 ppm
Cadmium (Cd)	0.06 ppm
Mercury (Hg)	not detected (detection limit 0.01 ppm)
Chromium (Cr)	1.1 ppm
Polychlorinated biphenyl (PCBs)	not detected (detection limit 0.01 ppm)
Total DDT*1	not detected (detection limit 0.05 ppm)
Total BHC*2	not detected (detection limit 0.05 ppm)

*1 Expressed as total amounts of op'-DDT , pp'-DDT ,op'-DDD , pp-DDD , op'-DDE and pp'-DDE

*2 Expressed as total amounts of α -BHC, β -BHC, γ -BHC and δ -BHC

Appendix 6-1-2 Analysis of contaminants in animal feed

Authorized by the Ministry of Health & Welfare of Japan

TOKYO KENBIKYOIN FOUNDATION

CENTER FOR FOOD ENVIRONMENT HYGIENE

IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103, JAPAN
TEL:03(3663)9831 FAX:03(3663)9685

Heptachlor	not detected (detection limit 0.01 ppm)
Dieldrin	not detected (detection limit 0.01 ppm)
Aldrin	not detected (detection limit 0.01 ppm)
Parathion	not detected (detection limit 0.05 ppm)
Malathion	0.11 ppm

[redacted]
[redacted] D.V.M., Ph.D.
Director
Center for Food Environment Hygiene
TOKYO KENBIKYOIN FOUNDATION

DATE APR 21. 1999

MICROBIOROGICAL INSPECTION

Customer
RESEARCH INSTITUTE FOR ANIMAL SCIENCE
IN BIOCHEMISTORY AND TOXICOLOGY
Sample Designation
LABO MR STOCK
Lot No. 990373

S.P.C.·····1.3×10^4 CFU/g
Coliform Group·····Negative
Salmonella ·····Negative
Moids·····< 20 CFU/g

NIHON NOSAN KOGYO K.K.
R & D Center
Safety & QC Station
5246, TAKURA, TSUKUBASHI, 300-2615 JAPAN

[redacted] Director

[redacted]

Authorized by the Ministry of Health & Welfare of Japan

TOKYO KENBIKYOIN FOUNDATION

CENTER FOR FOOD ENVIRONMENT HYGIENE

IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103, JAPAN
TEL:03(3663)9681 FAX:03(3663)9685

Date : July 23 , 1999

CERTIFICATE

Applicant : NIHON NOSAN KOGYO K. K
Samples : LABO MR-STOCK, Lot No.990653
Date of Application : July 2, 1999
Date of Examination : July 2 ～ July 23 , 1999
Examination No. : 3907803

As a result of tests carried out on the sample submitted under the above mentioned name on July 2, 1999. We herewith report as follows :

RESUTS

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)
N-Nitrosodimethylamine	not detected (detection limit 10 ppb)
N-Nitrosodiethylamine	not detected (detection limit 10 ppb)
Arsenic (As)	0.29 ppm
Lead (Pb)	0.2 ppm
Cadmium (Cd)	0.08 ppm
Mercury (Hg)	not detected (detection limit 0.01 ppm)
Chromium (Cr)	1.7 ppm
Polychlorinated biphenyl (PCBs)	not detected (detection limit 0.01 ppm)
Total DDT*1	not detected (detection limit 0.05 ppm)
Total BHC*2	not detected (detection limit 0.05 ppm)

*1 Expressed as total amounts of op'-DDT , pp'-DDT ,op'-DDD , pp-DDD , op'-DDE and pp'-DDE

*2 Expressed as total amounts of α -BHC, β -BHC, γ -BHC and δ -BHC

Appendix 6-2-2 Analysis of contaminants in animal feed

Authorized by the Ministry of Health & Welfare of Japan

TOKYO KENBIKYOIN FOUNDATION

CENTER FOR FOOD ENVIRONMENT HYGIENE

IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103, JAPAN
TEL:03(3663)9681 FAX:03(3663)9636

Heptachlor	not detected (detection limit 0.01 ppm)
Dieldrin	not detected (detection limit 0.01 ppm)
Aldrin	not detected (detection limit 0.01 ppm)
Parathion	not detected (detection limit 0.05 ppm)
Malathion	0.10 ppm

[redacted], D.V.M., Ph.D.
Director
Center for Food Environment Hygiene
TOKYO KENBIKYOIN FOUNDATION

DATE JULY 16. 1999

MICROBIOROGICAL INSPECTION

Customer
RESEARCH INSTITUTE FOR ANIMAL SCIENCE
IN BIOCHEMISTORY AND TOXICOLOGY
Sample Designation
LABO MR STOCK
Lot No. 990653

S.P.C.·····1.0×10^4 CFU/g
Coliform Group·····Negative
Salmonella ·····Negative
Moids·····< 20 CFU/g

NIHON NOSAN KOGYO K.K.
R & D Center
Safety & QC Station
5246, TAKURA, TSUKUBASHI, 300-2615 JAPAN

[redacted] Director

[redacted]

Appendix 6-3-1 Analysis of contaminants in animal feed

Authorized by the Ministry of Health & Welfare of Japan

TOKYO KENBIKYOIN FOUNDATION

CENTER FOR FOOD ENVIRONMENT HYGIENE

IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103, JAPAN
TEL:03(3663)9631 FAX:03(3663)9635

Date : Aug. 12 , 1999

CERTIFICATE

Applicant : NIHON NOSAN KOGYO K. K
Samples : LABO MR-STOCK, Lot No.990755
Date of Application : July 26, 1999
Date of Examination : July 26 ~ Aug. 12 , 1999
Examination No. : 3907807

As a result of tests carried out on the sample submitted under the above mentioned name on July 26, 1999. We herewith report as follows :

RESUTS

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)
N-Nitrosodimethylamine	not detected (detection limit 10 ppb)
N-Nitrosodiethylamine	not detected (detection limit 10 ppb)
Arsenic (As)	0.17 ppm
Lead (Pb)	0.4 ppm
Cadmium (Cd)	0.10 ppm
Mercury (Hg)	not detected (detection limit 0.01 ppm)
Chromium (Cr)	1.8 ppm
Polychlorinated biphenyl (PCBs)	not detected (detection limit 0.01 ppm)
Total DDT*1	not detected (detection limit 0.05 ppm)
Total BHC*2	not detected (detection limit 0.05 ppm)

*1 Expressed as total amounts of op'-DDT , pp'-DDT ,op'-DDD , pp-DDD , op'-DDE and pp'-DDE

*2 Expressed as total amounts of α -BHC, β -BHC, γ -BHC and δ -BHC

Appendix 6-3-2 Analysis of contaminants in animal feed

Authorized by the Ministry of Health & Welfare of Japan

TOKYO KENBIKYOIN FOUNDATION

CENTER FOR FOOD ENVIRONMENT HYGIENE

IMAS-HAKOZAKI BLDG., 44-1, Nihonbashi hakozaki-cho, Chuo-Ku, Tokyo 103, JAPAN
TEL:03(3663)9681 FAX:03(3663)9633

Heptachlor	not detected (detection limit 0.01 ppm)
Dieldrin	not detected (detection limit 0.01 ppm)
Aldrin	not detected (detection limit 0.01 ppm)
Parathion	not detected (detection limit 0.05 ppm)
Malathion	0.05 ppm

[redacted], D.V.M., Ph.D.
Director
Center for Food Environment Hygiene
TOKYO KENBIKYOIN FOUNDATION

DATE AUG 2. 1999

MICROBIOROGICAL INSPECTION

Customer
RESEARCH INSTITUTE FOR ANIMAL SCIENCE
IN BIOCHEMISTORY AND TOXICOLOGY
Sample Designation
LABO MR STOCK
Lot No. 990755

S.P.C.·····1.7×10^4 CFU/g
Coliform Group·····Negative
Salmonella ·····Negative
Moids·····< 20 CFU/g

NIHON NOSAN KOGYO K.K.
R & D Center
Safety & QC Station
5246, TAKURA, TSUKUBASHI, 300-2615 JAPAN

[redacted] Director

[redacted]

Appendix 7-1 Analysis of contaminants in drinking water

Quality Analysis & Certificate for Drinking Water

Certificate No: D-990079

Date : 1999. FEB. 5th

Messrs. Research Institute for Animal in Biochemistry and Toxicology

Place of take up sample:

Drinking Water for animal of a BS area

Date of take up sample : '99 JAN. 28th

Examination purpose :

Propriety of a water quality standard in water supply law

Tokyo Technic[redacted]o., Ltd.

6chome-7-6 Nakaka[redacted] Tokyo

TEL 03(3688[redacted]

(Tokyo Metropolice Registered %56W327)

Responsible person : [redacted]

Items	Results	Regulative Standard
Bacteria	0 group/ml	Bellow 100groups/ml
Escherchia	Negative	Negative
Nitrogen (as nitric & nitrous acid)	1.7	Below 10 mg/l
Chloride	8.0	Below 200 mg/l
Organic (chemical oxygen demand)	0.7	Below 10 mg/l
pH	7.7	5.8 ~ 8.6
Taste	Normal	Normal
Odor	Normal	Normal
Color Standard Solution	Below 1 °	Below 5'
Turbidity Standard Solution	Below 1 °	Below 2'

Method of Analysis are based on The Ministry of Health and Welfare Order No. 69

Appendix 7-2 Analysis of contaminants in drinking water

Quality Analysis & Certificate for Drinking Water

Certificate No: D－990779

Date : 1999. Aug. 4th

Messrs. Research Institute for Animal in Biochemistry and Toxicology

Place of take up sample: Clean room

Date of take up sample : '99 July 9th

Examination purpose :
Propriety of a water quality standard in water supply law

Tokyo Tech [redacted] Co., Ltd.

6chome-7-6 Nak [redacted] ku Tokyo
TEL 03(368 [redacted]

(Tokyo Metropolice Registered №56W327)

Responsible person : [redacted]

Items	Results	Regulative Standard
Bacteria	0 group/ml	Bellow 100groups/ml
Escherchia	Negative	Negative
Nitrogen (as nitric & nitrous acid)	1.6	Below 10 mg/l
Chloride	6.8	Below 200 mg/l
Organic (chemical oxygen demand)	1.5	Below 10 mg/l
pH	7.5	5.8 ~ 8.6
Taste	Normal	Normal
Odor	Normal	Normal
Color Standard Solution	Below 1 °	Below 5'
Turbidity Standard Solution	Below 1 °	Below 2'
Lead	0.005 Under	0.05 Below
Zinc	0.1 Under	1.0 Below
Iron	0.03 Under	0.3 Below
Copper	0.1 Under	1.0 Below
Evaporated Residue	52	500 Below
Chloroform	0.0080	0.06 Below
Bromo-dichloromethane	0.0020	0.03 Below
Chloro-dibromomethane	0.001 Under	0.1 Below
Bromoform	0.0009 Under	0.09 Below
Total Trihalomethane	0.011	0.1 Below

Method of Analysis are based on The Ministry of Health and Welfare Order № 69

分析試験成績書

第199060425-001 号
平成 11 年 06 月 17 日

依 頼 者　　日本チャールス・リバー株式会社

検 体 名　　ホワイトフレーク

付記事項　　＊＊＊＊＊

財団法人
日本食品[redacted]
東京本部 〒15[redacted]元代々木町52番1号
大阪支所 〒56[redacted]豊津町3番1号
名古屋支所 〒46[redacted]大須4丁目5番13号
九州支所 〒81[redacted]下呉服町1番12号
多摩研究所 〒20[redacted]永山6丁目11番10号

平成 11 年 06 月 03 日当センターに提出された上記検体について分析試験した結果は次のとおりです。

分析試験結果

分析試験項目	結果	検出限界	注	分析方法
乾燥減量	7.1%		1	常圧加熱乾燥法
ヒ素(Asとして)	検出せず	0.1ppm		DDTC-Ag吸光光度法
鉛	0.23ppm			原子吸光光度法
カドミウム	0.11ppm			原子吸光光度法
総水銀	検出せず	0.01ppm		還元気化原子吸光光度法
BHC	検出せず	0.02ppm		ガスクロマトグラフ法
DDT	検出せず	0.02ppm		ガスクロマトグラフ法
アルドリン	検出せず	0.01ppm		ガスクロマトグラフ法
ディルドリン	検出せず	0.01ppm		ガスクロマトグラフ法
エンドリン	検出せず	0.01ppm		ガスクロマトグラフ法
ヘプタクロル	検出せず	0.01ppm		ガスクロマトグラフ法
ダイアジノン	検出せず	0.05ppm		ガスクロマトグラフ法
パラチオン	検出せず	0.05ppm		ガスクロマトグラフ法
パラチオンメチル	検出せず	0.05ppm		ガスクロマトグラフ法
マラチオン(マラソン)	検出せず	0.05ppm		ガスクロマトグラフ法
PCB	検出せず	0.1ppm		ガスクロマトグラフ法
アフラトキシンB_1	検出せず	5ppb		高速液体クロマトグラフ法
アフラトキシンB_2	検出せず	5ppb		高速液体クロマトグラフ法
アフラトキシンG_1	検出せず	5ppb		高速液体クロマトグラフ法
アフラトキシンG_2	検出せず	5ppb		高速液体クロマトグラフ法
一般細菌数(生菌数)	4.8×10^4／g			標準寒天平板培養法
大腸菌群	陰性／2.22g			BGLB法
サルモネラ	陰性／25g			増菌培養法
カビ数	60／g			ポテトデキストロース(10%)寒天平板培養法

注1. 測定条件：温度，105℃；時間，5時間

Appendix 9-1 Individual clinical signs of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
0	001	KT	22	NAD
	002	KT	22	NAD
	003	KT	22	NAD
	004	KT	22	NAD
	005	KT	22	NAD
	006	KT	22	NAD
	007	KR	85	NAD
	008	KR	85	NAD
	009	KR	85	NAD
	010	KR	85	NAD
	011	KR	85	NAD
	012	KR	85	NAD
40	013	KT	22	NAD
	014	KT	22	NAD
	015	KT	22	NAD
	016	KT	22	NAD
	017	KT	22	NAD
	018	KT	22	NAD
	019	KR	85	NAD
	020	KR	85	NAD
	021	KR	85	NAD
	022	KR	85	NAD
	023	KR	85	NAD
	024	KR	85	NAD

KT : Killed by design after administration period of 18 days ; KR : Killed by design after post-administration period of 63 days
NAD : No abnormalities detected

Appendix 9-2 Individual clinical signs of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
200	025	KT	22	Diarrhea, +(5)[a]
	026	KT	22	NAD
	027	KT	22	Diarrhea, +(9)[a]
	028	KT	22	Diarrhea, +(6)[a]
	029	KT	22	Diarrhea, +(8, 10)[a]
	030	KT	22	NAD
	031	KR	85	Diarrhea, +(6)[a]
	032	KR	85	NAD
	033	KR	85	Diarrhea, +(7, 10)[a]
	034	KR	85	NAD
	035	KR	85	Diarrhea, +(7)[a]
	036	KR	85	NAD
600	037	KT	22	Diarrhea, +(5-7, 9-11)[a]
	038	KT	22	Diarrhea, +(6, 14)[a]
	039	KT	22	Diarrhea, +(5-7, 9, 10)[a]
	040	KT	22	Diarrhea, +(5-7, 9-12, 16, 17)[a]
	041	KT	22	Diarrhea, +(5-17)[a]
	042	KT	22	Diarrhea, +(5-11)[a]
	043	KR	85	Diarrhea, +(5-7, 10, 13-15)[a]
	044	KE	28	Diarrhea, +(5-7, 16, 17)[a]
				Decrease in locomotor activity, +(25-28)[a]
				Piloerection, +(25-28)[a]
				Emaciation, +(25, 26)/++(27)/+++(28)[a]
				Pale skin, ++(28)[a]
				Abdomonal distension, +(28)[a]

KT : Killed by design after administration period of 18-days ; KR : Killed by design after post-administration period of 63-days
KE : Killed in extremis; NAD : No abnormalities detected; +: Slight; ++:Moderate; +++:Severe
a :Days of age when the sigh was observed

Appendix 9-3 Individual clinical signs of male rats treated orally with 4, 4'-isopropylidene bis(2, 6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
600	045	KR	85	Diarrhea, +(5-7, 9-10, 14)[a]
	046	FD	28	Diarrhea, +(5-7, 9-11)[a]
				Decrease in locomotor activity, +(25-27)[a]
				Piloerection, +(26, 27)[a]
				Emaciation, +(25, 26)/++(27)[a]
				Pale skin, ++(27)[a]
	047	KR	85	Diarrhea, +(5-8, 11, 16, 17)[a]
	048	KR	85	Diarrhea, +(5-10, 17)[a]

KT : Killed by design after administration period of 18-days ; KR : Killed by design after post-administration period of 63-days
FD: Found dead; NAD : No abnormalities detected; +: Slight; ++:Moderate
a :Days of age when the sigh was observed

Appendix 10-1 Individual clinical signs of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
0	501	KT		NAD
	502	KT	22	NAD
	503	KT	22	NAD
	504	KT	22	NAD
	505	KT	22	NAD
	506	KT	22	NAD
	507	KR	85	NAD
	508	KR	85	NAD
	509	KR	85	NAD
	510	KR	85	NAD
	511	KR	85	NAD
	512	KR	85	NAD
40	513	KT	22	NAD
	514	KT	22	NAD
	515	KT	22	NAD
	516	KT	22	NAD
	517	KT	22	NAD
	518	KT	22	NAD
	519	KR	85	NAD
	520	KR	85	NAD
	521	KR	85	NAD
	522	KR	85	NAD
	523	KR	85	NAD
	524	KR	85	NAD

KT : Killed by design after administration period of 18 day KR : Killed by design after post-administration period of 63-days
NAD : No abnormalities detected

Appendix 10-2 Individual clinical signs of female rats treated orally with 4, 4'-isopropylidene bis(2, 6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
200	525	KT	22	Diarrhea, +(8)[a]
	526	KT	22	Diarrhea, +(6)[a]
	527	KT	22	NAD
	528	KT	22	Diarrhea, +(10)[a]
	529	KT	22	NAD
	530	KT	22	Diarrhea, +(6, 10)[a]
	531	KR	85	Diarrhea, +(6)[a]
	532	KR	85	Diarrhea, +(5, 6)[a]
	533	KR	85	Diarrhea, +(5, 6)[a]
	534	KR	85	NAD
	535	KR	85	Diarrhea, +(7, 11)[a]
	536	KR	85	Diarrhea, +(5, 6)[a]
600	537	KT	22	Diarrhea, +(5-11, 14, 16, 17)[a]
	538	KT	22	Diarrhea, +(5-11, 13, 14, 16)[a]
	539	KT	22	Diarrhea, +(5-9, 13, 14, 16, 17)[a]
	540	KT	22	Diarrhea, +(5-7, 9, 10, 12, 14, 15)[a]
	541	KT	22	Diarrhea, +(5-7, 9-12, 15, 16)[a]
	542	KT	22	Diarrhea, +(5-10, 13-17[a]
	543	KR	85	Diarrhea, +(5-7, 9, 10, 12, 16, 17)[a]
	544	KR	85	Diarrhea, +(5-7, 9, 14, 16)[a]
	545	KR	85	Diarrhea, +(5-9, 11-13, 15, 16)[a]
	546	FD	28	Diarrhea, +(5-7, 10)[a] Decrease in locomotor activity, +(25-27)[a] Piloerection, +(25-27)[a] Emaciation, +(25, 26)/+++(27)[a] Pale skin, +(27)[a] Abdominal distension, +(26, 27)[a]
	547	KR	85	Diarrhea, +(5-7, 10)[a]
	548	KR	85	Diarrhea, +(5-10)[a]

