最 終 報 告 書

4-エチル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：98-097）

財団法人　畜産生物科学安全研究所

陳　述　書

試験の表題

4-エチル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：98-097）

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-エチル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：98-097）

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４月27日
母動物搬入	平成11年５月６日
分　　娩	平成11年５月13日
群 分 け	平成11年５月16日
投与開始	平成11年５月17日
投与終了・離乳	平成11年６月３日
投与終了時解剖	平成11年６月４日
観察終了	平成11年８月５日
観察終了時解剖	平成11年８月６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－エチル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　：　９８－０９７

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05月06日	平成11年05月06日	平成11年05月06日
検　疫 平成11年05月11日	平成11年05月11日	平成11年05月11日
分娩の確認 平成11年05月13日	平成11年05月13日	平成11年05月13日
哺育状態の観察・被験物質調製 平成11年05月14日	平成11年05月14日	平成11年05月14日
群分け・個体識別 平成11年05月16日	平成11年05月16日	平成11年05月16日
体重測定・投与・症状観察 平成11年05月17日	平成11年05月17日	平成11年05月17日
餌測定(給餌量) 平成11年05月19日	平成11年05月19日	平成11年05月19日
餌測定(残餌量)・症状観察・死亡動物の解剖 平成11年05月26日	平成11年05月26日	平成11年05月26日
被験物質調製 平成11年05月31日	平成11年05月31日	平成11年05月31日
感覚，反射機能検査 平成11年06月02日	平成11年06月02日	平成11年06月02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06月04日	平成11年06月04日	平成11年06月04日
病理組織標本作製の外部委託（病理検体の引き渡し）・血液学的検査 平成11年06月09日	平成11年06月09日	平成11年06月09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
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06月30日	平成11年06月30日	平成11年06月30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07月05日	平成11年07月05日	平成11年07月05日
体重測定・餌測定(残餌量) 平成11年07月22日	平成11年07月22日	平成11年07月22日
尿検査 平成11年07月30日	平成11年07月30日	平成11年07月30日
解　剖 平成11年08月06日	平成11年08月06日	平成11年08月06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18日 ～ 同年01月19日	平成12年01月19日	平成12年01月19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

最終報告書

4-エチル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：98-097）

財団法人　畜産生物科学安全研究所

要約

4-エチル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0，30，100 及び300mg/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，300mg/kg群で雌雄に自発運動低下，体温低下，振戦，挙尾，深大呼吸，削痩等の症状及び体重増加の有意な抑制，雌に2匹の死亡が認められた．感覚反射機能検査では，300mg/kg群で雄に面上正向反射の有意な遅延が認められた．器官重量では，明らかな体重増加抑制の認められた300mg/kg群の雄で，脳及び下垂体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．生存動物の血液学検査，血液生化学検査，剖検及び病理組織学検査では，被験物質の投与に起因する変化は認められなかった．

一方，投与後の観察及び観察期間終了時の検査では，器官重量で300mg/kg群の雄に脳の絶対重量の有意な減少が認められた．一般状態，外形分化状態，摂餌量，尿検査，血液学検査，血液生化学検査，剖検及び病理組織学検査では，被験物質の投与に起因する変化は認められず，体重も回復した．

以上の結果から，4-エチル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，中枢神経機能，脳重量，体重及び肝臓に対する影響であった．哺育期の投与により発現した変化のうち，脳重量の変化は観察期間終了後においても残存し，その他の変化は回復した．哺育期の投与によ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，100mg/kg/dayと推定された．

緒言

4-エチルフェノールは，反応性高分子（ポリパラビニルフェノール）や医薬品，農薬，染料等の原料並びに酸化防止剤として広く用いられている化学物質である．4-エチルフェノールの毒性について，類縁化合物の4-メチルフェノールには，中枢神経抑制や肝臓，腎臓，血液等に対する毒性があることが知られている[1]．しかしながら，本物質については，刺激性を有すること[2]並びに急性毒性[3]，変異原性[4, 5]及び生体内動態[6, 7]に関する報告はみられるものの，毒性学的性質の詳細についてほとんど知られていない．

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-エチル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-エチルフェノールは，分子量122.16，融点44.8℃，沸点219℃，水に不溶，アセトン，DMSO，エーテル，食物油に可溶な白色の結晶で，試験には[redacted]から提供されたロット番号81107A，純度98.4%（不純物としてフェノール 0.198%，4-メチルフェノール 0.206%，2-エチルフェノール 0.349%，3-エチルフェノール 0.588%，パライソプロピルフェノール 0.162%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．用いた被験物質を丸善石油化学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（Appendix2）．投与液は，局方オリブ油（宮澤薬品株式会社，ロット番号F107）を溶媒とし，約45℃に加温しながら所定の投与用量になるような濃度に溶解して調製した．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[9]ので週1回調製し，1日の使用量ごとに小分けして冷所（4℃）・遮光下で密栓して保管し，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22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 9.8(8.6－10.9)g，雌 8.9(8.3－9.7)g，その翌日の投与開始日平均体重（体重範囲）は雄 11.9(10.0－13.3)g，雌 10.8(9.7－12.1)gであった．各個体は，ラックおよ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21－24℃，湿度50－63%，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7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〔260w×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99.02.76，99.03.73，99.06.53）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（Appendices6～8），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．すな

わち，1群雌雄各5匹の4日齢ラットに，4-エチルフェノールを0（溶媒として用いた局方オリブ油のみ），100，300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 群では，雌雄の全例が死亡した．300mg/kg群では，雌の2例が死亡した．さらに，300mg/kg群の生存例においても，雌に軽度な体重増加の抑制傾向，雄に肝臓の相対重量増加が認められた．血液学及び血液生化学検査，剖検では，被験物質の投与に起因する変化は認められなかった．以上の結果から，本試験における投与量は，毒性影響が確実に発現すると予測される300mg/kg/dayを高用量，毒性影響が発現しないと予測される30mg/kg/day を低用量とし，これらの用量の間に100mg/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30mg/kg/day 投与群（30mg/kg 群），(3) 同100mg/kg/day投与群（100mg/kg群），(4) 同300mg/kg/ day 投与群（300mg/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，親動物から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）および白血球百分率（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．なお，300mg/kg群の投与期間終了時解剖動物の雌の1匹（No. 547）は採取できた血液量が少なく，血液学検査は実施できなかった．

(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-BM8型クリナライザー，日本電子株式会社）により総タンパク（ビューレット法），アルブミン（BCG法），A/G 比（計算値），血糖（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，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300mg/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．30及び100mg/kg群については，300mg/kg群の検査の結果，被験物質の投与による影響が認められなかったので，実施しなかった．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，300mg/kg群で，雌雄各12匹中親から隔離時の自発運動低下が雄の9匹及び雌の12匹，体温低下が雄の1匹及び雌の5匹，振戦が雄の1匹及び雌の6匹，挙尾が雄の4匹及び雌の7匹，深大呼吸が雄の3匹及び雌の5匹，痩削が雄の1匹及び雌の4匹に認められ，雌雄の自発運動低下並びに雌の体温低下，振戦，挙尾，深大呼吸及び痩削の発現率は，対照群に比べて有意差が認められた．なお，挙尾は対照群の雄の1匹にも認められた．死亡は300mg/kg群で雌の2匹認められ，1匹は13日齢（観察期間終了時解剖用），他の1匹は15日齢（投与期間終了時解剖用）時に死後発見された．

投与終了後の観察期間においては，一般状態の変化及び死亡は，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，100mg/kg群で雌の12匹中1匹，300mg/kg群で雄の12匹中4匹及び雌の11匹中1匹に反射の遅延が認められ，300mg/kg群の雄の発現率は，対照群に比べて統計学的に有意なものであった．

3）外形分化状態（Table 4, Appendices 13, 14）

腹部毛生，切歯萌出，眼瞼開裂，精巣下降及び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）

投与期間中において，300mg/kg群で投与4日（7日齢）以降に体重増加の抑制が認められ，雄の体重は投与期間を通じて，雌の体重は投与13日（16日齢）まで，いずれも対照群の体重を有意に下回り，雄では投与期間中の体重増加量も，対照群を有意に下回った．投与終了後の観察期間においては，300mg/kg群の体重は雌雄とも，28日齢時に対照群を有意に下回ったが，その後観察期間終了時まで対照群の体重と比べて有意差は認められず，観察期間中の体重増加量にも有意差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，各群の摂餌量に，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，被験物質の投与に起因すると考えられる変化は，認められなかった. 30mg/kg群の雄の赤血球数並びに100mg/kg群の雄の赤血球数及びヘマトクリット値は，対照群に比べて有意な高値を示したが，変化に用量相関性が認められず，また背景データにおける正常範囲内の変動であった.

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，各検査項目に有意な変化は認められなかった.