KT : Killed by design after administration period of 18-day KR : Killed by design after post-administration period of 63-days
FD: Found dead; NAD : No abnormalities detected; +: Slight; +++:Severe
a : Days of age when the sigh was observed

Appendix 11-1 Individual data on sensory functions of male treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg)	Animal number	State of gait	Pupil reflex	Pinna reflex	Corneal reflex	Visiual stepping reflex	Righting reflex	Air righting reflex	Ispilateral flexor reflex
	Score range	1~8	1,2	1~4	1~4	1~4	1~4	1~3	1~3
0	001	2	1	1	1	1	1	1	1
	002	2	1	1	1	1	1	1	1
	003	2	1	1	1	1	1	1	1
	004	2	1	1	1	1	1	1	1
	005	2	1	1	1	1	1	1	1
	006	2	1	1	1	1	1	1	1
	007	2	1	1	1	1	1	1	1
	008	2	1	1	1	1	1	1	1
	009	2	1	1	1	1	1	1	1
	010	2	1	1	1	1	1	1	1
	011	2	1	1	1	1	1	1	1
	012	2	1	1	1	1	1	1	1
40	013	2	1	1	1	1	1	1	1
	014	2	1	1	1	1	1	1	1
	015	2	1	1	1	1	1	1	1
	016	2	1	1	1	1	1	1	1
	017	2	1	1	1	1	1	1	1
	018	2	1	1	1	1	1	1	1
	019	2	1	1	1	1	1	1	1
	020	2	1	1	1	1	1	1	1
	021	2	1	1	1	1	1	1	1
	022	2	1	1	1	1	1	1	1
	023	2	1	1	1	1	1	1	1
	024	2	1	1	1	1	1	1	1

Appendix 11-2 Individual data on sensory functions of male treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg)	Animal number	State of gait	Pupil reflex	Pinna reflex	Corneal reflex	Visiual stepping reflex	Righting reflex	Air righting reflex	Ispilateral flexor reflex
	Score range	1~8	1,2	1~4	1~4	1~4	1~4	1~3	1~3
200	025	2	1	1	1	1	2	1	1
	026	2	1	1	1	1	1	1	1
	027	2	1	1	1	1	1	1	1
	028	2	1	1	1	1	1	1	1
	029	2	1	1	1	1	1	1	1
	030	2	1	1	1	1	1	1	1
	031	2	1	1	1	1	1	1	1
	032	2	1	1	1	1	1	1	1
	033	2	1	1	1	1	1	1	1
	034	2	1	1	1	1	1	1	1
	035	2	1	1	1	1	1	1	1
	036	2	1	1	1	1	1	1	1
600	037	2	1	1	1	1	1	1	1
	038	2	1	1	1	1	1	1	1
	039	2	1	1	1	1	1	1	1
	040	2	1	1	1	1	1	1	1
	041	2	1	1	1	1	1	1	1
	042	2	1	1	1	1	1	1	1
	043	2	1	1	1	1	1	1	1
	044	2	1	1	1	1	2	1	1
	045	2	1	1	1	1	1	1	1
	046	2	1	1	1	1	1	1	1
	047	2	1	1	1	1	1	1	1
	048	2	1	1	1	1	1	1	1

Appendix 12-1 Individual data on sensory functions of female treated orally with 4,4'-isopropylidene bis(2,6 dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg)	Animal number	State of gait	Pupil reflex	Pinna reflex	Corneal reflex	Visiual stepping reflex	Righting reflex	Air righting reflex	Ispilateral flexor reflex
	Score range	1~8	1,2	1~4	1~4	1~4	1~4	1~3	1~3
0	501	2	1	1	1	1	1	1	1
	502	2	1	1	1	1	1	1	1
	503	2	1	1	1	1	1	1	1
	504	2	1	1	1	1	1	1	1
	505	2	1	1	1	1	1	1	1
	506	2	1	1	1	1	1	1	1
	507	2	1	1	1	1	1	1	1
	508	2	1	1	1	1	1	1	1
	509	2	1	1	1	1	1	1	1
	510	2	1	1	1	1	1	1	1
	511	2	1	1	1	1	1	1	1
	512	2	1	1	1	1	1	1	1
40	513	2	1	1	1	1	1	1	1
	514	2	1	1	1	1	1	1	1
	515	2	1	1	1	1	1	1	1
	516	2	1	1	1	1	1	1	1
	517	2	1	1	1	1	1	1	1
	518	2	1	1	1	1	1	1	1
	519	2	1	1	1	1	1	1	1
	520	2	1	1	1	1	1	1	1
	521	2	1	1	1	1	1	1	1
	522	2	1	1	1	1	1	1	1
	523	2	1	1	1	1	1	1	1
	524	2	1	1	1	1	1	1	1

Appendix 12-2 Individual data on sensory functions of female treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg)	Animal number	State of gait	Pupil reflex	Pinna reflex	Corneal reflex	Visiual stepping reflex	Righting reflex	Air righting reflex	Ispilateral flexor reflex
	Score range	1~8	1,2	1~4	1~4	1~4	1~4	1~3	1~3
200	525	1	1	1	1	1	1	1	1
	526	1	1	1	1	1	1	1	1
	527	1	1	1	1	1	1	1	1
	528	1	1	1	1	1	1	1	1
	529	1	1	1	1	1	1	1	1
	530	1	1	1	1	1	1	1	1
	531	1	1	1	1	1	1	1	1
	532	1	1	1	1	1	1	1	1
	533	1	1	1	1	1	1	1	1
	534	1	1	1	1	1	1	1	1
	535	1	1	1	1	1	1	1	1
	536	1	1	1	1	1	1	1	1
600	537	1	1	1	1	1	1	1	1
	538	1	1	1	1	1	1	1	1
	539	1	1	1	1	1	1	1	1
	540	1	1	1	1	1	1	1	1
	541	1	1	1	1	1	1	1	1
	542	1	1	1	1	1	1	1	1
	543	1	1	1	1	1	2	1	1
	544	1	1	1	1	1	1	1	1
	545	1	1	1	1	1	1	1	1
	546	1	1	1	1	1	1	1	1
	547	1	1	1	1	1	1	1	1
	548	1	1	1	1	1	1	1	1

Appendix 13-1 Individual external differentiation of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Appearance of hair	Eruption of lower incisor	Separation of eyelids	Descent of testes
0	001	7	10	14	
	002	7	9	14	
	003	7	11	14	
	004	7	9	14	
	005	7	9	14	
	006	7	9	14	
	007	7	9	15	18
	008	7	10	14	18
	009	7	10	14	18
	010	7	9	14	18
	011	7	11	14	18
	012	7	10	14	18
	Mean	7.0	9.7	14.1	18.0
40	013	7	9	14	
	014	7	10	14	
	015	7	9	15	
	016	7	9	14	
	017	7	9	14	
	018	7	9	15	
	019	7	9	13	18
	020	7	10	14	18
	021	7	11	14	18
	022	7	9	14	19
	023	7	9	14	18
	024	7	9	14	18
	Mean	7.0	9.3	14.1	18.2

Each value is expressed as days of age.

Appendix 13-2 Individual external differentiation of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Appearance of hair	Eruption of lower incisor	Separation of eyelids	Descent of testes
200	025	7	11	14	
	026	7	9	14	
	027	7	9	13	
	028	7	10	14	
	029	7	9	14	
	030	7	10	14	
	031	7	9	14	18
	032	7	9	14	18
	033	7	9	15	18
	034	7	9	14	18
	035	7	10	14	18
	036	7	9	14	18
	Mean	7.0	9.4	14.0	18.0
600	037	7	9	15	
	038	7	11	15	
	039	7	9	14	
	040	7	9	14	
	041	7	9	12	
	042	7	9	15	
	043	7	9	14	18
	044	7	11	15	18
	045	7	9	13	18
	046	7	11	15	18
	047	7	9	15	18
	048	7	9	14	18
	Mean	7.0	9.5	14.3	18.0

Each value is expressed as days of age.

Appendix 14-1 Individual external differentiation of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Appearance of hair	Eruption of lower incisor	Separation of eyelids	Opening of vagina
0	501	7	9	14	
	502	7	10	14	
	503	7	9	14	
	504	7	9	14	
	505	7	9	14	
	506	7	10	14	
	507	7	9	14	33
	508	7	10	14	34
	509	7	9	14	33
	510	7	9	14	31
	511	7	9	14	34
	512	7	9	14	35
	Mean	7.0	9.3	14.0	33.3
40	513	7	9	14	
	514	7	10	14	
	515	7	11	14	
	516	7	9	13	
	517	7	11	14	
	518	7	9	15	
	519	7	10	14	39
	520	7	10	14	35
	521	7	9	14	30
	522	7	9	14	32
	523	7	9	13	34
	524	7	9	14	33
	Mean	7.0	9.6	13.9	33.8

Each value is expressed as days of age.

Appendix 14-2 Individual external differentiation of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Appearance of hair	Eruption of lower incisor	Separation of eyelids	Opening of vagina
200	525	7	9	14	
	526	7	9	14	
	527	7	9	14	
	528	7	9	14	
	529	7	11	12	
	530	7	10	14	
	531	7	9	14	32
	532	7	9	14	32
	533	7	9	13	32
	534	7	9	15	33
	535	7	9	14	30
	536	7	9	14	31
	Mean	7.0	9.3	13.8	31.7
600	537	7	9	14	
	538	7	10	14	
	539	7	9	13	
	540	7	9	14	
	541	7	9	13	
	542	7	11	14	
	543	7	11	14	32
	544	7	9	13	33
	545	7	9	13	37
	546	7	11	14	
	547	7	9	14	36
	548	7	9	13	32
	Mean	7.0	9.6	13.6	34.0

Each value is expressed as days of age.

Appendix 15-1 Individual body weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Dose (mg/kg/day)	Animal number	Days of age 3	4	7	10	13	16	19	21	Gain 4-21	21	28	35	42	49	56	63	70	77	84	Gain 21-84
0	001	11.0	12.7	19.2	27.0	34.3	42.1	49.5	56.2	43.5											
	002	10.7	12.3	18.5	24.9	31.0	38.6	48.1	58.9	46.6											
	003	9.9	11.0	16.3	22.6	29.3	35.9	43.5	53.8	42.8											
	004	10.6	12.9	18.8	26.2	33.6	42.6	51.8	63.4	50.5											
	005	10.4	13.0	20.5	26.8	34.3	41.9	51.7	60.6	47.6											
	006	10.1	12.2	18.8	25.7	33.5	41.8	49.6	58.7	46.5											
	007	10.0	12.0	18.8	25.0	33.3	42.6	51.3	62.2	50.2	62	103	161	225	286	349	392	428	468	482	420
	008	10.9	12.6	18.8	26.3	34.8	42.6	50.2	60.2	47.6	60	104	170	230	292	358	403	444	481	495	435
	009	10.7	13.0	20.7	28.7	36.0	43.8	52.0	60.9	47.9	61	100	161	225	279	330	362	386	412	425	364
	010	10.1	12.7	18.7	24.9	33.7	41.7	50.3	60.9	48.2	61	100	159	224	290	351	395	417	437	452	391
	011	10.3	12.7	19.9	27.3	33.6	40.8	48.9	59.3	46.6	59	98	162	220	282	338	382	414	447	468	409
	012	10.5	12.6	19.6	28.1	36.0	43.1	52.7	62.7	50.1	63	108	174	239	304	356	403	434	479	506	443
	Mean	10.4	12.5	19.1	26.1	33.6	41.5	50.0	59.8	47.3	61	102	165	227	289	347	390	421	454	471	410
40	013	10.0	11.6	17.0	23.5	30.9	38.0	47.1	55.1	43.5											
	014	11.0	13.0	19.0	25.4	32.3	39.6	49.6	59.3	46.3											
	015	9.8	11.8	17.9	24.4	31.3	38.5	47.2	57.7	45.9											
	016	10.4	12.6	19.3	26.0	33.1	41.2	48.7	59.6	47.0											
	017	10.5	13.1	20.7	28.6	36.4	45.6	58.1	65.7	52.6											
	018	10.9	13.1	19.4	26.8	34.2	41.6	49.7	57.7	44.6											
	019	9.9	11.8	18.8	25.9	34.9	44.7	54.4	62.7	50.9	63	97	151	209	268	324	369	402	435	452	389
	020	10.4	11.8	18.2	25.3	33.6	41.9	51.8	61.2	49.4	61	102	155	208	265	313	359	400	431	457	396
	021	10.3	12.1	19.4	27.0	35.0	43.3	53.1	63.4	51.3	63	108	175	249	310	362	402	423	453	465	402
	022	11.2	13.4	18.8	24.1	31.0	38.0	46.3	56.9	43.5	57	99	152	210	266	323	369	395	423	450	393
	023	10.0	12.2	19.2	26.7	34.4	42.3	52.7	62.4	50.2	62	107	167	231	303	369	419	462	500	520	458
	024	10.7	13.0	20.5	28.5	37.7	45.7	55.0	65.4	52.4	65	113	183	251	319	381	426	464	497	522	457
	Mean	10.4	12.5	19.0	26.0	33.7	41.7	51.1	60.6	48.1	62	104	164	226	289	345	391	424	457	478	416

Appendix 15-2 Individual body weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Dose (mg/kg/day)	Animal number	Days of age 3	4	7	10	13	16	19	21	Gain 4-21	21	28	35	42	49	56	63	70	77	84	Gain 21-84
200	025	10.2	12.6	19.0	26.5	34.3	42.1	50.2	60.1	47.5											
	026	10.3	12.2	18.3	24.7	32.4	39.7	49.1	57.1	44.9											
	027	11.1	12.4	18.4	25.2	32.1	38.6	45.6	56.0	43.6											
	028	10.6	13.4	19.9	27.2	35.0	42.7	52.6	61.3	47.9											
	029	10.0	12.5	19.2	27.3	35.3	42.9	52.8	61.4	48.9											
	030	10.8	12.7	18.7	25.5	33.0	38.8	48.7	58.1	45.4											
	031	11.0	13.4	19.8	27.6	36.8	46.2	57.4	67.7	54.3	68	108	173	245	314	378	423	460	493	528	460
	032	10.3	12.6	18.4	26.1	33.5	41.8	50.3	59.2	46.6	59	97	159	221	285	347	394	418	449	469	410
	033	10.2	13.0	20.2	27.7	36.4	45.2	53.6	63.8	50.8	64	104	169	238	299	353	395	432	469	493	429
	034	10.9	12.5	17.6	24.3	31.2	39.2	48.3	60.1	47.6	60	102	163	226	281	330	373	405	440	460	400
	035	10.7	13.1	19.9	27.7	35.4	42.5	49.4	60.1	47.0	60	102	175	253	322	386	436	485	522	557	497
	036	9.8	12.0	19.0	27.4	35.8	43.1	53.7	65.1	53.1	65	111	184	256	323	392	444	492	528	548	483
	Mean	10.5	12.7	19.0	26.4	34.3	41.9	51.0	60.8	48.1	63	104	171	240	304	364	411	449	484	509	447
600	037	10.0	11.8	16.7	24.0	31.6	39.6	47.0	55.9	44.1											
	038	10.5	12.3	17.2	23.2	30.3	36.9	44.9	54.8	42.5											
	039	11.0	12.4	18.1	24.6	31.1	37.3	44.8	56.3	43.9											
	040	9.9	12.0	17.0	24.3	31.2	39.4	48.0	57.6	45.6											
	041	10.7	13.1	19.0	26.0	33.0	40.0	50.7	60.8	47.7											
	042	10.3	12.8	18.1	25.7	33.4	40.8	49.6	60.8	48.0											
	043	10.5	13.0	18.9	26.9	36.4	45.2	54.0	64.4	51.4	64	103	159	223	286	338	376	410	427	452	388
	044	10.7	12.9	17.4	23.9	32.7	38.7	46.3	50.9	38.0	51	52									
	045	10.0	12.6	17.6	25.3	33.8	42.4	51.9	59.6	47.0	60	81	139	203	266	330	375	421	454	472	412
	046	10.2	12.3	16.8	23.6	30.8	37.8	44.5	52.7	40.4	53										
	047	11.0	13.5	18.7	26.6	34.0	41.2	49.0	59.8	46.3	60	100	173	246	310	372	419	464	501	535	475
	048	10.4	12.9	18.0	26.7	34.9	43.5	52.0	62.9	50.0	63	108	186	256	321	380	428	475	510	527	464
	Mean	10.4	12.6	17.8	25.1	32.8	40.2	48.6	58.0	45.4	59	89	164	232	296	355	400	443	473	497	435