観察期間終了時の検査においては，300mg/kg群で雄にトリグリセライドの有意な増加が認められた.

9) 剖検 (Tables 19－20, Appendices 29－32)

投与期間終了時及び観察期間終了時の解剖動物において，被験物質の投与に起因する変化は認められなかった. 300mg/kg群で雌に認められた2匹の投与期間中死亡動物においては，1匹に肺の暗赤色化，他の1匹に消化管のガスによる膨満が認められた.

なお，被験物質の投与とは無関係と思われる変化として，観察期間終了時解剖動物で対照群の雄の1匹に肺の赤色点，及び300mg/kg群の雌雄各1匹に胸腺の赤色斑が認められた.

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，300mg/kg群で雄に最終体重並びに脳及び下垂体の絶対重量の有意な減少，肝臓の相対重量の有意な増加が認められた.

観察期間終了時の解剖においては，300mg/kg群で雄に脳の絶対重量の有意な減少が認められた.

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

投与期間終了時及び観察期間終了時の解剖動物において，被験物質の投与に起因する変化は，認められなかった．

２匹の死亡動物においては，ガスにより膨満した消化管の認められた１匹には，胸腺皮質の萎縮が認められ，消化管には変化は認められなかった．肺の暗赤色化の認められた他の１匹には，肺のうっ血水腫が認められた．また，生存動物で投与とは無関係に認められた肺の赤色点には出血を伴う炎症巣，赤色斑の認められた胸腺には出血が認められた．以上の変化以外にも，300mg/kg群で投与期間終了時及び観察期間終了時解剖動物の各器官に変化が認められたが，散発的あるいは対照群における発現率や変化の程度と差の認められない変化であった．

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-エチル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，機能およ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，300mg/kg群で雌雄に自発運動低下，体温低下，振戦，挙尾及び深大呼吸等の症状，雄に面上正向反射の遅延が認められ，中枢神経機能に対する影響が伺われた．また，雌雄に体重増加の抑制及び雌に上述の症状を伴った2匹の死亡が認められた．

死亡動物の病理学検査では，1匹に消化管のガスによる膨満及びストレスによる変化と考えられる胸腺の萎縮が，他の1匹には肺のうっ血水腫が認められた．2匹に共通した変化が認められず，死因を特定することは困難であったが，2匹とも中枢神経機能に対する影響が背景にあって，死亡したものと推察される．

血液学及び血液生化学検査並びに剖検では，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，300mg/kg群で雄に脳及び下垂体の絶対重量減少，並びに肝臓の相対重量増加が認められた．

脳の絶対重量減少について，脳は栄養状態の影響を受けにくい器官で，毒性試験に一般的に用いられている5週齢以降のラットでは，経験上，成長抑制に伴う脳重量への影響は殆ど認められない．しかしながら，哺育期のラットの脳は，機能，形態とも著しい成長過程にあり，脳重量の減少は体重重増加の抑制の認められた用量での変化であることから，主に成長抑制に伴い，脳重量にも影響を受けたものと推察される．また，脳に病理組織学的変化が認められなかったことから，上述の中枢神経機能に対する影響とは関連性はないものと考えられる．

肝臓の相対重量増加についても，病理組織学検査を含む他の検査で関連する変化が認められなったが，本被験物質とは類縁の4-メチルフェノールのラットにおける13週間反復投与毒性試験において，肝臓に対する毒性影響が認められている[1]ことから，肝臓に対する軽度な影響を示唆する変化と考えられる．

一方，下垂体の絶対重量減少については，当該群の体重が対照群に比べて有意に少なく；相対重量の変化や病理組織学的変化が認められないことから，体重増加の抑制に伴う変化で，下垂体に対する毒性影響によるものではないと判断される．

なお，4-エチルフェノールは，眼，皮膚，粘膜等に対し刺激性を有することが知られているが，本試験においては投与経路である胃に変化は認められなかった．

投与後のラットの成長，機能及び形態に及ぼす影響については，300mg/kg群で雄に脳の絶対重量減少が認められた．一般状態，外形分化状態，尿検査，血液学及び血液生化

学検査，剖検，病理組織学検査では，被験物質の投与に起因する変化は，認められなかった．

体重に対する影響が回復傾向を示したにもかかわらず，脳重量の変化は63日後においても残存していたことは，哺育期に受けた脳重量に対する影響は非可逆的である可能性を示唆しているものと推察される．