Appendix 16-1 Individual body weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Dose (mg/kg/day)	Animal number	Days of age 3	4	7	10	13	16	19	21	Gain 4-21	21	28	35	42	49	56	63	70	77	84	Gain 21-84
0	501	9.5	11.5	17.3	24.2	32.1	38.2	45.9	54.3	42.8											
	502	9.8	11.7	17.4	23.8	30.6	37.0	43.4	49.1	37.4											
	503	9.9	11.9	17.8	25.0	31.6	38.0	44.4	53.2	41.3											
	504	10.5	12.9	20.2	27.3	33.6	40.6	48.7	57.9	45.0											
	505	10.2	13.0	19.6	27.2	34.3	42.5	51.6	59.9	46.9											
	506	10.1	11.8	18.1	25.5	33.0	40.2	49.9	58.8	47.0											
	507	10.3	11.9	18.9	26.7	34.7	42.8	52.7	62.3	50.4	62	91	134	169	196	220	238	256	267	276	214
	508	10.1	11.8	17.7	25.0	32.0	38.3	46.3	56.1	44.3	56	95	141	175	203	227	243	253	266	279	223
	509	10.4	12.9	20.7	27.7	37.2	45.1	54.2	64.8	51.9	65	101	153	188	215	245	264	280	292	306	241
	510	9.6	11.8	17.4	23.1	30.5	36.7	45.9	56.5	44.7	57	93	144	174	195	217	234	245	259	267	210
	511	9.9	12.1	18.9	26.1	32.5	39.8	47.8	57.7	45.6	58	91	131	162	185	205	222	232	241	248	190
	512	10.1	12.0	19.5	27.8	35.7	43.8	52.3	62.4	50.4	62	96	141	177	198	223	240	244	251	265	203
	Mean	10.0	12.1	18.6	25.8	33.2	40.3	48.6	57.8	45.6	60	95	141	174	199	223	240	252	263	274	214
40	513	9.9	12.2	19.1	27.5	34.5	41.5	49.8	55.9	43.7											
	514	9.9	12.1	17.7	23.9	30.6	38.4	47.6	56.8	44.7											
	515	10.1	11.9	18.2	24.4	31.7	38.3	45.5	53.2	41.3											
	516	10.3	12.4	19.2	26.0	33.2	41.5	48.7	57.6	45.2											
	517	9.4	11.4	17.9	24.8	31.5	37.4	47.8	54.1	42.7											
	518	10.4	12.8	18.8	25.7	33.3	40.8	50.1	59.2	46.4											
	519	9.8	11.7	18.9	25.9	34.3	43.3	50.9	58.4	46.7	58	88	126	161	189	215	234	245	259	269	211
	520	9.5	11.5	17.3	24.4	32.5	39.5	47.5	56.9	45.4	57	93	137	169	189	206	219	226	236	250	193
	521	10.0	12.4	20.2	28.0	35.8	45.4	56.8	67.0	54.6	67	108	152	184	198	224	231	250	255	266	199
	522	10.3	12.7	18.9	24.9	32.8	40.3	49.6	60.9	48.2	61	98	150	185	210	233	248	260	264	284	223
	523	10.2	12.7	19.6	27.1	32.9	39.2	48.4	57.4	44.7	57	90	133	167	191	209	226	244	259	267	210
	524	10.5	12.7	19.8	27.4	34.7	42.5	50.5	59.0	46.3	59	94	144	177	203	222	237	251	264	268	209
	Mean	10.0	12.2	18.8	25.8	33.2	40.7	49.4	58.0	45.8	60	95	140	174	197	218	233	246	256	267	208

Appendix 16-2 Individual body weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Dose (mg/kg/day)	Animal number	Days of age 3	4	7	10	13	16	19	21	Gain 4-21	21	28	35	42	49	56	63	70	77	84	Gain 21-84
200	525	9.7	11.5	17.5	25.4	32.5	39.4	47.1	54.9	43.4											
	526	10.4	12.4	18.1	24.6	31.4	37.8	47.8	53.6	41.2											
	527	9.8	10.7	15.8	21.4	28.2	34.4	43.7	52.8	42.1											
	528	10.0	12.4	18.6	26.1	32.8	40.6	49.4	55.0	42.6											
	529	10.1	12.2	18.3	25.4	33.2	41.7	52.0	59.5	47.3											
	530	10.2	12.8	18.0	23.5	30.7	37.9	46.4	55.7	42.9											
	531	10.4	12.1	18.2	26.2	33.3	41.3	51.1	59.7	47.6	60	102	153	183	204	228	248	265	279	282	222
	532	9.8	12.0	18.1	24.6	32.9	38.8	48.7	54.2	42.2	54	87	131	169	190	211	232	249	264	264	210
	533	10.2	13.0	20.0	27.5	36.3	44.2	54.1	64.6	51.6	65	109	165	204	222	250	264	275	292	310	245
	534	9.6	11.5	16.9	23.9	31.9	36.7	45.1	54.5	43.0	55	90	140	176	197	220	234	251	254	268	213
	535	10.3	12.2	18.3	25.0	32.0	39.5	48.3	57.3	45.1	57	97	143	175	199	221	237	245	261	271	214
	536	10.0	12.3	18.5	26.1	34.3	41.8	50.5	60.3	48.0	60	98	145	188	213	235	248	269	285	293	233
	Mean	10.0	12.1	18.0	25.0	32.5	39.5	48.7	56.8	44.8	59	97	146	183	204	228	244	259	273	281	223
600	537	10.4	12.5	17.2	25.0	32.5															
	538	10.3	12.5	17.5	23.4	30.7	34.9	44.3	52.0	39.5											
	539	9.5	11.3	16.6	23.1	30.7	38.2	47.2	54.9	43.6											
	540	9.9	11.9	17.0	22.8	29.4	36.0	43.3	46.6	34.7											
	541	9.9	12.6	17.9	25.5	32.9	41.2	52.5	61.3	48.7											
	542	10.1	12.6	17.9	24.9	32.8	40.0	48.1	58.6	46.0											
	543	10.2	12.3	17.7	24.9	34.5	42.4	49.3	59.3	47.0	59	99	156	194	222	251	263	282	293	306	247
	544	9.7	11.8	16.7	24.0	31.8	38.6	48.4	59.0	47.2	59	93	140	177	204	231	249	266	280	295	236
	545	10.4	12.2	18.0	25.0	34.3	42.2	50.6	58.9	46.7	59	87	136	173	201	224	241	255	274	283	224
	546	10.1	11.6	16.5	22.0	31.0	38.9	46.7	55.7	44.1	56										
	547	9.7	12.2	18.7	26.1	32.5															
	548	10.3	12.3	17.8	26.6	32.5	40.1	49.1	58.2	45.9	58	98	148	184	205	229	247	265	274	285	227
	Mean	10.0	12.2	17.5	24.4	32.1	39.3	48.0	56.5	44.3	58	94	145	182	208	234	250	267	280	292	234

Appendix 17 Individual food consumption of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Dose (mg/kg/day)	Animal number	Days of age 28	35	42	49	56	63	70	77	84
0	007	18	26	30	38	41	37	42	42	37
	008	20	27	32	34	38	35	36	43	36
	009	17	23	29	30	30	30	30	34	26
	010	29	24	32	32	37	38	37	35	32
	011	18	25	29	31	35	37	35	38	33
	012	18	25	30	36	35	32	33	40	36
	Mean	20	25	30	34	36	35	36	39	33
40	019	17	24	27	32	35	35	32	36	32
	020	19	24	26	33	33	33	35	35	33
	021	19	28	33	34	35	38	32	34	30
	022	19	24	28	33	35	36	33	31	31
	023	20	27	33	37	41	42	45	47	40
	024	19	29	32	37	42	38	38	37	33
	Mean	19	26	30	34	37	37	36	37	33
200	031	19	25	34	36	43	42	40	37	41
	032	18	22	29	30	33	35	33	34	31
	033	19	26	31	33	34	33	35	38	37
	034	18	24	31	32	35	36	36	37	38
	035	20	31	39	42	46	49	47	48	42
	036	19	28	33	12	43	39	40	44	36
	Mean	19	26	33	31	39	39	39	40	38
600	043	18	23	32	32	34	34	36	32	33
	044									
	045	13	23	31	36	40	33	43	39	36
	046									
	047	20	29	38	39	44	39	43	41	42
	048	19	30	35	42	42	39	48	45	38
	Mean	18	26	34	37	40	36	43	39	37

Appendix 18 Individual food consumption of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Dose (mg/kg/day)	Animal number	Days of age 28	35	42	49	56	63	70	77	84
0	507	14	20	20	22	24	25	26	25	22
	508	17	22	23	24	26	23	21	22	24
	509	17	23	25	22	26	25	26	23	28
	510	17	24	22	21	22	23	23	23	23
	511	18	20	22	25	25	25	28	26	25
	512	16	21	23	21	25	26	23	21	26
	Mean	17	22	23	23	25	25	25	23	25
40	519	16	20	21	25	26	25	22	25	25
	520	18	20	21	21	23	22	21	23	24
	521	19	21	22	21	24	19	24	19	21
	522	20	25	26	26	27	30	27	24	29
	523	16	22	20	22	25	24	23	26	24
	524	15	21	21	23	22	23	24	26	22
	Mean	17	22	22	23	25	24	24	24	24
200	531	18	24	20	24	23	22	27	27	24
	532	17	20	24	25	22	25	26	27	20
	533	22	27	29	30	30	27	27	28	30
	534	18	22	24	23	26	24	25	21	23
	535	18	23	22	22	26	25	24	26	26
	536	17	22	26	28	28	26	30	30	28
	Mean	18	23	24	25	26	25	27	27	25
600	543	20	27	26	28	29	27	28	25	28
	544	17	24	25	27	30	25	23	26	26
	545	17	23	26	27	28	29	23	32	30
	546									
	547	15	20	24	26	26	27	31	27	27
	548	18	23	26	21	25	24	29	22	25
	Mean	17	23	25	26	28	26	27	26	27

Appendix 19 - 1 Individual urinary findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Color	Cloudy	Volume (mL/18hrs)	Specific gravity	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0	007	PY	−	13.9	1.052	8.0	+	−	−	−	0.1	−
	008	PY	+	8.5	1.022	8.5	+	−	−	−	0.1	−
	009	PY	−	10.0	1.052	8.0	+	−	±	−	0.1	−
	010	PY	+	10.7	1.058	8.0	+	−	±	−	0.1	−
	011	PY	−	9.9	1.074	8.0	++	−	−	−	0.1	−
	012	PY	−	12.3	1.068	7.0	+	−	±	+	0.1	−
40	019	PY	−	11.0	1.070	8.0	+	−	+	−	0.1	−
	020	PY	−	11.2	1.022	8.5	+	−	−	−	0.1	−
	021	PY	−	9.2	1.032	8.5	+	−	±	−	0.1	−
	022	PY	−	10.9	1.032	8.0	+	−	−	−	0.1	−
	023	PY	−	15.4	1.038	8.0	±	−	−	−	0.1	−
	024	PY	−	7.5	1.056	8.0	+	−	±	−	0.1	−

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

Appendix 19 - 2 Individual urinary findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Color	Cloudy	Volume (mL/18hrs)	Specific gravity	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
200	031	PY	−	9.5	1.060	8.5	+	−	±	−	0.1	−
	032	PY	−	9.5	1.048	8.5	+	−	±	−	0.1	−
	033	PY	−	8.0	1.030	8.0	±	−	−	−	0.1	−
	034	PY	+	11.5	1.042	8.5	±	−	−	−	0.1	−
	035	PY	+	15.5	1.070	7.5	++	−	+	−	0.1	−
	036	PY	−	27.8	1.036	8.0	+	−	±	−	0.1	−
600	043	PY	−	21.9	1.026	8.5	±	−	−	−	0.1	−
	044	----	----	----	----	----	----	----	----	----	----	----
	045	PY	−	18.5	1.026	8.5	++	−	±	++	0.1	−
	046	----	----	----	----	----	----	----	----	----	----	----
	047	PY	−	16.0	1.042	8.5	+	−	−	−	0.1	−
	048	PY	−	10.4	1.040	8.5	+	−	−	+	0.1	−

---- : Not available

Appendix 19 - 3 Individual urinary findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Erythro-cytes	Leuko-cytes	Crystals			Epithelial cells			Casts			Fat globules
				Mg	Ca	Ams	Sq	R	S	G	H	W	
0	007	−	−	++	−	−	+	−	−	−	−	−	−
	008	−	−	+	−	−	+	−	−	−	−	−	−
	009	−	−	+	−	−	+	−	−	−	−	−	−
	010	−	−	+	−	−	+	−	−	−	−	−	−
	011	−	−	+++	−	−	++	−	−	−	−	−	−
	012	−	−	−	++	−	+	−	−	−	−	−	−
40	019	−	−	++	−	−	+	−	−	−	−	−	−
	020	−	−	−	−	−	+	−	−	−	−	−	−
	021	−	−	++	−	−	+	−	−	−	−	−	−
	022	−	−	++	−	−	+	−	−	−	−	−	−
	023	−	−	+	−	−	+	−	−	−	−	−	−
	024	−	−	++	−	−	+	−	−	−	−	−	−

− : Not observed; + : A few in some fields; ++ : A few in all fields; +++ : Many in all fields

Crystals
- Mg(ammonium magnesium phosphate)
- Ca(calcium phosphate)
- Ams(amorphous)

Epithelial cells
- Sq(squamous)
- R(round)
- S(spindle)

Casts
- G(granule)
- H(hyaline)
- W(waxy)

Appendix 19 - 4 Individual urinary findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Erythro-cytes	Leuko-cytes	Crystals			Epithelial cells			Casts			Fat globules
				Mg	Ca	Ams	Sq	R	S	G	H	W	
200	031	−	−	++	−	−	+	−	−	−	−	−	−
	032	−	−	++	−	−	+	−	−	−	−	−	−
	033	−	−	+	−	−	+	−	−	−	−	−	−
	034	−	−	++	−	−	+	−	−	−	−	−	−
	035	−	−	+	−	−	+	−	−	−	−	−	−
	036	−	−	+	−	−	+	−	−	−	−	−	−
600	043	−	−	+	−	−	+	−	−	−	−	−	−
	044	----	----	----	----	----	----	----	----	----	----	----	----
	045	−	−	+	−	−	+	−	−	−	−	−	−
	046	----	----	----	----	----	----	----	----	----	----	----	----
	047	−	−	++	−	−	+	−	−	−	−	−	−
	048	−	−	++	−	−	+	−	−	−	−	−	−

---- : Not available

Appendix 20 - 1 Individual urinary findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Color	Cloudy	Volume (mL/18hrs)	Specific gravity	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
0	507	PY	−	8.0	1.058	7.5	±	−	−	−	0.1	−
	508	PY	−	5.5	1.058	8.5	+	−	−	−	0.1	−
	509	PY	+	10.5	1.066	8.5	±	−	−	−	0.1	−
	510	PY	−	13.5	1.068	6.0	±	−	−	−	0.1	−
	511	PY	−	30.5	1.044	8.5	±	−	−	−	0.1	−
	512	PY	+	7.0	1.078	8.0	+	−	−	−	0.1	−
40	519	PY	−	8.5	1.032	6.0	±	−	−	−	0.1	−
	520	PY	+	23.0	1.052	8.0	±	−	−	−	0.1	−
	521	PY	−	10.0	1.074	8.0	±	−	−	−	0.1	−
	522	PY	−	8.0	1.080	8.5	+	−	±	−	0.1	−
	523	PY	−	8.0	1.032	8.0	±	−	−	−	0.1	−
	524	PY	−	12.0	1.046	7.5	±	−	−	−	0.1	−

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

Appendix 20 - 2 Individual urinary findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Color	Cloudy	Volume (mL/18hrs)	Specific gravity	pH	Protein	Glucose	Ketone body	Occult blood	Urobilinogen	Bilirubin
200	531	PY	−	11.0	1.032	8.5	±	−	−	−	0.1	−
	532	PY	−	11.5	1.032	8.5	±	−	−	−	0.1	−
	533	PY	−	8.5	1.032	8.0	±	−	−	−	0.1	−
	534	PY	−	7.0	1.096	8.5	+	−	±	−	0.1	−
	535	PY	+	13.5	1.058	8.0	±	−	−	−	0.1	−
	536	PY	−	5.5	1.060	8.0	±	−	−	−	0.1	−
600	543	PY	+	11.0	1.052	7.5	+	−	−	−	0.1	−
	544	PY	+	17.5	1.026	8.5	±	−	−	−	0.1	−
	545	PY	−	10.5	1.040	8.5	±	−	−	−	0.1	−
	546	----	----	----	----	----	----	----	----	----	----	----
	547	PY	−	34.0	1.040	6.5	+	−	−	−	0.1	−
	548	PY	−	13.5	1.070	8.0	+	−	−	−	0.1	−

---- : Not available

Appendix 20 - 3 Individual urinary findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Erythro-cytes	Leuko-cytes	Crystals			Epithelial cells			Casts			Fat globules
				Mg	Ca	Ams	Sq	R	S	G	H	W	
0	507	−	−	−	−	−	+	−	−	−	−	−	−
	508	−	−	−	−	−	+	−	−	−	−	−	−
	509	−	−	+	−	−	+	−	−	−	−	−	−
	510	−	−	++	−	−	++	−	−	−	−	−	−
	511	−	−	−	−	−	+	−	−	−	−	−	−
	512	−	−	++	−	−	+	−	−	−	−	−	−
40	519	−	−	−	−	−	+	−	−	−	−	−	−
	520	−	−	−	−	−	+	−	−	−	−	−	−
	521	−	−	−	−	−	+	−	−	−	−	−	−
	522	−	−	−	−	−	+	−	−	−	−	−	−
	523	−	−	−	−	−	+	−	−	−	−	−	−
	524	−	−	−	−	−	+	−	−	−	−	−	−

− : Not observed; + : A few in some fields; ++ : A few in all fields

Crystals
- Mg(ammonium magnesium phosphate)
- Ca(calcium phosphate)
- Ams(amorphous)

Epithelial cells
- Sq(squamous)
- R(round)
- S(spindle)

Casts
- G(granule)
- H(hyaline)
- W(waxy)

Appendix 20 - 4 Individual urinary findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age weaning

< 11 weeks of age >

Dose (mg/kg)	Animal number	Erythro-cytes	Leuko-cytes	Crystals			Epithelial cells			Casts			Fat globules
				Mg	Ca	Ams	Sq	R	S	G	H	W	
200	531	−	−	+	−	−	+	−	−	−	−	−	−
	532	−	−	+	−	−	+	−	−	−	−	−	−
	533	−	−	−	−	−	+	−	−	−	−	−	−
	534	−	−	−	−	−	−	−	−	−	−	−	−
	535	−	−	++	−	−	+	−	−	−	−	−	−
	536	−	−	++	−	−	++	−	−	−	−	−	−
600	543	−	−	−	−	−	+	−	−	−	−	−	−
	544	−	−	+	−	−	+	−	−	−	−	−	−
	545	−	−	−	−	−	+	−	−	−	−	−	−
	546	----	----	----	----	----	----	----	----	----	----	----	----
	547	−	−	−	−	−	+	−	−	−	−	−	−
	548	−	−	−	−	−	+	−	−	−	−	−	−

---- : Not available

Appendix 21 - 1 Individual hematological findings of male rats treated orally 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	001	470	9.4	29.2	62	20.0	32.2	202	13.6	15.1
	002	472	9.1	30.1	64	19.3	30.2	246	13.2	15.6
	003	487	9.5	31.2	64	19.5	30.4	289	13.7	15.5
	004	490	10.2	32.4	66	20.8	31.5	224	14.0	14.9
	005	472	9.6	30.5	65	20.3	31.5	241	13.3	15.6
	006	487	10.2	32.1	66	20.9	31.8	158	14.0	14.7
	Mean	480	9.7	30.9	65	20.1	31.3	227	13.6	15.2
40	013	455	8.9	28.6	63	19.6	31.1	200	13.2	15.3
	014	489	10.3	33.0	67	21.1	31.2	298	13.9	14.8
	015	482	9.6	30.5	63	19.9	31.5	270	14.1	14.1
	016	493	10.1	32.4	66	20.5	31.2	220	13.5	15.0
	017	483	9.5	30.5	63	19.7	31.1	200	13.4	13.7
	018	474	9.4	29.3	62	19.8	32.1	193	13.8	13.5
	Mean	479	9.6	30.7	64	20.1	31.4	230	13.7	14.4
200	025	490	8.2	27.8	57	16.7	29.5	239	13.2	13.9
	026	443	8.2	27.4	62	18.5	29.9	236	14.0	14.5
	027	488	9.8	31.6	65	20.1	31.0	246	13.5	14.7
	028	515	10.5	33.3	65	20.4	31.5	210	13.6	15.4
	029	469	9.4	30.2	64	20.0	31.1	165	13.6	13.0
	030	490	9.8	31.8	65	20.0	30.8	229	14.1	14.7
	Mean	483	9.3	30.4	63	19.3	30.6	221	13.7	14.4
600	037	476	8.5	28.2	59	17.9	30.1	268	13.7	13.9
	038	457	8.2	26.9	59	17.9	30.5	252	13.6	14.3
	039	501	10.1	31.6	63	20.2	32.0	240	13.5	14.7
	040	510	8.8	29.3	57	17.3	30.0	256	12.9	14.2
	041	475	8.7	28.8	61	18.3	30.2	226	12.8	13.8
	042	476	9.1	30.0	63	19.1	30.3	195	13.5	14.5
	Mean	483	8.9	29.1	60	18.5	30.5	240	13.3	14.2