なお，観察期間終了時の血液生化学検査で，300mg/kg群の雄にトリグリセライドの有意な増加が認められたが，背景データにおける正常範囲（Appendix 43を参照）内の変動で，他に関連する変化が認められなかったことから，遅発的な毒性影響を示唆する変化ではなく，偶発的な変化と判断された．

以上の結果から，4-エチルフェノールのラット新生児に対する反復投与毒性は，中枢神経機能，脳重量，体重及び肝臓に対する影響であった．哺育期の投与により発現した変化のうち，脳重量の変化は観察期間終了時においても回復傾向が認めらず，その他の変化はいずれも回復した．哺育期の投与によ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100mg/kg/dayと推定された．

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4-エチル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：98-097）

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

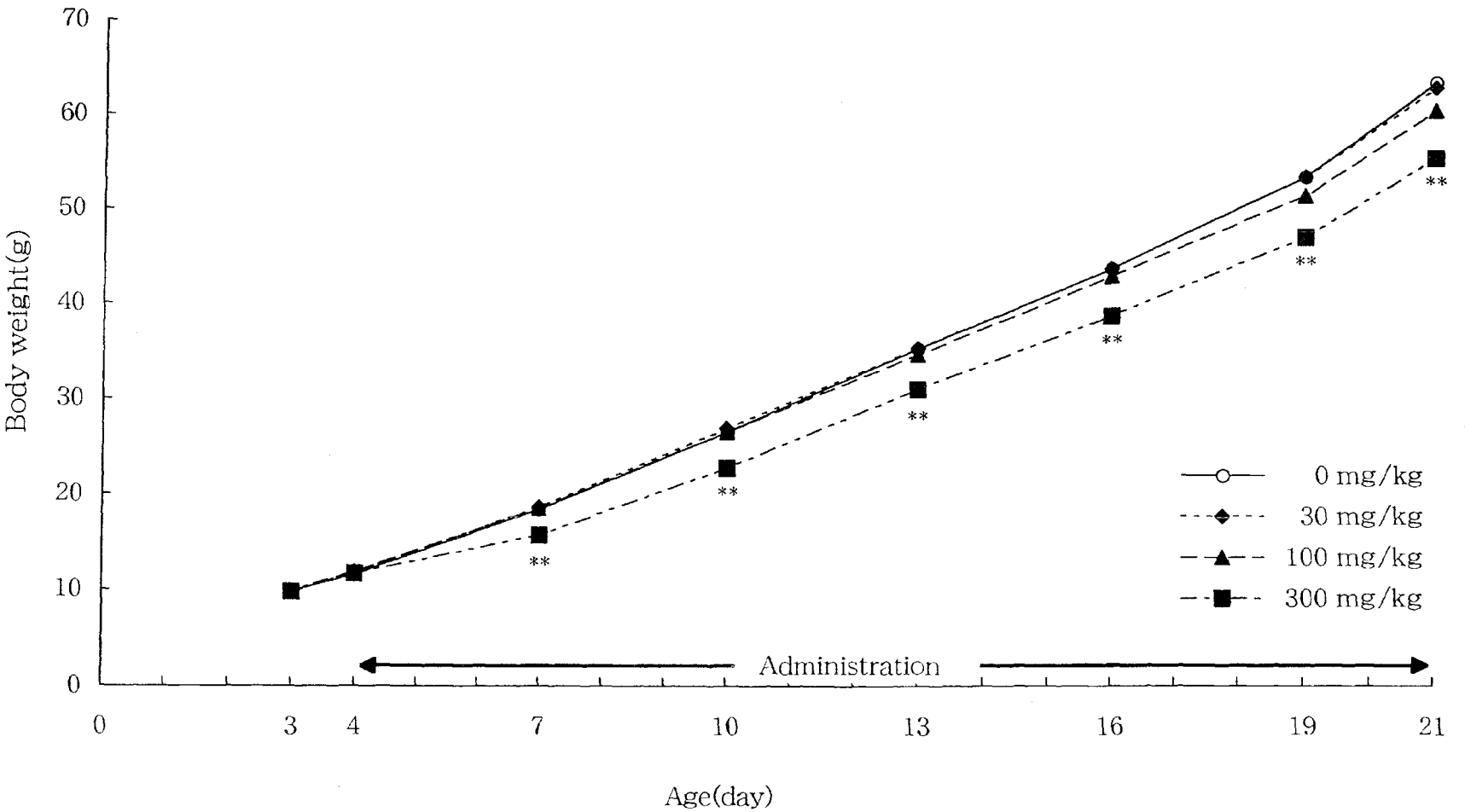


Fig.1-1 Body weight changes of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning
Significantly different from control (** : $p < 0.01$)