Appendix 21 - 2 Individual hematological findings of male rats treated orally 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)							Plat. ($10^4/\mu L$)
					Neutro.					
			Baso.	Eosin.	Stab	Seg.	Lymph.	Mono.	Other	
0	001	16	0	0	0	25	71	4	0	161
	002	13	0	0	0	18	78	4	0	132
	003	15	0	0	0	19	76	5	0	123
	004	21	0	0	0	24	73	3	0	150
	005	8	0	3	0	13	81	3	0	152
	006	23	0	0	0	10	86	4	0	153
	Mean	16	0	1	0	18	78	4	0	145
40	013	24	0	0	0	12	85	3	0	136
	014	12	0	0	0	12	84	4	0	155
	015	19	0	1	0	10	87	2	0	134
	016	15	0	0	0	21	76	3	0	149
	017	15	0	0	0	15	84	1	0	125
	018	25	0	0	0	7	89	4	0	133
	Mean	18	0	0	0	13	84	3	0	139
200	025	15	0	0	0	10	87	3	0	145
	026	9	0	0	0	22	77	1	0	149
	027	15	0	0	1	12	85	2	0	124
	028	18	0	0	0	17	82	1	0	142
	029	27	0	0	1	19	75	5	0	140
	030	10	0	0	0	12	86	2	0	148
	Mean	16	0	0	0	15	82	2	0	141
600	037	19	0	0	0	12	85	3	0	174
	038	15	0	1	0	11	88	0	0	142
	039	24	0	0	1	21	76	2	0	156
	040	10	0	0	0	8	89	3	0	150
	041	29	0	0	0	18	80	2	0	165
	042	13	0	0	0	21	78	1	0	132
	Mean	18	0	0	0	15	83	2	0	153

Appendix 22 - 1 Individual hematological findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	501	463	9.1	29.3	63	19.7	31.1	188	14.0	14.7
	502	494	9.2	29.1	59	18.6	31.6	152	14.2	13.9
	503	517	10.5	33.0	64	20.3	31.8	191	13.7	13.7
	504	541	11.1	34.3	63	20.5	32.4	202	13.6	14.7
	505	512	10.1	31.6	62	19.7	32.0	212	14.0	15.4
	506	517	10.2	31.9	62	19.7	32.0	235	13.9	13.9
	Mean	507	10.0	31.5	62	19.8	31.8	197	13.9	14.4
40	513	490	9.7	30.6	62	19.8	31.7	227	14.5	14.9
	514	513	10.1	32.8	64	19.7	30.8	202	14.7	16.1
	515	514	10.4	33.0	64	20.2	31.5	229	14.0	17.2
	516	520	10.8	34.1	66	20.8	31.7	215	13.0	15.4
	517	508	10.4	33.6	66	20.5	31.0	178	14.0	14.9
	518	524	10.0	31.9	61	19.1	31.3	190	14.0	15.3
	Mean	512	10.2	32.7	64	20.0	31.3	207	14.0	15.6
200	525	531	9.7	32.4	61	18.3	29.9	231	13.9	14.7
	526	501	9.8	31.9	64	19.6	30.7	234	13.8	14.3
	527	475	9.2	29.1	61	19.4	31.6	191	14.1	13.9
	528	513	10.6	33.4	65	20.7	31.7	218	13.0	13.5
	529	491	9.9	31.0	63	20.2	31.9	195	13.2	13.7
	530	533	10.4	34.0	64	19.5	30.6	223	13.7	14.9
	Mean	507	9.9	32.0	63	19.6	31.1	215	13.6	14.2
600	537	504	8.9	28.9	57	17.7	30.8	181	13.6	14.1
	538	505	8.6	28.3	56	17.0	30.4	196	13.5	13.3
	539	522	9.3	30.5	58	17.8	30.5	226	14.1	14.7
	540	500	8.8	30.0	60	17.6	29.3	190	13.2	12.0
	541	483	8.9	28.7	59	18.4	31.0	227	13.1	12.9
	542	504	9.6	30.8	61	19.0	31.2	242	13.9	13.7
	Mean	503	9.0	29.5	59	17.9	30.5	210	13.6	13.5

Appendix 22 - 2 Individual hematological findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)							Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	501	17	0	0	0	10	87	3	0	159
	502	24	0	1	0	13	86	0	0	134
	503	20	0	0	0	19	80	1	0	142
	504	22	0	0	0	11	87	2	0	128
	505	35	0	0	0	16	83	1	0	123
	506	18	0	0	0	13	86	1	0	166
	Mean	23	0	0	0	14	85	1	0	142
40	513	20	0	0	0	13	86	1	0	155
	514	20	0	0	0	20	79	1	0	171
	515	16	0	0	0	20	77	3	0	155
	516	23	0	0	0	18	80	2	0	140
	517	34	0	0	0	20	78	2	0	137
	518	24	0	0	0	21	78	1	0	174
	Mean	23	0	0	0	19	80	2	0	155
200	525	18	0	1	0	10	86	3	0	165
	526	12	0	0	0	17	82	1	0	178
	527	15	0	0	0	5	94	1	0	135
	528	31	0	1	0	9	84	6	0	172
	529	50	0	1	2	27	67	3	0	131
	530	32	0	0	0	8	92	0	0	132
	Mean	26	0	1	0	13	84	2	0	152
600	537	23	0	1	0	11	87	1	0	142
	538	21	0	1	1	14	82	2	0	153
	539	22	0	0	0	14	83	3	0	136
	540	30	0	0	0	13	85	2	0	184
	541	30	0	1	0	7	92	0	0	193
	542	24	0	0	1	10	88	1	0	154
	Mean	25	0	1	0	12	86	2	0	160

Appendix 23 - 1 Individual hematological findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	007	871	16.3	46.1	53	18.7	35.4	24	12.8	19.1
	008	821	15.6	43.9	53	19.0	35.5	32	12.9	18.9
	009	837	15.7	44.0	53	18.8	35.7	46	12.2	18.6
	010	865	16.4	45.4	52	19.0	36.1	21	12.7	18.6
	011	799	15.3	42.8	54	19.1	35.7	32	12.7	18.6
	012	837	15.7	44.6	53	18.8	35.2	36	13.0	18.3
	Mean	838	15.8	44.5	53	18.9	35.6	32	12.7	18.7
40	019	871	16.3	45.6	52	18.7	35.7	26	13.2	19.6
	020	807	15.5	44.6	55	19.2	34.8	26	13.5	16.6
	021	883	16.8	47.1	53	19.0	35.7	31	12.9	17.0
	022	854	15.3	43.2	51	17.9	35.4	41	12.3	17.3
	023	844	15.5	44.6	53	18.4	34.8	38	12.6	18.2
	024	856	14.9	42.7	50	17.4	34.9	21	13.0	18.6
	Mean	853	15.7	44.6	52	18.4	35.2	31	12.9	17.9
200	031	864	16.2	45.9	53	18.8	35.3	19	12.5	18.2
	032	857	15.1	43.0	50	17.6	35.1	22	12.5	17.2
	033	861	16.2	45.6	53	18.8	35.5	38	12.4	17.3
	034	831	14.9	42.9	52	17.9	34.7	45	12.4	17.1
	035	790	14.7	42.5	54	18.6	34.6	56	12.8	18.3
	036	780	14.7	42.0	54	18.8	35.0	48	12.4	15.9
	Mean	831	15.3	43.7	53	18.4	35.0	38	12.5	17.3
600	043	865	15.8	44.9	52	18.3	35.2	32	12.1	16.3
	044	----	----	----	----	----	----	----	----	----
	045	773	14.8	42.9	55	19.1	34.5	47	12.8	18.7
	046	----	----	----	----	----	----	----	----	----
	047	794	15.3	44.0	55	19.3	34.8	41	12.6	17.9
	048	835	16.3	46.4	56	19.5	35.1	48	12.4	17.5
	Mean	817	15.6	44.6	55	19.1	34.9	42	12.5	17.6

---- : Not available

Appendix 23 - 2 Individual hematological findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)							Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	007	60	0	0	0	8	92	0	0	121
	008	77	0	0	0	5	95	0	0	145
	009	84	0	0	0	11	88	1	0	116
	010	48	0	0	0	21	79	0	0	120
	011	72	0	0	0	14	85	1	0	122
	012	61	0	0	0	12	86	2	0	127
	Mean	67	0	0	0	12	88	1	0	125
40	019	53	0	1	0	13	83	3	0	126
	020	58	0	1	0	12	87	0	0	147
	021	58	0	1	0	20	77	2	0	131
	022	52	0	1	0	7	90	2	0	110
	023	79	0	2	0	11	87	0	0	130
	024	70	0	1	0	6	93	0	0	128
	Mean	62	0	1	0	12	86	1	0	129
200	031	75	0	0	0	17	81	2	0	128
	032	63	0	0	0	17	83	0	0	119
	033	50	0	0	0	8	90	2	0	141
	034	60	0	0	0	15	82	3	0	128
	035	54	0	1	0	16	83	0	0	134
	036	91	0	2	0	21	75	2	0	126
	Mean	66	0	1	0	16	82	2	0	129
600	043	66	0	0	0	9	88	3	0	121
	044	----	----	----	----	----	----	----	----	----
	045	60	0	1	0	18	81	0	0	146
	046	----	----	----	----	----	----	----	----	----
	047	59	0	1	0	27	69	3	0	129
	048	69	0	1	0	21	76	2	0	132
	Mean	64	0	1	0	19	79	2	0	132

---- : Not available

Appendix 24 - 1 Individual hematological findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	RBC ($10^4/\mu L$)	Hb (g/dL)	Ht (%)	MCV (fL)	MCH (pg)	MCHC (%)	Ret. (‰)	PT (sec)	APTT (sec)
0	507	833	16.4	45.7	55	19.7	35.9	15	12.6	16.5
	508	831	15.5	44.3	53	18.7	35.0	22	12.5	17.6
	509	759	15.4	42.7	56	20.3	36.1	31	12.9	18.6
	510	783	14.2	41.0	52	18.1	34.6	36	12.2	14.5
	511	809	15.6	43.9	54	19.3	35.5	17	13.0	15.1
	512	805	15.7	43.7	54	19.5	35.9	39	12.9	17.9
	Mean	803	15.5	43.6	54	19.3	35.5	27	12.7	16.7
40	519	892	16.5	46.4	52	18.5	35.6	18	13.7	15.7
	520	----	----	----	----	----	----	----	----	----
	521	744	14.3	40.8	55	19.2	35.0	15	12.3	15.1
	522	797	15.6	43.7	55	19.6	35.7	21	12.4	15.0
	523	785	14.6	41.6	53	18.6	35.1	33	13.4	15.9
	524	795	15.1	42.3	53	19.0	35.7	31	12.7	17.2
	Mean	803	15.2	43.0	54	19.0	35.4	24	12.9	15.8
200	531	794	15.7	43.2	54	19.8	36.3	26	12.6	15.8
	532	772	14.4	41.2	53	18.7	35.0	19	12.0	17.2
	533	797	15.4	43.2	54	19.3	35.6	28	12.3	16.1
	534	774	14.4	41.1	53	18.6	35.0	21	12.5	16.2
	535	818	14.6	43.5	53	17.8	33.6	33	12.5	16.4
	536	797	15.6	43.9	55	19.6	35.5	23	12.2	15.6
	Mean	792	15.0	42.7	54	19.0	35.2	25	12.4	16.2
600	543	831	15.9	44.5	54	19.1	35.7	45	12.1	16.3
	544	800	16.5	45.8	57	20.6	36.0	30	12.9	16.8
	545	840	15.8	44.5	53	18.8	35.5	23	12.6	16.1
	546	----	----	----	----	----	----	----	----	----
	547	756	14.4	40.2	53	19.0	35.8	23	11.9	15.1
	548	746	14.2	40.8	55	19.0	34.8	49	11.6	15.0
	Mean	795	15.4	43.2	54	19.3	35.6	34	12.2	15.9

---- : Not available

Appendix 24 - 2 Individual hematological findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	WBC ($10^2/\mu L$)	Differential leukocyte counts (%)							Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	507	44	0	1	0	12	86	1	0	122
	508	33	0	1	0	7	91	1	0	129
	509	53	0	2	0	10	88	0	0	140
	510	38	0	0	0	5	92	3	0	123
	511	29	0	2	0	6	90	2	0	122
	512	44	0	0	0	15	80	5	0	111
	Mean	40	0	1	0	9	88	2	0	125
40	519	53	0	0	0	8	90	2	0	90
	520	----	----	----	----	----	----	----	----	----
	521	38	0	0	0	14	86	0	0	132
	522	35	0	0	0	13	83	4	0	138
	523	47	0	0	1	5	94	0	0	121
	524	49	0	0	0	10	90	0	0	153
	Mean	44	0	0	0	10	89	1	0	127
200	531	50	0	0	0	8	91	1	0	119
	532	37	0	0	0	15	83	2	0	163
	533	29	0	1	0	6	91	2	0	146
	534	32	0	0	0	17	82	1	0	131
	535	51	0	2	0	14	84	0	0	138
	536	33	0	2	0	14	82	2	0	126
	Mean	39	0	1	0	12	86	1	0	137
600	543	31	0	0	0	11	88	1	0	162
	544	31	0	1	0	13	86	0	0	147
	545	24	0	2	0	14	82	2	0	105
	546	----	----	----	----	----	----	----	----	----
	547	59	0	0	0	14	85	1	0	120
	548	42	0	0	0	11	89	0	0	121
	Mean	37	0	1	0	13	86	1	0	131

---- : Not available

Appendix 25 - 1 Individual blood biochemical findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	001	548	121	26	1108	1.06	137	4.97	3.07	1.62	108	20
	002	406	113	27	1190	1.03	83	4.80	3.12	1.86	73	33
	003	575	137	25	1165	1.42	72	4.88	3.26	2.01	80	29
	004	534	134	24	836	1.04	97	4.79	3.09	1.82	80	35
	005	365	114	26	753	0.99	103	5.00	3.09	1.62	74	24
	006	695	140	23	916	0.98	74	5.11	3.15	1.61	63	32
	Mean	521	127	25	995	1.09	94	4.93	3.13	1.76	80	29
40	013	791	134	34	1076	1.01	87	5.10	3.12	1.58	84	23
	014	442	127	24	1228	1.29	107	4.73	3.19	2.07	75	24
	015	469	124	32	943	1.16	99	4.43	2.82	1.75	74	19
	016	241	113	24	1146	0.98	84	4.57	3.14	2.20	87	26
	017	285	128	23	885	0.94	93	4.58	2.64	1.36	82	29
	018	543	147	30	1193	1.10	116	4.85	2.99	1.61	92	22
	Mean	462	129	28	1079	1.08	98	4.71	2.98	1.76	82	24
200	025	669	129	33	945	0.70	84	4.44	2.72	1.58	82	24
	026	475	133	31	974	0.71	84	4.90	2.98	1.55	79	27
	027	794	136	32	1143	1.10	83	4.94	3.11	1.70	91	26
	028	429	116	27	1087	0.63	82	4.37	2.75	1.70	73	30
	029	502	132	22	1107	0.85	63	4.75	3.08	1.84	58	21
	030	472	146	25	1191	1.03	99	4.71	3.08	1.89	61	19
	Mean	557	132	28	1075	0.84	83	4.69	2.95	1.71	74	25
600	037	659	139	27	1337	0.91	77	4.87	3.10	1.75	63	27
	038	600	149	35	1324	0.93	97	4.71	2.91	1.62	94	30
	039	428	156	39	1374	1.28	99	4.43	2.85	1.80	78	20
	040	362	109	28	1107	0.84	66	4.86	3.21	1.95	90	15
	041	719	135	27	1008	0.82	101	4.70	2.90	1.61	82	28
	042	449	148	28	1195	0.93	96	4.65	2.95	1.74	70	25
	Mean	536	139	31	1224	0.95	89	4.70	2.99	1.75	80	24

Appendix 25 - 2 Individual blood biochemical findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	PL (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	152	155	17.2	0.49	0.41	9.5	9.1	142	7.55	109
	002	112	137	14.9	0.39	0.39	9.8	9.6	142	6.26	106
	003	120	136	20.5	0.47	0.41	9.6	8.9	143	6.49	109
	004	124	131	15.0	0.44	0.44	10.0	9.5	142	7.87	106
	005	109	148	13.1	0.44	0.40	10.2	9.2	143	6.50	106
	006	106	134	10.5	0.44	0.39	10.2	10.1	144	6.93	106
	Mean	121	140	15.2	0.45	0.41	9.9	9.4	143	6.93	107
40	013	125	148	14.8	0.51	0.39	10.1	8.8	143	7.11	110
	014	113	130	14.1	0.38	0.43	9.5	9.1	142	7.52	108
	015	107	138	13.4	0.38	0.44	9.5	9.0	141	7.23	106
	016	134	139	12.3	0.42	0.38	10.0	9.4	142	7.00	109
	017	116	137	18.0	0.43	0.39	10.1	9.4	142	6.60	107
	018	133	150	20.0	0.44	0.37	9.6	9.0	143	6.96	108
	Mean	121	140	15.4	0.43	0.40	9.8	9.1	142	7.07	108
200	025	124	143	9.9	0.46	0.39	9.7	8.5	142	7.77	107
	026	121	146	14.7	0.44	0.39	10.0	9.1	142	7.18	106
	027	132	147	18.2	0.44	0.42	9.7	8.6	142	7.61	108
	028	118	135	15.2	0.48	0.43	9.7	8.8	142	6.27	106
	029	99	139	15.6	0.44	0.48	10.3	8.6	143	6.66	107
	030	98	154	22.1	0.44	0.44	9.2	8.8	141	7.62	108
	Mean	115	144	16.0	0.45	0.43	9.8	8.7	142	7.19	107
600	037	102	134	16.6	0.47	0.56	10.0	9.3	141	6.98	105
	038	140	147	18.3	0.45	0.42	9.6	9.9	143	6.71	108
	039	116	145	19.7	0.43	0.55	9.6	9.3	142	6.94	109
	040	129	154	8.4	0.43	0.47	10.2	8.9	141	7.42	104
	041	123	130	11.9	0.49	0.49	9.9	8.9	142	6.93	105
	042	117	142	13.9	0.44	0.51	9.9	8.0	143	5.79	105
	Mean	121	142	14.8	0.45	0.50	9.9	9.1	142	6.80	106