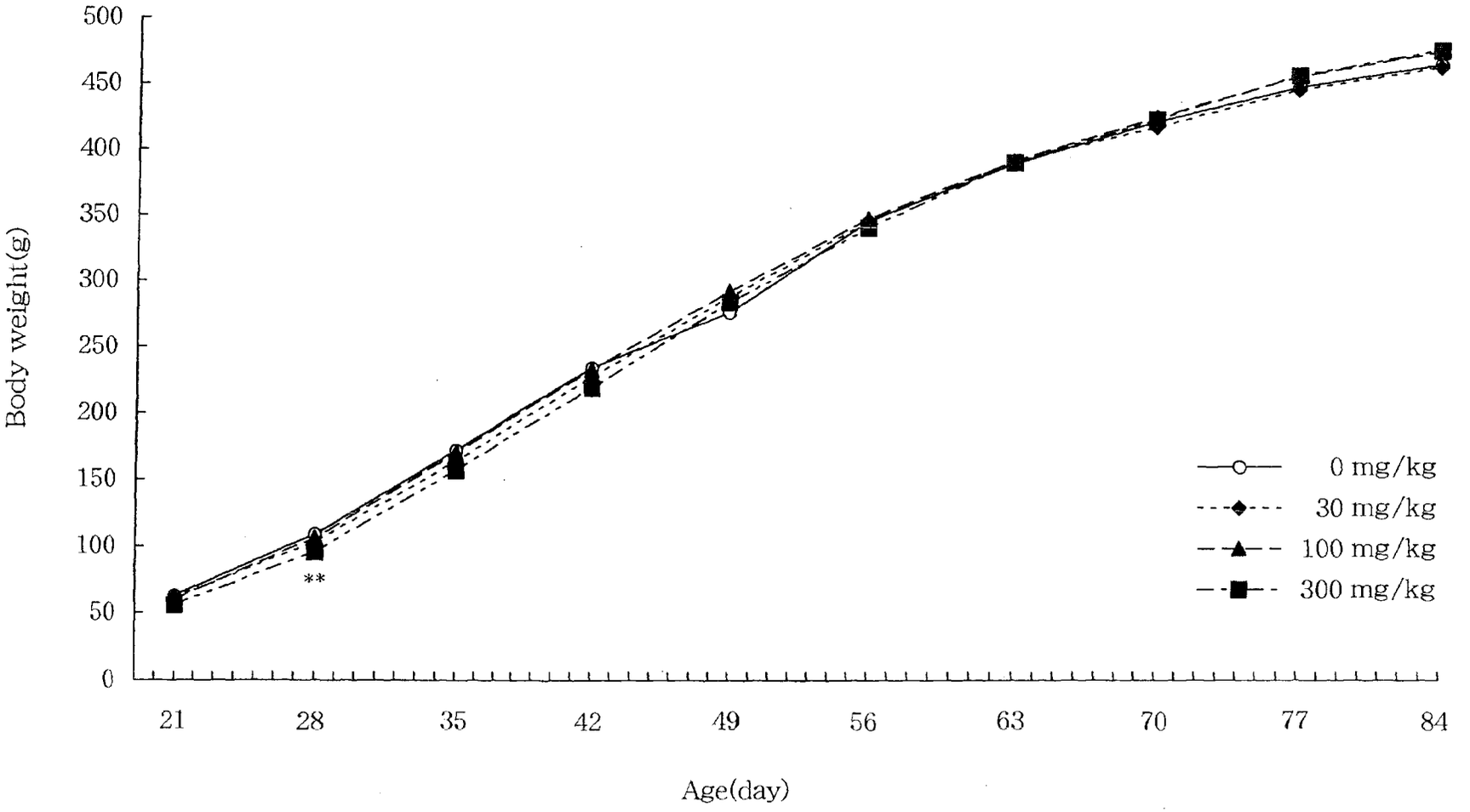


Fig.1-2 Body weight changes of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning
Significantly different from control (** : $p < 0.01$)