Appendix 26 - 1 Individual blood biochemical findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	501	556	133	18	883	0.80	87	5.01	3.24	1.83	60	22
	502	1052	154	22	1086	1.16	98	5.06	3.07	1.54	73	21
	503	687	159	20	1200	1.31	74	5.36	3.59	2.03	49	21
	504	470	116	17	863	0.85	89	5.17	3.34	1.83	87	30
	505	348	122	18	669	0.94	77	4.74	3.12	1.93	77	31
	506	476	125	20	851	0.65	75	4.71	3.11	1.94	68	27
	Mean	598	135	19	925	0.95	83	5.01	3.25	1.85	69	25
40	513	688	134	24	1074	1.00	100	5.04	3.14	1.65	93	24
	514	595	153	24	899	1.42	93	4.98	3.34	2.04	60	22
	515	630	145	23	926	1.45	78	4.87	3.10	1.75	68	28
	516	556	113	17	1163	0.95	76	4.85	3.13	1.82	110	41
	517	575	151	19	967	0.80	75	4.90	3.00	1.58	58	27
	518	632	126	16	1013	0.95	90	4.98	3.19	1.78	53	21
	Mean	613	137	21	1007	1.10	85	4.94	3.15	1.77	74	27
200	525	582	126	20	972	0.77	75	4.89	3.27	2.02	60	20
	526	430	114	23	1026	0.75	95	4.93	3.02	1.58	66	14
	527	583	136	26	1193	0.94	67	4.66	3.10	1.99	76	34
	528	486	107	16	999	0.64	97	4.55	2.81	1.62	74	29
	529	423	107	15	985	0.59	73	4.63	2.83	1.57	65	32
	530	369	121	21	725	0.79	89	4.94	3.12	1.71	90	29
	Mean	479	119	20	983	0.75	83	4.77	3.03	1.75	72	26
600	537	371	130	23	1075	0.67	119	4.69	3.00	1.78	84	35
	538	758	153	30	1171	1.14	68	4.69	3.04	1.84	94	29
	539	483	140	23	1134	1.01	71	4.48	2.94	1.91	71	21
	540	757	189	19	1053	12.70	79	5.58	3.12	1.27	154	67
	541	618	123	21	977	0.61	101	4.78	2.94	1.60	70	22
	542	703	152	22	1243	0.97	91	4.70	3.11	1.96	82	23
	Mean	615	148	23	1109	2.85	88	4.82	3.03	1.73	93	33

Appendix 26 - 2 Individual blood biochemical findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	PL (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	501	95	145	13.6	0.51	0.43	9.7	8.5	143	7.27	108
	502	111	160	23.1	0.48	0.34	9.1	9.7	141	6.54	110
	503	84	146	23.0	0.48	0.38	9.7	7.9	144	6.14	110
	504	129	108	17.3	0.45	0.40	10.2	8.8	142	7.66	108
	505	116	114	14.4	0.42	0.38	10.2	9.7	140	7.79	104
	506	110	139	19.4	0.41	0.37	9.8	9.3	141	7.69	108
	Mean	108	135	18.5	0.46	0.38	9.8	9.0	142	7.18	108
40	513	136	148	13.7	0.53	0.39	9.7	9.7	142	7.94	109
	514	99	140	16.9	0.47	0.40	9.6	9.1	142	7.57	107
	515	110	141	18.4	0.46	0.39	9.4	8.9	142	6.71	109
	516	160	134	13.1	0.43	0.39	10.0	9.4	143	7.29	108
	517	96	131	18.4	0.49	0.33	9.5	8.4	144	7.12	110
	518	91	142	19.1	0.45	0.42	9.9	9.2	141	7.09	107
	Mean	115	139	16.6	0.47	0.39	9.7	9.1	142	7.29	108
200	525	99	142	13.9	0.45	0.45	10.0	9.5	141	7.22	106
	526	101	141	15.3	0.42	0.40	9.7	9.6	143	6.92	109
	527	118	123	11.1	0.46	0.43	10.2	9.5	141	7.34	105
	528	117	135	15.8	0.40	0.39	10.0	9.5	142	7.26	107
	529	108	122	14.5	0.40	0.40	10.2	9.8	142	7.15	106
	530	129	135	17.1	0.42	0.39	10.0	9.3	142	7.53	107
	Mean	112	133	14.6	0.43	0.41	10.0	9.5	142	7.24	107
600	537	131	139	16.7	0.49	0.45	9.6	9.2	142	6.65	107
	538	134	119	13.2	0.41	0.45	10.3	9.4	142	6.93	105
	539	102	134	19.0	0.45	0.46	9.4	9.6	142	7.51	108
	540	203	150	48.8	0.69	0.76	10.1	8.8	142	6.24	101
	541	110	141	16.2	0.46	0.40	9.9	10.1	144	7.05	106
	542	116	133	15.8	0.40	0.48	9.6	8.9	141	7.65	107
	Mean	133	136	21.6	0.48	0.50	9.8	9.3	142	7.01	106

Appendix 27 - 1 Individual blood biochemical findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	007	265	70	33	401	1.11	43	6.45	3.42	1.13	58	33
	008	322	81	34	463	0.82	43	6.30	3.37	1.15	78	98
	009	388	75	41	479	0.96	60	6.35	3.17	1.00	68	50
	010	836	99	54	597	0.49	31	6.28	3.32	1.12	52	50
	011	244	73	43	463	0.78	34	6.28	3.13	0.99	74	82
	012	239	82	40	550	1.06	60	6.05	3.26	1.17	62	60
	Mean	382	80	41	492	0.87	45	6.29	3.28	1.09	65	62
40	019	302	75	39	510	0.98	40	6.11	3.23	1.12	58	41
	020	285	84	39	484	0.83	40	5.83	3.36	1.36	69	118
	021	252	69	34	681	1.18	36	6.14	3.21	1.10	85	49
	022	1510	92	42	516	0.98	42	6.40	3.30	1.06	101	138
	023	261	66	36	376	0.76	46	6.68	3.48	1.09	61	91
	024	331	74	37	364	0.81	39	6.27	3.23	1.06	88	81
	Mean	490	77	38	489	0.92	41	6.24	3.30	1.13	77	86
200	031	228	80	37	702	0.61	43	6.27	3.16	1.02	70	93
	032	434	87	42	463	0.74	67	5.96	2.97	0.99	76	104
	033	245	86	49	552	0.65	41	6.07	3.10	1.04	74	91
	034	214	65	38	559	0.83	69	6.24	3.19	1.05	84	52
	035	247	79	41	475	0.62	44	6.13	3.26	1.14	67	80
	036	220	79	41	586	0.79	64	6.17	2.88	0.88	88	114
	Mean	265	79	41	556	0.71	55	6.14	3.09	1.02	77	89
600	043	403	103	48	560	0.61	36	5.93	3.08	1.08	73	96
	044	(448)	(138)	(44)	(1765)	(6.31)	(86)	(5.35)	(2.87)	(1.16)	(89)	(29)
	045	418	87	41	829	1.53	49	6.07	3.10	1.04	77	43
	046	----	----	----	----	----	----	----	----	----	----	----
	047	239	86	38	568	0.84	47	5.99	3.01	1.01	84	55
	048	179	71	35	550	0.69	41	6.29	3.29	1.10	74	62
	Mean	310	87	41	627	0.92	43	6.07	3.12	1.06	77	64

( ) : Not included in statistics because of a case killed in extremis
---- : Not available

Appendix 27 - 2 Individual blood biochemical findings of male rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	PL (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	007	87	159	14.2	0.59	0.38	10.2	7.5	146	4.98	102
	008	126	156	13.7	0.56	0.32	9.6	7.2	144	5.04	102
	009	108	157	17.8	0.64	0.34	9.5	7.3	144	5.10	104
	010	90	139	13.1	0.55	0.36	10.1	7.2	144	5.40	105
	011	109	141	16.6	0.53	0.34	9.9	7.7	144	5.04	102
	012	101	164	12.3	0.54	0.34	10.3	7.5	144	4.89	101
	Mean	104	153	14.6	0.57	0.35	9.9	7.4	144	5.08	103
40	019	94	154	14.5	0.58	0.35	9.5	7.3	144	4.97	104
	020	116	154	15.9	0.64	0.31	9.4	7.8	144	4.92	102
	021	114	164	18.7	0.58	0.34	9.9	6.6	146	5.31	102
	022	155	159	14.3	0.59	0.30	10.3	7.4	145	5.62	103
	023	115	182	17.0	0.60	0.26	10.4	7.3	145	5.02	104
	024	133	150	15.3	0.57	0.32	10.3	7.6	146	5.24	105
	Mean	121	161	16.0	0.59	0.31	10.0	7.3	145	5.18	103
200	031	123	189	18.5	0.70	0.31	10.2	9.0	144	4.66	100
	032	129	143	14.0	0.54	0.37	10.0	6.9	143	5.25	102
	033	125	151	15.3	0.54	0.36	10.2	7.4	146	4.89	103
	034	122	183	16.3	0.65	0.34	10.1	6.9	144	4.74	104
	035	112	141	13.2	0.54	0.33	10.4	7.4	144	4.78	102
	036	135	140	12.2	0.56	0.34	10.0	7.3	144	4.98	103
	Mean	124	158	14.9	0.59	0.34	10.2	7.5	144	4.88	102
600	043	128	136	14.7	0.59	0.40	9.9	7.5	144	5.04	104
	044	(142)	(167)	(52.1)	(0.56)	(0.37)	(9.5)	(7.4)	----	----	----
	045	106	131	21.3	0.64	0.33	9.8	7.1	146	5.21	103
	046	----	----	----	----	----	----	----	----	----	----
	047	119	162	17.1	0.55	0.36	10.1	8.2	147	4.73	100
	048	114	184	18.2	0.63	0.34	10.3	8.0	146	4.66	100
	Mean	117	153	17.8	0.60	0.36	10.0	7.7	146	4.91	102

( ) : Not included in statistics because of a case killed in extremis
---- : Not available

Appendix 28 - 1 Individual blood biochemical findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	LDH (IU/L)	GOT (IU/L)	GPT (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)	T.G. (mg/dL)
0	507	211	73	33	406	1.36	515	6.39	3.63	1.32	88	13
	508	241	68	32	190	1.12	259	6.38	3.60	1.29	82	32
	509	587	72	26	379	1.33	535	6.97	3.73	1.15	108	40
	510	354	75	32	325	1.70	455	5.83	3.23	1.24	101	31
	511	274	74	24	482	1.92	315	6.14	3.54	1.36	64	17
	512	298	110	73	517	2.01	394	6.60	3.58	1.19	91	16
	Mean	328	79	37	383	1.57	412	6.39	3.55	1.26	89	25
40	519	412	95	29	416	4.38	83	5.62	3.28	1.40	77	10
	520	----	----	----	----	----	----	----	----	----	----	----
	521	358	66	27	322	0.87	538	6.13	3.44	1.28	95	21
	522	331	75	35	408	1.56	489	6.45	3.81	1.44	71	28
	523	234	70	35	206	2.34	245	6.03	3.22	1.15	115	22
	524	341	60	22	204	2.25	518	6.58	3.68	1.27	90	18
	Mean	335	73	30	311	2.28	375	6.16	3.49	1.31	90	20
200	531	322	64	29	197	3.07	301	6.52	3.69	1.30	101	24
	532	591	76	28	339	0.90	556	6.84	3.71	1.19	112	22
	533	586	69	22	351	1.54	349	6.32	3.54	1.27	115	45
	534	385	67	32	457	0.85	532	6.69	3.97	1.46	85	22
	535	329	67	25	324	1.13	498	6.63	3.83	1.37	79	7
	536	249	90	42	286	1.61	501	6.91	3.95	1.33	94	19
	Mean	410	72	30	326	1.52	456	6.65	3.78	1.32	98	23
600	543	401	73	24	291	1.74	465	6.43	3.62	1.29	92	22
	544	282	75	25	358	1.52	498	6.48	3.50	1.17	110	20
	545	270	66	27	360	1.49	244	6.52	3.76	1.36	87	23
	546	----	----	----	----	----	----	----	----	----	----	----
	547	265	68	27	265	1.27	538	6.04	3.30	1.20	102	31
	548	284	67	22	312	1.01	375	6.32	3.62	1.34	86	14
	Mean	300	70	25	317	1.41	424	6.36	3.56	1.27	95	22

---- : Not available

Appendix 28 - 2 Individual blood biochemical findings of female rats treated orally with 4,4'-isopropylidene bis (2,6-dibromophenol) during 18 days from 4 days of age to weaning

< 85 days of age >

Dose (mg/kg)	Animal number	PL (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	507	142	137	15.2	0.65	0.32	10.5	7.6	146	4.41	106
	508	140	146	11.5	0.55	0.30	10.1	6.5	145	4.37	105
	509	166	126	14.5	0.66	0.33	10.4	6.8	145	4.90	103
	510	163	133	12.3	0.55	0.32	10.3	7.4	144	4.53	106
	511	117	127	13.7	0.63	0.31	9.5	6.8	144	4.53	105
	512	151	117	13.4	0.57	0.27	10.1	7.3	143	4.44	104
	Mean	147	131	13.4	0.60	0.31	10.2	7.1	145	4.53	105
40	519	111	124	11.4	0.55	0.37	9.8	7.0	145	4.43	104
	520	----	----	----	----	----	----	----	----	----	----
	521	151	133	13.3	0.59	0.33	10.1	6.9	144	5.03	104
	522	130	142	13.0	0.65	0.37	10.4	7.3	144	4.41	103
	523	168	110	12.8	0.58	0.32	9.9	6.9	144	5.01	105
	524	141	145	14.1	0.61	0.28	10.3	6.4	144	4.74	105
	Mean	140	131	12.9	0.60	0.33	10.1	6.9	144	4.72	104
200	531	156	146	12.7	0.58	0.29	10.2	6.4	144	4.85	105
	532	164	119	16.8	0.63	0.30	10.1	6.3	144	4.93	105
	533	173	143	13.4	0.57	0.37	9.8	6.7	144	4.97	102
	534	152	138	12.0	0.55	0.33	10.4	6.8	143	4.85	102
	535	127	133	16.0	0.64	0.32	9.6	6.7	146	4.85	107
	536	160	119	20.3	0.63	0.32	10.7	7.4	146	4.57	104
	Mean	155	133	15.2	0.60	0.32	10.1	6.7	145	4.84	104
600	543	154	131	14.2	0.67	0.36	10.0	7.6	146	4.45	106
	544	149	127	18.0	0.66	0.33	10.0	6.8	148	4.50	106
	545	138	140	12.8	0.60	0.29	9.8	5.7	146	4.95	109
	546	----	----	----	----	----	----	----	----	----	----
	547	164	131	16.3	0.61	0.27	10.1	7.3	142	4.54	103
	548	141	140	12.1	0.57	0.29	10.5	7.0	145	4.58	105
	Mean	149	134	14.7	0.62	0.31	10.1	6.9	145	4.60	106

---- : Not available

Appendix 29-1 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
0	001	NAD	a Heart	: Degeneration, myocardial, focal +
			Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
				Dilatation, renal pelvis, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++
	002	NAD	a Lung	: Metaplasia, osseous +
			Liver	: Hematopoiesis, extramedullary +
			Spleen	: Hematopoiesis, extramedullary ++
	003	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++
	004	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	005	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary, unilateral +
				Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	006	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Pancreas	: Proliferation, ductule, focal +
			Spleen	: Hematopoiesis, extramedullary ++

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

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

Appendix 29-2 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
40	013	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
	014	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: NAD
	015	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary, unilateral +
				Basophilic tubules, unilateral +
	016	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
	017	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary, unilateral +
				Basophilic tubules +
				Cellular infiltration, lymphocyte, cortex, unilateral +
	018	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +

NAD : No abnormalities detected; + : Slight

Appendix 29-3 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
200	025	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary +
	026	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary, unilateral +
				Basophilic tubules +
				Dilatation, renal pelvis, unilateral +
	027	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary +
				Basophilic tubules +
				Degeneration, collecting tubular epithelium +
	028	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, multiple, unilateral +
				Basophilic tubules +
	029	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, multiple, unilateral +
				Basophilic tubules +
	030	NAD	Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary, unilateral +
				Basophilic tubules +
				Degeneration/hyperplasia, collecting tubular epithelium, unilateral +

NAD : No abnormalities detected; + : Slight

Appendix 29-4-1 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined	Findings
600	037	Kidney : Enlargement ++	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, multiple +++
				Cast, hyaline +
				Atrophy, cortical +
				Basophilic tubules +
				Degeneration/hyperplasia, collecting tubular epithelium +
			Spleen	: Hematopoiesis, extramedullary ++
	038	Kidney : Enlargement ++	a Liver	: Hematopoiesis, extramedullary +
				Hypertrophy, hepatocyte, centrilobular +
			Kidney	: Cyst, multiple +++
				Atrophy, cortical +
				Basophilic tubules +
				Degeneration/hyperplasia, collecting tubular epithelium, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++
	039	Kidney : Enlargement ++	a Liver	: Hematopoiesis, extramedullary +
				Hypertrophy, hepatocyte, centrilobular +
			Kidney	: Cyst, multiple +++
				Cast, hyaline, unilateral +
				Atrophy, cortical +
				Basophilic tubules ++
				Degeneration/hyperplasia, collecting tubular epithelium, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++

NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis, prostate and seminal vesicle were examined microscopically.

Appendix 29-4-2 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined		Findings
600 (Continued)	040	Kidney : Enlargement ++	a	Liver	: Hematopoiesis, extramedullary +
					Hypertrophy, hepatocyte, centrilobular +
				Kidney	: Cyst, multiple +++
					Atrophy, cortical +
					Basophilic tubules ++
					Degeneration/hyperplasia, collecting tubular epithelium, unilateral +
				Spleen	: Hematopoiesis, extramedullary ++
	041	Cecum : Dilatation +	a	Liver	: Hematopoiesis, extramedullary +
		Kidney : Enlargement +++		Cecum	: NAD
				Kidney	: Cyst, multiple +++
					Atrophy, cortical ++
					Basophilic tubules +
					Degeneration/hyperplasia, collecting tubular epithelium, unilateral +
				Parathyroid	: Not in section
				Spleen	: Hematopoiesis, extramedullary ++
	042	Cecum : Dilatation +	a	Liver	: Hematopoiesis, extramedullary +
		Kidney : Enlargement +++		Cecum	: NAD
				Kidney	: Cyst, multiple +++
					Atrophy, cortical +
					Basophilic tubules +
					Degeneration/hyperplasia, collecting tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary ++

NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis, prostate and seminal vesicle were examined microscopically.