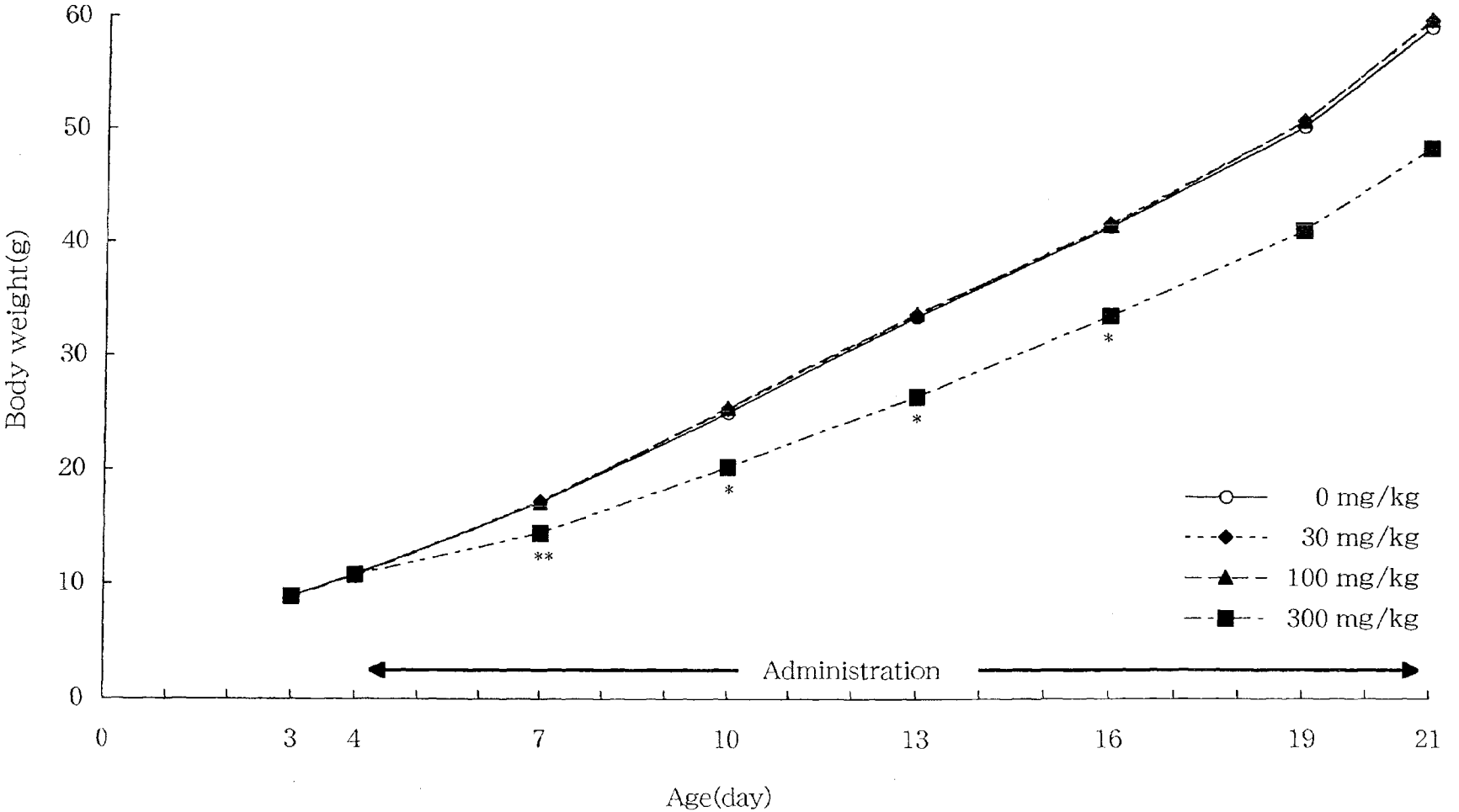


Fig.2-1 Body weight changes of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning
Significantly different from control (* : $p < 0.05$; ** : $p < 0.01$)

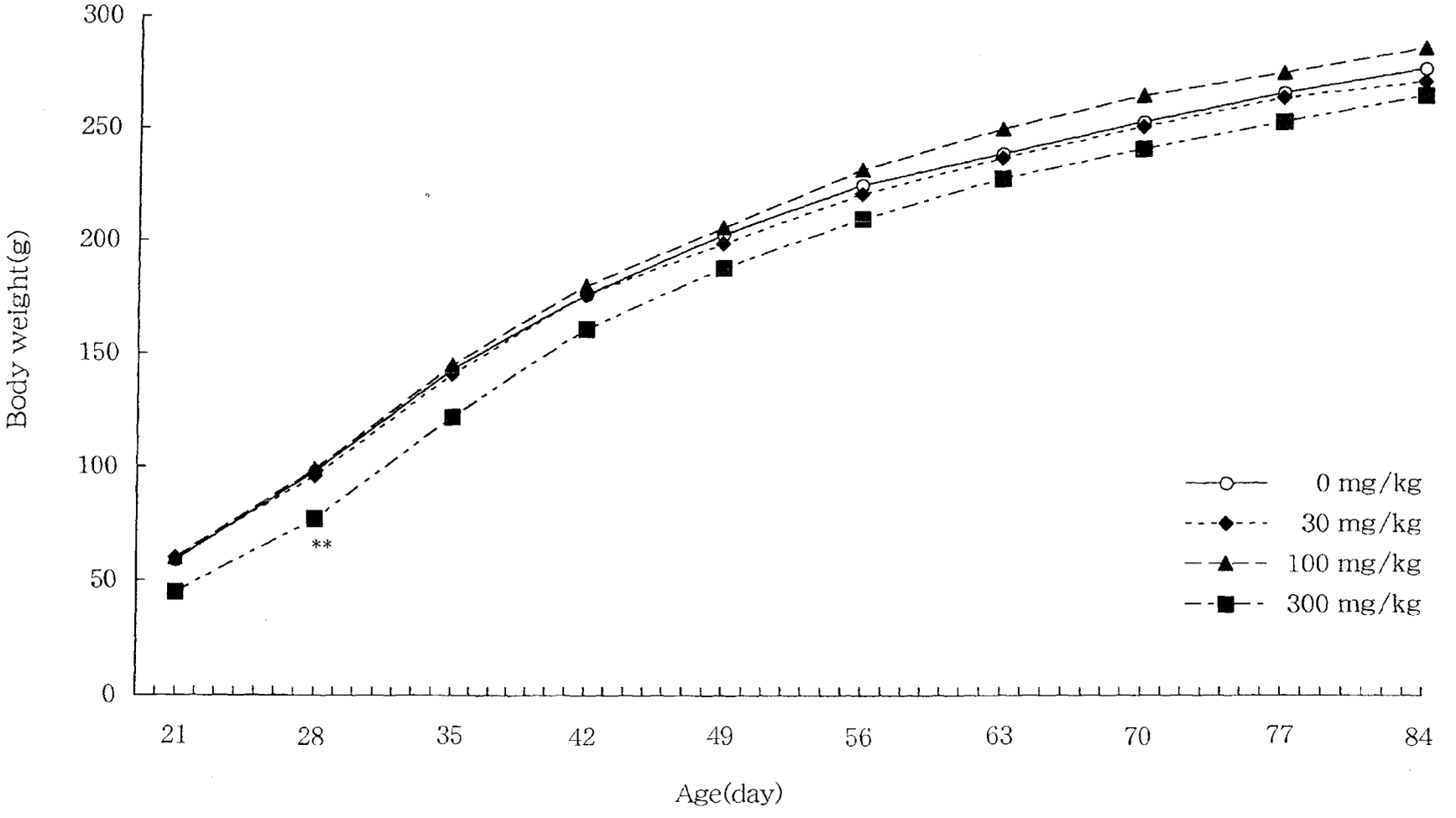


Fig.2-2 Body weight changes of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning
Significantly different from control (** : $p < 0.01$)

Table 1 Mortality rate and incidence of clinical signs of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

		Administration period				Post-administration period			
Dose (mg/kg/day)		0	30	100	300	0	30	100	300
Fate		TK	TK	TK	TK	TK	TK	TK	TK
No. of animals examined		12	12	12	12	6	6	6	6
Mortality (%)	Grade	0	0	0	0	0	0	0	0
Clinical signs									
Decrease in locomotor activity	−	12	12	12	3	6	6	6	6
	+	0	0	0	9 **	0	0	0	0
Subnormal temperature	−	12	12	12	11	6	6	6	6
	+	0	0	0	1	0	0	0	0
Tremor	−	12	12	12	11	6	6	6	6
	+～++	0	0	0	1	0	0	0	0
Straub tail	−	11	12	12	8	6	6	6	6
	+	1	0	0	4	0	0	0	0
Deep respiration	−	12	12	12	9	6	6	6	6
	+	0	0	0	3	0	0	0	0
Emaciation	−	12	12	12	11	6	6	6	6
	+	0	0	0	1	0	0	0	0

TK : Terminal kill; + : Slight; ++ : Moderate
Significantly different from control (**: $p<0.01$)