Appendix 30-1-1 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology		
			Organs examined		Findings
0	501	NAD	a Liver	:	Hematopoiesis, extramedullary +
			Kidney	:	Basophilic tubules +
			Spleen	:	Hematopoiesis, extramedullary +
	502	NAD	a Lung	:	Accumulation, foam cell +
			Liver	:	Hematopoiesis, extramedullary +
			Kidney	:	Basophilic tubules, uninlateral +
			Spleen	:	Hematopoiesis, extramedullary +
	503	NAD	a Liver	:	Hematopoiesis, extramedullary +
			Pancreas	:	Atrophy, acinar cell, focal +
			Kidney	:	Basophilic tubules +
			Parathyroid	:	Not in section
			Spleen		Hematopoiesis, extramedullary +
	504	NAD	a Lung	:	Accumulation, foam cell +
			Liver	:	Hematopoiesis, extramedullary +
			Kidney	:	Basophilic tubules -
			Spleen	:	Hematopoiesis, extramedullary ++
	505	NAD	a Liver	:	Hematopoiesis, extramedullary +
			Kidney	:	Cyst, solitary, unilateral +
					Basophilic tubules, uninlateral +
			Spleen	:	Hematopoiesis, extramedullary ++

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

a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 30-1-2 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
0 (Continued)	506	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary +

NAD : No abnormalities detected; + : Slight

a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 30-2 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
40	513	NAD	Kidney	: Basophilic tubules, uninlateral +
	514	NAD	Kidney	: Cyst, solitary, unilateral + Fibrosis, unilateral +
	515	NAD	Kidney	: Cyst, solitary, unilateral + Basophilic tubules + Degeneration, vacuolar, proximal tubular epithelium +
	516	NAD	Kidney	: Basophilic tubules +
	517	NAD	Kidney	: Cyst, solitary + Basophilic tubules, uninlateral +
	518	NAD	Kidney	: Basophilic tubules, uninlateral +

NAD : No abnormalities detected; + : Slight

Appendix 30-3 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
200	525	NAD	Kidney	: Basophilic tubules, uninlateral + Hyperplasia, pelvic epithelium, unilateral +
	526	NAD	Kidney	: Cyst, solitary, unilateral + Basophilic tubules +
	527	NAD	Kidney	: Cyst, solitary, unilateral + Basophilic tubules +
	528	NAD	Kidney	: NAD
	529	NAD	Kidney	: Basophilic tubules, uninlateral +
	530	NAD	Kidney	: Basophilic tubules +

NAD : No abnormalities detected; + : Slight

Appendix 30-4-1 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined		Findings
600	537	Kidney : Enlargement +++	a	Liver	: Hematopoiesis, extramedullary +
				Kidney	: Cyst, multiple +++
					Atrophy, cortical +
					Basophilic tubules +
					Degeneration/hyperplasia, collecting tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
	538	Cecum : Dilatation +	a	Liver	: Hematopoiesis, extramedullary +
		Kidney : Enlargement ++		Kidney	: Cyst, multiple, unilateral +++
					Atrophy, cortical +
					Basophilic tubules ++
					Degeneration/hyperplasia, collecting tubular epithelium +
				Cecum	: NAD
				Parathyroid	: Not in section
				Spleen	: Hematopoiesis, extramedullary +
	539	Cecum : Dilatation +	a	Liver	: Hematopoiesis, extramedullary +
		Kidney : Enlargement ++		Cecum	: NAD
				Kidney	: Cyst, multiple +++
					Cast, hyaline, unilateral +
					Atrophy, cortical +
					Basophilic tubules +
				Spleen	: Hematopoiesis, extramedullary +

NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe

a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 30-4-2 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 22 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined	Findings
600 (Continued)	540	Kidney : Enlargement +++ Red/dark red /grayish white spots/areas ++	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, multiple +++
				Atrophy, cortical ++
				Degeneration/hyperplasia, collecting tubular epithelium ++
				Inflammation, suppurative +++
			Spleen	: Hematopoiesis, extramedullary ++
	541	Cecum : Dilatation + Kidney : Enlargement +++	a Liver	: Hematopoiesis, extramedullary +
			Cecum	: NAD
			Kidney	: Cyst, multiple +++
				Cast, hyaline, unilateral +
				Atrophy, cortical +
				Basophilic tubules +
				Degeneration/hyperplasia, collecting tubular epithelium +
			Spleen	: Hematopoiesis, extramedullary +
	542	Cecum : Dilatation + Kidney : Enlargement ++	a Liver	: Hematopoiesis, extramedullary +
			Cecum	: NAD
			Kidney	: Cyst, multiple +++
				Cast, hyaline +
				Atrophy, cortical +
				Basophilic tubules, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++

NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 31-1-1 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined	Findings
0	007	NAD	a Kidney	: Hyaline droplet, proximal tubular epithelium +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	008	NAD	a Lung	: Mineralization, artery +
			Kidney	: Eosinophilic body, proximal tubular epithelium ++
				Hyaline droplet, proximal tubular epithelium +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	009	NAD	a Lung	: Mineralization, artery +
			Kidney	: Basophilic tubules, unilateral +
				Hyaline droplet, proximal tubular epithelium +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	010	NAD	a Liver	: Microgranuloma +
			Kidney	: Eosinophilic body, proximal tubular epithelium +
				Hyaline droplet, proximal tubular epithelium +
			Prostate	: Cellular infiltration, lymphocyte, interstitium +
			Parathyroid	: Not in section
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +

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

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

Appendix 31-1-2 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined	Findings
0 (Continued)	011	NAD	a Liver	: Microgranuloma +
			Kidney	: Basophilic tubules, unilateral +
				Eosinophilic body, proximal tubular epithelium +
				Hyaline droplet, proximal tubular epithelium +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	012	Lung : Black spot +	a Heart	: Myocardial degeneration/fibrosis +
			Lung	: Hemorrhage/inflammation, focal +
			Liver	: Microgranuloma +
			Kidney	: Hyaline droplet, proximal tubular epithelium +
			Prostate	: Cellular infiltration, lymphocyte, interstitium +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +

NAD : No abnormalities detected; + : Slight

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

Appendix 31-2 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
40	019	NAD	Kidney	: Hyaline droplet, proximal tubular epithelium +
	020	NAD	Kidney	: Eosinophilic body, proximal tubular epithelium + Hyaline droplet, proximal tubular epithelium + Cellular infiltration, lymphocyte, cortex, unilateral +
	021	NAD	Kidney	: Basophilic tubules, unilateral + Hyaline droplet, proximal tubular epithelium +
	022	NAD	Kidney	: Basophilic tubules, unilateral + Hyaline droplet, proximal tubular epithelium +
	023	NAD	Kidney	: Basophilic tubules, unilateral + Hyaline droplet, proximal tubular epithelium +
	024	NAD	Kidney	: Hyaline droplet, proximal tubular epithelium + Dilatation, renal pelvis, unilateral +

NAD : No abnormalities detected; + : Slight

Appendix 31-3 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
200	031	NAD	Kidney	: Basophilic tubules + Hyaline droplet, proximal tubular epithelium + Cellular infiltration, lymphocyte, cortex, unilateral +
	032	NAD	Kidney	: Cyst, multiple + Eosinophilic body, proximal tubular epithelium + Hyaline droplet, proximal tubular epithelium +
	033	NAD	Kidney	: Basophilic tubules + Hyaline droplet, proximal tubular epithelium +
	034	NAD	Kidney	: Hyaline droplet, proximal tubular epithelium +
	035	NAD	Kidney	: Hyaline droplet, proximal tubular epithelium +
	036	NAD	Kidney	: Basophilic tubules, unilateral + Hyaline droplet, proximal tubular epithelium +

NAD : No abnormalities detected; + : Slight

Appendix 31-4-1 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings		Histology Organs examined		Findings
600	043	Kidney	: Hydronephrosis + a	Liver	:	Microgranuloma +
			Recessed area +	Kidney	:	Cyst, multiple ++
						Cast, hyaline +
						Basophilic tubules ++
						Eosinophilic body, proximal tubular epithelium +
						Hyaline droplet, proximal tubular epithelium +
						Cellular infiltration, lymphocyte, cortex, unilateral +
						Fibrosis ++
				Spleen	:	Hematopoiesis, extramedullary +
						Deposit, brown pigment +
	044	KE Kidney	: Enlargement +++ a	Stomach	:	Erosion, glandular stomach +
			Dark red spots ++	Kidney	:	Cyst, multiple +++
						Cast, hyaline +++
						Cast, granular +
						Atrophy, cortical ++
						Basophilic tubules ++
						Degeneration/hyperplasia, collecting tubular epithelium ++
						Necrosis, tubular epithelium ++
				Prostate	:	Cellular infiltration, lymphocyte, interstitium +
				Thymus	:	Atrophy, cortical +
				Spleen	:	Hematopoiesis, extramedullary ++
						Deposit, brown pigment +

KE : Killed in extremis; NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis, prostate and seminal vesicle were examined microscopically.

Appendix 31-4-2 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings		Histology Organs examined		Findings
600 (Continued)	045	Kidney	: Recessed area ++	a Lung	:	Mineralization, artery +
				Kidney	:	Cyst, multiple +++
						Cast, hyaline, unilateral ++
						Cast, granular +
						Atrophy, cortical +
						Hyaline droplet, proximal tubular epithelium +
						Cellular infiltration, lymphocyte, cortex ++
						Degeneration/hyperplasia, collecting tubular epithelium +
						Fibrosis +++
				Spleen	:	Hematopoiesis, extramedullary +
						Deposit, brown pigment +
	046	FD Kidney	: Enlargement +++	a Lung	:	Metaplasia, osseous +
			Dark red spots	Liver	:	Necrosis, focal ++
			/area ++	Kidney	:	Cyst, multiple +++
						Cast, hyaline ++
						Cast, granular +
						Atrophy, cortical +++
						Basophilic tubules +++
						Hyaline droplet, proximal tubular epithelium +
						Degeneration/hyperplasia, collecting tubular epithelium +
						Necrosis, tubular epithelium ++
				Parathyroid	:	Not in section
				Thymus	:	Atrophy, cortical +
				Spleen	:	Hematopoiesis, extramedullary ++
						Atrophy, white pulp +

FD : Found dead; NAD : No abnormalities detected; + : Slight; ++ : Moderate; +-+ : Severe
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis, prostate and seminal vesicle were examined microscopically.

Appendix 31-4-3 Individual pathological findings of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology Organs examined		Findings
600 (Continued)	047	Kidney : Recessed area +	a	Heart	: Myocardial degeneration/fibrosis +
				Lung	: Mineralization, artery +
				Kidney	: Cyst, multiple ++
					Cast, hyaline, unilateral ++
					Basophilic tubules ++
					Hyaline droplet, proximal tubular epithelium +
					Cellular infiltration, lymphocyte, cortex ++
					Degeneration/hyperplasia, collecting tubular epithelium +
					Fibrosis ++
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	048	NAD	a	Pancreas	: Cellular infiltration, lymphocyte, focal +
				Kidney	: Cyst, multiple, unilateral ++
					Basophilic tubules +
					Hyaline droplet, proximal tubular epithelium +
					Cellular infiltration, lymphocyte, cortex +
					Dilatation, renal pelvis, unilateral +
					Fibrosis, unilateral +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +

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

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

Appendix 32-1 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
0	507	NAD	a Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	508	NAD	a Lung	: Mineralization, artery +
			Pancreas	: Cellular infiltration, neutrophil, focal +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	509	NAD	a Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	510	NAD	a Kidney	: Cyst, solitary, unilateral + Cellular infiltration, lymphocyte, cortex, unilateral +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	511	NAD	a Liver	: Microgranuloma +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	512	NAD	a Lung	: Mineralization, artery +
			Kidney	: Mineralization, cortico-medullary junction +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +

NAD : No abnormalities detected; + : Slight

a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 32-2 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
40	519	NAD	Kidney	: NAD
	520	NAD	Kidney	: Basophilic tubules, unilateral +
	521	NAD	Kidney	: Cyst, solitary, unilateral + Basophilic tubules, unilateral +
	522	NAD	Kidney	: NAD
	523	NAD	Kidney	: NAD
	524	NAD	Kidney	: NAD

NAD : No abnormalities detected; + : Slight

Appendix 32-3 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
200	531	NAD	Kidney	: Cyst, solitary, unilateral +
	532	NAD	Kidney	: Cyst, solitary, unilateral +
	533	NAD	Kidney	: NAD
	534	NAD	Kidney	: Cyst, multiple + Basophilic tubules, unilateral +
	535	NAD	Kidney	: NAD
	536	NAD	Kidney	: NAD

NAD : No abnormalities detected; + : Slight

Appendix 32-4-1 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings	Histology	
			Organs examined	Findings
600	543	Kidney : Recessed area +	a Lung	: Mineralization, artery +
			Kidney	: Cyst, multiple, unilateral +
				Cast, hyaline, unilateral +
				Basophilic tubules +
				Cellular infiltration, lymphocyte, cortex +
			Thymus	: Hemorrhage +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	544	Kidney : Recessed area +	a Lung	: Mineralization, artery +
			Kidney	: Cyst, multiple ++
				Cast, hyaline ++
				Fibrosis ++
				Tubular necrosis, granular, unilateral +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +

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

a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 32-4-2 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings		Histology Organs examined		Findings
600 (Continued)	545	Kidney	: Recessed area + Deformity, right +	a Kidney	:	Cyst, multiple ++ Cast, hyaline + Basophilic tubules + Degeneration/hyperplasia, collecting tubular epithelium + Deposit, brown pigment + Fibrosis ++ Mineralization, cortex +
				Parathyroid	:	Not in section
				Spleen	:	Hematopoiesis, extramedullary + Deposit, brown pigment +
	546	FD Kidney	: Enlargement +++ Dark red spots/ area ++	a Lung	:	Congestive edema ++
				Kidney	:	Cyst, multiple +++ Cast, hyaline ++ Cast, granular ++ Atrophy, cortical ++ Degeneration/hyperplasia, collecting tubular epithelium ++ Necrosis, tubular ++
				Ovary	:	Atrophy ++
				Uterus	:	Atrophy ++
				Spleen	:	Hematopoiesis, extramedullary ++ Atrophy, white pulp +

FD : Found dead; NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 32-4-3 Individual pathological findings of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
< 85 days of age>

Dose (mg/kg)	Animal Number	Necropsy Findings		Histology Organs examined		Findings
600 (Continued)	547	Kidney	: Recessed area ++ Deformity +	a Lung	:	Metaplasia, osseous +
				Liver	:	Micrograniuloma +
				Kidney	:	Cyst, multiple ++
						Cast, hyaline ++
						Basophilic tubules ++
						Cellular infiltration, lymphocyte, cortex ++
						Degeneration/hyperplasia, collecting tubular epithelium +
						Deposit, brown pigment +
						Fibrosis ++
				Spleen	:	Hematopoiesis, extramedullary +
						Deposit, brown pigment +
	548	Kidney	: Recessed area +	a Lung	:	Mineralization, artery +
				Pancreas	:	Cellular infiltration, lymphocyte, focal +
				Kidney	:	Cyst, multiple ++
						Basophilic tubules +
						Cellular infiltration, lymphocyte, cortex ++
						Fibrosis +
				Spleen	:	Hematopoiesis, extramedullary +
						Deposit, brown pigment +

NAD : No abnormalities detected; + : Slight; ++ : Moderate
a: Organs of brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, liver, pancreas, spleen, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus were examined microscopically.

Appendix 33 Individual absolute organ weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (mg)	Heart (mg)	Lung (mg)	Thymus (mg)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Testis (mg)	Prost.† (mg)	Epidid. (mg)
0	001	51.0	1.52	1.55	0.65	189	299	433	211	9.2	2.9	23.9	307	99.6	58.6
	002	50.7	1.58	1.71	0.63	188	286	420	209	7.5	3.2	25.5	338	98.3	56.1
	003	46.0	1.50	1.52	0.60	188	254	390	269	9.5	2.9	24.4	267	77.2	49.7
	004	53.6	1.48	1.78	0.65	214	286	399	248	9.6	3.0	26.3	293	81.4	52.4
	005	54.2	1.52	1.81	0.71	163	315	393	250	9.1	3.2	24.5	264	107.7	53.8
	006	52.9	1.42	1.64	0.66	178	263	444	192	9.6	2.9	28.2	270	91.4	49.7
	Mean	51.4	1.50	1.67	0.65	187	284	413	230	9.1	3.0	25.5	290	92.6	53.4
40	013	49.0	1.51	1.68	0.62	185	328	409	217	8.6	3.0	24.2	314	61.8	54.6
	014	51.9	1.53	1.64	0.65	197	293	433	227	9.7	3.1	24.0	316	96.5	57.0
	015	50.9	1.53	1.65	0.64	205	290	416	251	10.9	3.3	25.0	316	93.4	60.7
	016	51.5	1.59	1.63	0.68	228	304	443	260	9.4	2.9	25.7	322	99.4	62.9
	017	58.8	1.59	1.99	0.72	234	290	480	290	10.0	3.5	29.9	315	84.9	59.7
	018	51.0	1.51	1.64	0.68	168	287	398	235	9.6	3.0	25.3	285	80.2	52.4
	Mean	52.2	1.54	1.71	0.67	203	299	430	247	9.7	3.1	25.7	311	86.0	57.9
200	025	53.8	1.59	1.82	0.65	210	305	457	244	9.1	3.3	26.4	313	109.6	63.5
	026	49.7	1.44	1.70	0.60	165	296	433	216	10.4	3.4	24.3	290	81.7	46.6
	027	47.3	1.54	1.66	0.60	168	266	416	211	9.3	2.9	20.4	316	81.2	60.2
	028	53.2	1.59	1.72	0.63	209	276	452	252	9.2	3.5	27.9	310	95.3	56.1
	029	54.3	1.60	1.81	0.65	171	286	407	238	9.2	3.0	18.7	303	71.8	57.1
	030	51.7	1.54	1.72	0.64	174	287	433	254	9.5	3.0	26.4	322	71.9	54.9
	Mean	51.7	1.55	1.74	0.63	183	286	433	236	9.5	3.2	24.0	309	85.3	56.4
600	037	49.8	1.61	1.71	1.39	139	314	430	179	7.1	3.0	20.7	274	47.5	42.5
	038	47.6	1.45	1.64	1.81	160	280	387	187	8.2	2.8	20.4	275	94.6	52.7
	039	49.0	1.54	1.71	1.77	183	280	426	174	7.2	3.1	20.7	310	87.3	52.7
	040	51.4	1.49	1.91	1.30	172	312	404	210	8.2	2.9	17.5	314	99.1	57.8
	041	52.5	1.53	1.94	2.36	180	303	442	248	9.3	2.9	24.0	306	77.5	49.5
	042	53.7	1.55	2.05	2.25	239	332	402	217	6.9	2.9	27.0	290	88.8	48.6
	Mean	50.7	1.53	1.83	1.81	179	304	415	203	7.8	2.9	21.7	295	82.5	50.6

† : Total weights of the prostate and seminal vesicle

Appendix 34 Individual absolute organ weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (mg)	Heart (mg)	Lung (mg)	Thymus (mg)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Ovary (mg)	Uterus (mg)
0	501	47.8	1.49	1.65	0.64	118	301	410	214	9.3	3.1	24.6	13.9	38.9
	502	41.9	1.43	1.39	0.59	131	265	373	161	10.9	3.0	22.4	13.1	41.9
	503	43.8	1.50	1.43	0.54	91	266	365	170	8.7	2.5	20.0	9.1	40.2
	504	48.8	1.54	1.45	0.63	166	286	397	280	8.6	2.9	26.6	14.8	44.3
	505	52.7	1.51	1.54	0.74	233	265	452	257	9.4	3.0	26.5	14.9	49.4
	506	50.5	1.56	1.67	0.67	149	276	422	293	9.1	3.0	21.9	14.8	42.5
	Mean	47.6	1.51	1.52	0.64	148	277	403	229	9.3	2.9	23.7	13.4	42.9
40	513	49.1	1.48	1.59	0.65	160	273	455	212	10.7	3.0	24.5	15.2	40.9
	514	47.8	1.41	1.56	0.62	130	299	386	237	9.1	2.6	19.4	20.5	35.3
	515	45.0	1.44	1.48	0.61	107	244	397	196	8.2	3.1	24.9	19.8	45.4
	516	50.3	1.48	1.66	0.66	169	289	473	301	10.0	3.3	23.1	14.4	52.7
	517	47.1	1.47	1.49	0.60	159	260	378	274	9.7	3.3	18.7	10.6	39.2
	518	50.9	1.53	1.63	0.73	125	273	437	205	9.0	2.7	24.0	16.1	35.7
	Mean	48.4	1.47	1.57	0.65	142	273	421	238	9.5	3.0	22.4	16.1	41.5
200	525	48.4	1.55	1.59	0.65	174	313	438	246	10.4	3.3	19.1	17.9	34.7
	526	46.4	1.40	1.60	0.72	114	293	388	202	9.6	2.8	21.6	16.9	48.0
	527	45.7	1.49	1.46	0.58	190	270	451	254	7.7	3.2	19.2	8.1	39.8
	528	48.1	1.42	1.55	0.64	147	263	417	241	7.9	3.0	22.3	17.7	52.0
	529	52.6	1.48	1.81	0.70	193	295	439	305	9.2	3.1	26.2	16.1	36.0
	530	48.2	1.50	1.61	0.66	171	241	393	226	8.0	3.1	22.8	11.7	50.8
	Mean	48.2	1.47	1.60	0.66	165	279	421	246	8.8	3.1	21.9	14.7	43.6
600	537	50.6	1.43	1.74	1.97	167	283	399	196	8.2	3.0	28.1	12.0	49.7
	538	46.0	1.45	1.51	1.08	134	276	375	260	8.9	2.8	16.0	16.8	45.0
	539	48.4	1.41	1.54	1.53	132	256	390	190	9.7	3.0	20.1	14.7	44.1
	540	41.2	1.39	1.60	5.72	111	313	325	139	8.1	2.6	21.5	7.5	49.7
	541	52.4	1.45	1.89	1.94	140	329	427	199	8.8	2.9	25.1	13.8	43.0
	542	51.4	1.54	1.68	1.11	187	291	442	226	8.9	3.2	21.7	18.3	38.0
	Mean	48.3	1.45	1.66	2.23	145	291	393	202	8.8	2.9	22.1	13.9	44.9

Appendix 35 Individual relative organ weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (%)	Liver (%)	Kidney (%)	Spleen (mg%)	Heart (mg%)	Lung (mg%)	Thymus (mg%)	Thyr. (mg%)	Pitui. (mg%)	Adrenal (mg%)	Testis (mg%)	Prost. (mg%)	Epidid. (mg%)
0	001	51.0	2.98	3.04	1.27	371	586	849	414	18.0	5.7	46.9	602	195.3	114.9
	002	50.7	3.12	3.37	1.24	371	564	828	412	14.8	6.3	50.3	667	193.9	110.7
	003	46.0	3.26	3.30	1.30	409	552	848	585	20.7	6.3	53.0	580	167.8	108.0
	004	53.6	2.76	3.32	1.21	399	534	744	463	17.9	5.6	49.1	547	151.9	97.8
	005	54.2	2.80	3.34	1.31	301	581	725	461	16.8	5.9	45.2	487	198.7	99.3
	006	52.9	2.68	3.10	1.25	336	497	839	363	18.1	5.5	53.3	510	172.8	94.0
	Mean	51.4	2.93	3.25	1.26	365	552	806	450	17.7	5.9	49.6	566	180.1	104.1
40	013	49.0	3.08	3.43	1.27	378	669	835	443	17.6	6.1	49.4	641	126.1	111.4
	014	51.9	2.95	3.16	1.25	380	565	834	437	18.7	6.0	46.2	609	185.9	109.8
	015	50.9	3.01	3.24	1.26	403	570	817	493	21.4	6.5	49.1	621	183.5	119.3
	016	51.5	3.09	3.17	1.32	443	590	860	505	18.3	5.6	49.9	625	193.0	122.1
	017	58.8	2.70	3.38	1.22	398	493	816	493	17.0	6.0	50.9	536	144.4	101.5
	018	51.0	2.96	3.22	1.33	329	563	780	461	18.8	5.9	49.6	559	157.3	102.7
	Mean	52.2	2.97	3.27	1.28	389	575	824	472	18.6	6.0	49.2	599	165.0	111.1
200	025	53.8	2.96	3.38	1.21	390	567	849	454	16.9	6.1	49.1	582	203.7	118.0
	026	49.7	2.90	3.42	1.21	332	596	871	435	20.9	6.8	48.9	584	164.4	93.8
	027	47.3	3.26	3.51	1.27	355	562	879	446	19.7	6.1	43.1	668	171.7	127.3
	028	53.2	2.99	3.23	1.18	393	519	850	474	17.3	6.6	52.4	583	179.1	105.5
	029	54.3	2.95	3.33	1.20	315	527	750	438	16.9	5.5	34.4	558	132.2	105.2
	030	51.7	2.98	3.33	1.24	337	555	838	491	18.4	5.8	51.1	623	139.1	106.2
	Mean	51.7	3.01	3.37	1.22	354	554	840	456	18.4	6.2	46.5	600	165.0	109.3
600	037	49.8	3.23	3.43	2.79	279	631	863	359	14.3	6.0	41.6	550	95.4	85.3
	038	47.6	3.05	3.45	3.80	336	588	813	393	17.2	5.9	42.9	578	198.7	110.7
	039	49.0	3.14	3.49	3.61	373	571	869	355	14.7	6.3	42.2	633	178.2	107.6
	040	51.4	2.90	3.72	2.53	335	607	786	409	16.0	5.6	34.0	611	192.8	112.5
	041	52.5	2.91	3.70	4.50	343	577	842	472	17.7	5.5	45.7	583	147.6	94.3
	042	53.7	2.89	3.82	4.19	445	618	749	404	12.8	5.4	50.3	540	165.4	90.5
	Mean	50.7	3.02	3.60	3.57	352	599	820	399	15.5	5.8	42.8	583	163.0	100.2

† : Total weights of the prostate and seminal vesicle

Appendix 36 Individual relative organ weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<22 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (%)	Liver (%)	Kidney (%)	Spleen (mg%)	Heart (mg%)	Lung (mg%)	Thymus (mg%)	Thyr. (mg%)	Pitui. (mg%)	Adrenal (mg%)	Ovary (mg%)	Uterus (mg%)
0	501	47.8	3.12	3.45	1.34	247	630	858	448	19.5	6.5	51.5	29.1	81.4
	502	41.9	3.41	3.32	1.41	313	632	890	384	26.0	7.2	53.5	31.3	100.0
	503	43.8	3.42	3.26	1.23	208	607	833	388	19.9	5.7	45.7	20.8	91.8
	504	48.8	3.16	2.97	1.29	340	586	814	574	17.6	5.9	54.5	30.3	90.8
	505	52.7	2.87	2.92	1.40	442	503	858	488	17.8	5.7	50.3	28.3	93.7
	506	50.5	3.09	3.31	1.33	295	547	836	580	18.0	5.9	43.4	29.3	84.2
	Mean	47.6	3.18	3.21	1.33	308	584	848	477	19.8	6.2	49.8	28.2	90.3
40	513	49.1	3.01	3.24	1.32	326	556	927	432	21.8	6.1	49.9	31.0	83.3
	514	47.8	2.95	3.26	1.30	272	626	808	496	19.0	5.4	40.6	42.9	73.8
	515	45.0	3.20	3.29	1.36	238	542	882	436	18.2	6.9	55.3	44.0	100.9
	516	50.3	2.94	3.30	1.31	336	575	940	598	19.9	6.6	45.9	28.6	104.8
	517	47.1	3.12	3.16	1.27	338	552	803	582	20.6	7.0	39.7	22.5	83.2
	518	50.9	3.01	3.20	1.43	246	536	859	403	17.7	5.3	47.2	31.6	70.1
	Mean	48.4	3.04	3.24	1.33	293	565	870	491	19.5	6.2	46.4	33.4	86.0
200	525	48.4	3.20	3.29	1.34	360	647	905	508	21.5	6.8	39.5	37.0	71.7
	526	46.4	3.02	3.45	1.55	246	631	836	435	20.7	6.0	46.6	36.4	103.4
	527	45.7	3.26	3.19	1.27	416	591	987	556	16.8	7.0	42.0	17.7	87.1
	528	48.1	2.95	3.22	1.33	306	547	867	501	16.4	6.2	46.4	36.8	108.1
	529	52.6	2.81	3.44	1.33	367	561	835	580	17.5	5.9	49.8	30.6	68.4
	530	48.2	3.11	3.34	1.37	355	500	815	469	16.6	6.4	47.3	24.3	105.4
	Mean	48.2	3.06	3.32	1.37	342	580	874	508	18.3	6.4	45.3	30.5	90.7
600	537	50.6	2.83	3.44	3.89	330	559	789	387	16.2	5.9	55.5	23.7	98.2
	538	46.0	3.15	3.28	2.35	291	600	815	565	19.3	6.1	34.8	36.5	97.8
	539	48.4	2.91	3.18	3.16	273	529	806	393	20.0	6.2	41.5	30.4	91.1
	540	41.2	3.37	3.88	13.88	269	760	789	337	19.7	6.3	52.2	18.2	120.6
	541	52.4	2.77	3.61	3.70	267	628	815	380	16.8	5.5	47.9	26.3	82.1
	542	51.4	3.00	3.27	2.16	364	566	860	440	17.3	6.2	42.2	35.6	73.9
	Mean	48.3	3.01	3.44	4.86	299	607	812	417	18.2	6.0	45.7	28.5	94.0

Appendix 37 Individual absolute organ weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Testis (g)	Prost. (g)	Semi.v (g)	Epidid. (g)
0	007	444	2.04	11.89	2.89	0.74	1.63	1.50	0.55	34.3	14.4	69.9	3.26	0.61	2.14	1.11
	008	458	2.02	15.04	3.38	0.92	1.52	1.45	0.70	36.2	14.3	74.5	3.27	0.76	1.80	1.22
	009	395	2.01	10.73	2.82	0.85	1.17	1.34	0.35	27.6	12.5	73.8	3.43	0.65	1.94	1.18
	010	419	2.06	11.92	3.13	0.70	1.33	1.34	0.46	33.0	12.5	63.7	3.30	0.61	1.98	1.25
	011	441	2.01	14.57	3.54	0.91	1.38	1.62	0.42	33.7	15.6	66.7	3.37	0.85	1.93	1.27
	012	462	2.15	11.30	3.20	0.84	1.41	1.48	0.62	37.6	14.7	73.8	3.54	0.71	2.06	1.22
	Mean	437	2.05	12.58	3.16	0.83	1.41	1.46	0.52	33.7	14.0	70.4	3.36	0.70	1.98	1.21
40	019	418	1.94	11.72	2.94	0.78	1.27	1.41	0.38	25.6	14.7	60.5	3.81	0.74	1.95	1.26
	020	426	1.98	12.67	2.73	0.73	1.30	1.37	0.39	29.1	12.5	45.8	2.97	0.59	1.79	1.13
	021	434	2.12	13.09	3.30	0.74	1.39	1.44	0.55	38.6	14.7	75.9	4.03	0.85	1.98	1.34
	022	419	2.09	13.01	2.86	0.78	1.33	1.20	0.49	36.4	12.2	59.0	3.00	0.48	0.96	1.12
	023	483	2.10	16.38	3.12	1.02	1.48	1.42	0.57	38.3	13.1	75.2	3.56	0.47	1.82	1.31
	024	490	2.13	14.20	3.30	0.93	1.48	1.58	0.51	32.2	15.5	64.1	3.26	0.38	1.76	1.38
	Mean	445	2.06	13.51	3.04	0.83	1.38	1.40	0.48	33.4	13.8	63.4	3.44	0.59	1.71	1.26
200	031	482	2.25	15.12	3.20	0.89	1.57	1.59	0.45	39.2	15.9	84.7	3.38	0.65	1.78	1.22
	032	430	2.19	13.06	3.31	0.93	1.45	1.41	0.53	32.2	13.2	67.6	3.20	0.61	1.91	1.24
	033	447	2.19	12.45	3.03	0.74	1.35	1.44	0.46	37.4	15.4	63.3	3.83	0.60	1.60	1.18
	034	437	2.01	13.24	2.89	0.91	1.34	1.40	0.47	37.0	15.7	76.0	3.75	0.68	1.92	1.34
	035	517	2.20	14.09	3.34	0.96	1.59	1.65	0.58	35.6	13.5	96.0	4.29	0.34	2.29	1.49
	036	515	2.16	15.50	3.39	0.90	1.56	1.71	0.62	32.6	15.9	58.9	3.77	0.81	2.12	1.36
	Mean	471	2.17	13.91	3.19	0.89	1.48	1.53	0.52	35.7	14.9	74.4	3.70	0.62	1.94	1.31
600	043	415	2.12	11.85	3.25	0.87	1.47	1.39	0.53	30.4	12.2	53.0	3.45	0.52	1.89	1.27
	044	(51)	(1.56)	(1.84)	(4.59)	(0.20)	(0.55)	(0.49)	(0.03)	(7.2)	(2.0)	(20.4)	(0.40)	(0.09)†	†	(0.03)
	045	435	2.05	12.01	4.98	1.00	1.54	1.60	0.61	30.6	13.2	62.7	3.59	0.65	1.96	1.11
	046	(38)	(1.54)	(1.73)	(4.57)	(0.19)	(0.46)	(0.42)	(0.03)	(6.0)	(2.4)	(23.9)	(0.36)	(0.09)†	†	(0.03)
	047	499	2.21	15.23	4.80	0.91	1.60	1.63	0.38	34.4	16.9	63.0	3.42	0.84	1.69	1.22
	048	487	2.14	15.57	3.68	0.91	1.50	1.62	0.47	33.9	15.7	93.1	3.58	0.71	1.84	1.33
	Mean	459	2.13	13.67	4.18	0.92	1.53	1.56	0.50	32.3	14.5	68.0	3.51	0.68	1.85	1.23

( ) : Not included in statistics because of a case killed in extremis or found dead; † : Total weights of the prostate and seminal vesicle

Appendix 38 Individual absolute organ weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (g)	Liver (g)	Kidney (g)	Spleen (g)	Heart (g)	Lung (g)	Thymus (g)	Thyr. (mg)	Pitui. (mg)	Adrenal (mg)	Ovary (mg)	Uterus (g)
0	507	253	1.92	6.10	1.84	0.39	0.89	1.02	0.35	25.7	12.3	65.4	63.2	0.44
	508	256	1.91	6.25	1.86	0.49	0.87	0.99	0.55	29.7	15.1	74.0	73.2	1.03
	509	277	2.00	7.78	2.19	0.57	0.97	1.28	0.53	24.0	18.2	79.8	100.7	0.54
	510	246	1.96	7.06	1.92	0.65	0.88	1.09	0.39	21.9	18.9	76.4	79.8	0.52
	511	228	1.76	6.69	1.70	0.48	0.90	1.12	0.37	22.2	13.5	74.3	117.8	0.45
	512	249	1.91	6.81	2.11	0.47	0.86	1.10	0.40	21.9	19.7	87.0	70.3	0.55
	Mean	252	1.91	6.78	1.94	0.51	0.90	1.10	0.43	24.2	16.3	76.2	84.2	0.59
40	519	245	1.98	4.65	2.12	0.56	1.03	1.05	0.37	27.4	9.7	62.7	37.3	0.46
	520	225	1.85	6.36	1.65	0.50	0.84	1.09	0.33	20.8	13.8	58.8	63.1	0.49
	521	250	2.05	7.56	1.99	0.54	0.92	1.00	0.38	21.8	17.7	67.7	87.6	0.53
	522	256	2.03	7.49	2.05	0.51	1.00	1.21	0.45	22.5	16.1	82.9	119.7	0.51
	523	249	2.01	6.30	1.83	0.59	0.80	1.09	0.44	23.9	12.3	73.0	85.4	0.63
	524	249	1.91	6.97	2.03	0.53	0.82	1.01	0.43	26.2	15.1	74.2	71.9	0.56
	Mean	246	1.97	6.56	1.95	0.54	0.90	1.08	0.40	23.8	14.1	77.5	0.5	
200	531	262	1.94	7.20	1.98	0.61	0.78	1.07	0.55	25.4	16.4	63.2	65.9	0.58
	532	251	1.89	7.07	1.88	0.51	0.89	1.06	0.42	22.5	15.1	72.8	81.4	0.44
	533	285	2.10	7.96	2.31	0.61	0.96	1.20	0.53	23.0	19.4	71.9	95.5	0.94
	534	249	2.08	7.14	2.08	0.54	0.87	1.07	0.41	23.0	17.4	88.3	76.5	0.52
	535	254	1.88	6.80	1.98	0.52	0.82	1.15	0.49	34.2	15.2	61.5	94.2	0.37
	536	271	2.07	7.46	2.18	0.49	1.03	1.16	0.36	24.7	15.6	78.9	120.1	0.58
	Mean	262	1.99	7.27	2.07	0.55	0.89	1.12	0.46	25.5	16.5	72.8	88.9	0.57
600	543	285	2.06	7.64	2.04	0.48	0.96	1.17	0.47	23.7	15.8	63.7	87.2	0.58
	544	276	1.91	7.32	2.62	0.77	0.97	1.12	0.57	23.3	14.5	71.1	86.0	0.98
	545	255	1.88	7.03	2.64	0.55	0.88	1.08	0.46	22.1	17.3	63.8	77.8	0.70
	546	(40)	(1.55)	(1.58)	(6.24)	(0.14)	(0.38)	(0.49)	(0.03)	(6.2)	(2.6)	(26.1)	(10.8)	(0.05)
	547	268	1.91	8.63	2.78	0.69	1.12	1.27	0.43	23.1	19.4	72.6	84.6	0.58
	548	265	1.94	7.44	2.31	0.54	0.96	1.22	0.47	24.6	15.4	60.1	87.4	0.59
	Mean	270	1.94	7.61	2.48	0.61	0.98	1.17	0.48	23.4	16.5	66.3	84.6	0.69

( ) : Not included in statistics because of a case found dead

Appendix 39 Individual relative organ weights of male rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (%)	Liver (%)	Kidney (%)	Spleen (%)	Heart (%)	Lung (%)	Thymus (%)	Thyr. (mg%)	Pitui. (mg%)	Adrenal (mg%)	Testis (%)	Prost. (%)	Semi.v (%)	Epidid. (%)
0	007	444	0.46	2.68	0.65	0.17	0.37	0.34	0.12	7.7	3.2	15.7	0.73	0.14	0.48	0.25
	008	458	0.44	3.28	0.74	0.20	0.33	0.32	0.15	7.9	3.1	16.3	0.71	0.17	0.39	0.27
	009	395	0.51	2.72	0.71	0.22	0.30	0.34	0.09	7.0	3.2	18.7	0.87	0.16	0.49	0.30
	010	419	0.49	2.84	0.75	0.17	0.32	0.32	0.11	7.9	3.0	15.2	0.79	0.15	0.47	0.30
	011	441	0.46	3.30	0.80	0.21	0.31	0.37	0.10	7.6	3.5	15.1	0.76	0.19	0.44	0.29
	012	462	0.47	2.45	0.69	0.18	0.31	0.32	0.13	8.1	3.2	16.0	0.77	0.15	0.45	0.26
	Mean	437	0.47	2.88	0.72	0.19	0.32	0.34	0.12	7.7	3.2	16.2	0.77	0.16	0.45	0.28
40	019	418	0.46	2.80	0.70	0.19	0.30	0.34	0.09	6.1	3.5	14.5	0.91	0.18	0.47	0.30
	020	426	0.46	2.97	0.64	0.17	0.31	0.32	0.09	6.8	2.9	10.8	0.70	0.14	0.42	0.27
	021	434	0.49	3.02	0.76	0.17	0.32	0.33	0.13	8.9	3.4	17.5	0.93	0.20	0.46	0.31
	022	419	0.50	3.11	0.68	0.19	0.32	0.29	0.12	8.7	2.9	14.1	0.72	0.11	0.23	0.27
	023	483	0.43	3.39	0.65	0.21	0.31	0.29	0.12	7.9	2.7	15.6	0.74	0.10	0.38	0.27
	024	490	0.43	2.90	0.67	0.19	0.30	0.32	0.10	6.6	3.2	13.1	0.67	0.08	0.36	0.28
	Mean	445	0.46	3.03	0.68	0.19	0.31	0.32	0.11	7.5	3.1	14.3	0.78	0.14	0.39	0.28
200	031	482	0.47	3.14	0.66	0.18	0.33	0.33	0.09	8.1	3.3	17.6	0.70	0.13	0.37	0.25
	032	430	0.51	3.04	0.77	0.22	0.34	0.33	0.12	7.5	3.1	15.7	0.74	0.14	0.44	0.29
	033	447	0.49	2.79	0.68	0.17	0.30	0.32	0.10	8.4	3.4	14.2	0.86	0.13	0.36	0.26
	034	437	0.46	3.03	0.66	0.21	0.31	0.32	0.11	8.5	3.6	17.4	0.86	0.16	0.44	0.31
	035	517	0.43	2.73	0.65	0.19	0.31	0.32	0.11	6.9	2.6	18.6	0.83	0.07	0.44	0.29
	036	515	0.42	3.01	0.66	0.17	0.30	0.33	0.12	6.3	3.1	11.4	0.73	0.16	0.41	0.26
	Mean	471	0.46	2.96	0.68	0.19	0.32	0.33	0.11	7.6	3.2	15.8	0.79	0.13	0.41	0.28
600	043	415	0.51	2.86	0.78	0.21	0.35	0.33	0.13	7.3	2.9	12.8	0.83	0.13	0.46	0.31
	044	(51)	(3.06)	(3.61)	(9.00)	(0.39)	(1.08)	(0.96)	(0.06)	(14.1)	(3.9)	(40.0)	(0.78)	(0.18)†	†	(0.06)
	045	435	0.47	2.76	1.14	0.23	0.35	0.37	0.14	7.0	3.0	14.4	0.83	0.15	0.45	0.26
	046	(38)	(4.05)	(4.55)	(12.03)	(0.50)	(1.21)	(1.11)	(0.08)	(15.8)	(6.3)	(62.9)	(0.95)	(0.24)†	†	(0.08)
	047	499	0.44	3.05	0.96	0.18	0.32	0.33	0.08	6.9	3.4	12.6	0.69	0.17	0.34	0.24
	048	487	0.44	3.20	0.76	0.19	0.31	0.33	0.10	7.0	3.2	19.1	0.74	0.15	0.38	0.27
	Mean	459	0.47	2.97	0.91	0.20	0.33	0.34	0.11	7.1	3.1	14.7	0.77	0.15	0.41	0.27

( ) : Not included in statistics because of a case killed in extremis or found dead; † : Total weights of the prostate and seminal vesicle

Appendix 40 Individual relative organ weights of female rats treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning
<85 days of age>

Dose (mg/kg)	Animal numbers	B.W. (g)	Brain (%)	Liver (%)	Kidney (%)	Spleen (%)	Heart (%)	Lung (%)	Thymus (%)	Thyr. (mg%)	Pitui. (mg%)	Adrenal (mg%)	Ovary (mg%)	Uterus (%)
0	507	253	0.76	2.41	0.73	0.15	0.35	0.40	0.14	10.2	4.9	25.8	25.0	0.17
	508	256	0.75	2.44	0.73	0.19	0.34	0.39	0.21	11.6	5.9	28.9	28.6	0.40
	509	277	0.72	2.81	0.79	0.21	0.35	0.46	0.19	8.7	6.6	28.8	36.4	0.19
	510	246	0.80	2.87	0.78	0.26	0.36	0.44	0.16	8.9	7.7	31.1	32.4	0.21
	511	228	0.77	2.93	0.75	0.21	0.39	0.49	0.16	9.7	5.9	32.6	51.7	0.20
	512	249	0.77	2.73	0.85	0.19	0.35	0.44	0.16	8.8	7.9	34.9	28.2	0.22
	Mean	252	0.76	2.70	0.77	0.20	0.36	0.44	0.17	9.7	6.5	30.4	33.7	0.23
40	519	245	0.81	1.90	0.87	0.23	0.42	0.43	0.15	11.2	4.0	25.6	15.2	0.19
	520	225	0.82	2.83	0.73	0.22	0.37	0.48	0.15	9.2	6.1	26.1	28.0	0.22
	521	250	0.82	3.02	0.80	0.22	0.37	0.40	0.15	8.7	7.1	27.1	35.0	0.21
	522	256	0.79	2.93	0.80	0.20	0.39	0.47	0.18	8.8	6.3	32.4	46.8	0.20
	523	249	0.81	2.53	0.73	0.24	0.32	0.44	0.18	9.6	4.9	29.3	34.3	0.25
	524	249	0.77	2.80	0.82	0.21	0.33	0.41	0.17	10.5	6.1	29.8	28.9	0.22
	Mean	246	0.80	2.67	0.79	0.22	0.37	0.44	0.16	9.7	5.8	28.4	31.4	0.22
200	531	262	0.74	2.75	0.76	0.23	0.30	0.41	0.21	9.7	6.3	24.1	25.2	0.22
	532	251	0.75	2.82	0.75	0.20	0.35	0.42	0.17	9.0	6.0	29.0	32.4	0.18
	533	285	0.74	2.79	0.81	0.21	0.34	0.42	0.19	8.1	6.8	25.2	33.5	0.33
	534	249	0.84	2.87	0.84	0.22	0.35	0.43	0.16	9.2	7.0	35.5	30.7	0.21
	535	254	0.74	2.68	0.78	0.20	0.32	0.45	0.19	13.5	6.0	24.2	37.1	0.15
	536	271	0.76	2.75	0.80	0.18	0.38	0.43	0.13	9.1	5.8	29.1	44.3	0.21
	Mean	262	0.76	2.78	0.79	0.21	0.34	0.43	0.18	9.8	6.3	27.9	33.9	0.22
600	543	285	0.72	2.68	0.72	0.17	0.34	0.41	0.16	8.3	5.5	22.4	30.6	0.20
	544	276	0.69	2.65	0.95	0.28	0.35	0.41	0.21	8.4	5.3	25.8	31.2	0.36
	545	255	0.74	2.76	1.04	0.22	0.35	0.42	0.18	8.7	6.8	25.0	30.5	0.27
	546	(40)	(3.87)	(3.95)	(15.60)	(0.35)	(0.95)	(1.22)	(0.07)	(15.5)	(6.5)	(65.3)	(27.0)	(0.12)
	547	268	0.71	3.22	1.04	0.26	0.42	0.47	0.16	8.6	7.2	27.1	31.6	0.22
	548	265	0.73	2.81	0.87	0.20	0.36	0.46	0.18	9.3	5.8	22.7	33.0	0.22
	Mean	270	0.72	2.82	0.92	0.23	0.36	0.43	0.18	8.7	6.1	24.6	31.4	0.25

( ) : Not included in statistics because of a case found dead

Appendix 41 Individual body weights of foster mother rats that reared pups treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Animal number	Days of age 4	10	16	21	Gain 4-21
601	250	302	311	290	40
602	252	307	328	309	57
603	257	311	319	314	57
604	256	335	337	308	52
605	298	322	348	335	37
606	263	290	300	297	34
607	247	285	297	289	42
608	255	308	333	324	69
609	320	358	368	360	40
610	301	348	365	361	60
611	266	339	339	333	67
612	266	295	301	311	45
Mean	269	317	329	319	50

Appendix 42 Individual food consumption of foster mother rats that reared pups treated orally with 4,4'-isopropylidene bis(2,6-dibromophenol) during 18 days from 4 days of age to weaning

(g)

Animal number	Days of age 7	13	19
601	53	64	76
602	57	73	77
603	50	63	70
604	56	67	65
605	57	69	74
606	51	66	73
607	48	57	72
608	59	69	86
609	75	80	86
610	63	80	80
611	58	71	79
612	49	62	85
Mean	56	68	77

Appendix 43 Historical baseline data of the Crj:CD(SD)IGS strain male rats on the hematological and biochemical parameters

Parameters	22 days of age		85 days of age	
	Mean	Normal range[a)]	Mean	Normal range[a)]
Hematological parameters				
Erythrocyte count ($10^4/\mu L$)	513(69)	443 ~ 583	849(103)	785 ~ 913
Hemoglobin concentration (g/dL)	10.2(69)	8.3 ~ 12.1	15.9(106)	14.6 ~ 17.2
Hematocrit value (%)	32.7(69)	27.7 ~ 37.8	45.3(106)	42.2 ~ 48.4
Mean corpuscular volume (pg)	64(69)	58 ~ 70	53(106)	50 ~ 56
Mean corpuscular hemoglobin (fL)	19.9(69)	17.6 ~ 22.2	18.7(106)	17.5 ~ 19.8
Mean corpuscular hemoglobin concentration (%)	31.2(69)	29.4 ~ 33.0	35.1(106)	33.7 ~ 36.5
Reticulocyte count (‰)	223(69)	171 ~ 274	26(103)	16 ~ 36
Prothrombin time (sec)	13.6(56)	12.6 ~ 14.5	13.0(106)	12.2 ~ 13.9
Activated partialthromboplastin time (sec)	14.7(60)	12.8 ~ 16.5	18.2(106)	15.9 ~ 20.5
Total leukocyte count ($10^2/\mu L$)	24(69)	10 ~ 53*	77(104)	42 ~ 112
Platelet count ($10^4/\mu L$)	157(67)	127 ~ 187	127(106)	104 ~ 150
Biochemical parameters				
Lactate dehydrogenase (IU/L)*	482(53)	241 ~ 965*	345(59)	174 ~ 678*
Glutamic oxaloacetic transaminase (IU/L)	118(53)	91 ~ 144	78(60)	58 ~ 98
Glutamic pyruvic transaminase (IU/L)	32(53)	17 ~ 47	39(59)	23 ~ 54
Alkaline phosphatase (IU/L)*	978(53)	673 ~ 1282	479(60)	226 ~ 731
γ-Glutamyl transpeptidase (IU/L)*	0.85(48)	0.24 ~ 1.46	0.67(60)	0.16 ~ 1.19
Cholinesterase (IU/L)	90(33)	63 ~ 127	47(48)	22 ~ 73
Total protein (g/dL)	4.74(53)	4.18 ~ 5.30	6.32(56)	5.65 ~ 7.00
Albumin (g/dL)	2.96(53)	2.59 ~ 3.32	3.22(60)	2.73 ~ 3.71
A/G ratio	1.67(53)	1.32 ~ 2.02	1.05(60)	0.83 ~ 1.26
Total cholesterol (mg/dL)	82(53)	57 ~ 116*	73(60)	41 ~ 105
Triglyceride (mg/dL)*	40(53)	16 ~ 95*	71(60)	16 ~ 127
Phospholipid(mg/dL)	122(48)	93 ~ 160*	117(59)	69 ~ 164
Glucose (mg/dL)	113(53)	72 ~ 155	143(60)	101 ~ 184
Total bilirubin (mg/dL)	0.40(53)	0.30 ~ 0.49	0.29(58)	0.23 ~ 0.35
Urea nitrogen (mg/dL)*	12.3(53)	1.9 ~ 22.7	15.2(60)	10.3 ~ 20.1
Creatinine (mg/dL)	0.42(53)	0.29 ~ 0.55	0.58(59)	0.47 ~ 0.69
Calcium (mg/dL)	9.8(53)	9.0 ~ 10.6	10.0(53)	9.2 ~ 10.7
Inorganic phosphorus (mg/dL)	9.1(53)	8.0 ~ 10.1	7.1(56)	5.9 ~ 8.4
Sodium (mEq/L)	143(46)	135 ~ 150*	144(60)	138 ~ 149
Potassium (mEq/L)	6.80(52)	5.42 ~ 8.19	4.83(60)	4.10 ~ 5.56
Chloride (mEq/L)	106(49)	101 ~ 112	104(60)	99 ~ 109

a) : (mean−2S.D.) ~ (mean+2S.D.)
( ) : Number of animals
* : Calculated from log-transformed data

Appendix 44 Historical baseline data of the Crj:CD(SD)IGS strain female rats on the hematological and biochemical parameters

Parameters	22 days of age		85 days of age	
	Mean	Normal range[a)]	Mean	Normal range[a)]
Hematological parameters				
Erythrocyte count ($10^4/\mu L$)	532(65)	455 ~ 608	806(102)	760 ~ 852
Hemoglobin concentration (g/dL)	10.6(66)	8.6 ~ 12.7	15.3(104)	14.2 ~ 14.4
Hematocrit value (%)	33.7(66)	28.2 ~ 39.3	43.4(104)	40.8 ~ 46.0
Mean corpuscular volume (pg)	63(66)	57 ~ 69	54(105)	51 ~ 56
Mean corpuscular hemoglobin (fL)	19.9(66)	17.7 ~ 22.1	19.0(106)	17.7 ~ 20.3
Mean corpuscular hemoglobin concentration (%)	31.5(64)	30.2 ~ 32.8	35.3(106)	34.0 ~ 36.6
Reticulocyte count (‰)	207(66)	151 ~ 262	22(104)	12 ~ 33
Prothrombin time (sec)	13.4(54)	12.3 ~ 14.5	13.4(102)	12.2 ~ 14.7
Activated partialthromboplastin time (sec)	14.1(60)	12.0 ~ 16.2	15.7(98)	14.1 ~ 18.0
Total leukocyte count ($10^2/\mu L$)	24(66)	13 ~ 47*	45(104)	19 ~ 72
Platelet count ($10^4/\mu L$)	153(66)	112 ~ 195	131(105)	101 ~ 161
Biochemical parameters				
Lactate dehydrogenase (IU/L)*	471(53)	236 ~ 938*	346(55)	190 ~ 627*
Glutamic oxaloacetic transaminase (IU/L)	118(53)	94 ~ 148*	76(57)	56 ~ 104*
Glutamic pyruvic transaminase (IU/L)	27(53)	15 ~ 46*	33(55)	22 ~ 47*
Alkaline phosphatase (IU/L)*	958(53)	661 ~ 1388*	335(58)	164 ~ 507
γ-Glutamyl transpeptidase (IU/L)*	0.93(48)	0.36 ~ 1.50	1.63(58)	0.63 ~ 2.64
Cholinesterase (IU/L)	89(32)	67 ~ 118	441(58)	148 ~ 734
Total protein (g/dL)	4.87(53)	4.39 ~ 5.36	6.40(58)	5.78 ~ 7.02
Albumin (g/dL)	3.08(53)	2.72 ~ 3.43	3.57(58)	3.15 ~ 3.98
A/G ratio	1.73(53)	1.36 ~ 2.09	1.25(58)	1.00 ~ 1.50
Total cholesterol (mg/dL)	86(53)	47 ~ 125	85(58)	58 ~ 111
Triglyceride (mg/dL)*	38(53)	15 ~ 95*	24(58)	10 ~ 56*
Phospholipid(mg/dL)	120(48)	79 ~ 154	141(58)	108 ~ 173
Glucose (mg/dL)	117(53)	79 ~ 154	134(58)	108 ~ 160
Total bilirubin (mg/dL)	0.38(53)	0.30 ~ 0.46	0.29(58)	0.23 ~ 0.35
Urea nitrogen (mg/dL)*	13.4(53)	4.1 ~ 22.8	15.0(57)	10.5 ~ 20.3
Creatinine (mg/dL)	0.41(52)	0.29 ~ 0.53	0.61(55)	0.52 ~ 0.70
Calcium (mg/dL)	10.0(53)	9.4 ~ 10.6	10.0(58)	9.3 ~ 10.7
Inorganic phosphorus (mg/dL)	9.5(53)	8.4 ~ 10.6	6.7(58)	5.3 ~ 8.1
Sodium (mEq/L)	141(47)	136 ~ 147	144(58)	141 ~ 147
Potassium (mEq/L)	6.98(52)	5.67 ~ 8.29	4.61(58)	4.04 ~ 5.19
Chloride (mEq/L)	106(52)	99 ~ 112	104(58)	101 ~ 107

a) : (mean−2S.D.) ~ (mean+2S.D.)
( ) : Number of animals
* : Calculated from log-transformed data