Table 2 Mortality rate and incidence of clinical signs of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

		Administration period							Post-administration period			
Dose (mg/kg/day)		0	30	100	300				0	30	100	300
Fate		TK	TK	TK	TK	FD	T		TK	TK	TK	TK
No. of animals examined		12	12	12	10	2	(12)		6	6	6	5
Mortality (%)	Grade	0	0	0	17				0	0	0	0
Decrease in locomotor activity	−	12	12	12	0	0	(0)		6	6	6	5
	+〜++	0	0	0	10	2	(12)	**	0	0	0	0
Subnormal temperature	−	12	12	12	6	1	(7)		6	6	6	5
	+	0	0	0	4	1	(5)	*	0	0	0	0
Tremor	−	12	12	12	5	1	(6)		6	6	6	5
	+	0	0	0	5	1	(6)	**	0	0	0	0
Straub tail	−	12	12	12	4	1	(5)		6	6	6	5
	+〜++	0	0	0	6	1	(7)	**	0	0	0	0
Deep respiration	−	12	12	12	6	1	(7)		6	6	6	5
	+	0	0	0	4	1	(5)	*	0	0	0	0
Emaciation	−	12	12	12	7	1	(8)		6	6	6	6
	+〜++	0	0	0	3	1	(4)	*	0	0	0	0

TK : Terminal kill; FD : Found dead; T : Total; + : Slight; ++ : Moderate
Significantly different from control (*: $p<0.05$; **: $p<0.01$)

Table 3 Sensory functions of rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

Sex	Contents	Dose(mg/kg)	0	30	100	300
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	12	8 4 *
	Air righting reflex	Normal	12	12	12	12
	Ispilateral flexor reflex	Normal	12	12	12	11
Female		No. of animals examined	12	12	12	11
	State of gait	Normal	12	12	12	11
	Pupil reflex	Normal	12	12	12	11
	Pinna reflex	Normal	12	12	12	11
	Corneal reflex	Normal	12	12	12	11
	Visiual stepping reflex	Normal	12	12	12	11
	Righting reflex	Normal Slightly slow	12	12	11 1	10 1
	Air righting reflex	Normal	12	12	12	11
	Ispilateral flexor reflex	Normal	12	12	12	11

Significantly different from control(*:$p<0.05$)

Table 4 External differentiation and estrous cycle of rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	0	30	100	300
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)	10.0 ± 0.4 (12)	10.0 ± 0.0 (12)	10.2 ± 0.4 (12)	9.7 ± 0.5 (12)
Separation of eyelids (days of age)	14.1 ± 0.5 (12)	14.2 ± 0.4 (12)	14.4 ± 0.5 (12)	14.1 ± 0.7 (12)
Descent of testes (days of age)	20.0 ± 0.0 (6)	20.2 ± 0.4 (6)	20.2 ± 0.4 (6)	20.3 ± 0.5 (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)	10.1 ± 0.3 (12)	9.9 ± 0.3 (12)	10.1 ± 0.3 (12)	9.8 ± 0.4 (12)
Separation of eyelids (days of age)	14.1 ± 0.3 (12)	14.2 ± 0.4 (12)	14.1 ± 0.3 (12)	13.8 ± 0.5 (12)
Opening of vagina (days of age)	34.5 ± 3.3 (6)	32.8 ± 0.8 (6)	33.0 ± 0.6 (6)	35.4 ± 3.4 (5)

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

Table 5-1 Body weights of male rats treated orally with 4-ethylphenol 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	9.8 ± 0.7 (12)	11.6 ± 0.8 (12)	18.4 ± 1.2 (12)	26.5 ± 1.6 (12)	35.2 ± 2.4 (12)	43.7 ± 3.0 (12)	53.4 ± 2.9 (12)	63.4 ± 3.1 (12)	51.8 ± 2.8 (12)
30	9.9 ± 0.7 (12)	11.8 ± 0.8 (12)	18.6 ± 1.1 (12)	26.9 ± 1.1 (12)	35.3 ± 1.5 (12)	43.7 ± 2.1 (12)	53.4 ± 2.4 (12)	62.8 ± 2.9 (12)	51.0 ± 2.6 (12)
100	9.9 ± 0.7 (12)	11.9 ± 0.8 (12)	18.5 ± 1.2 (12)	26.5 ± 1.4 (12)	34.6 ± 1.8 (12)	42.9 ± 2.0 (12)	51.4 ± 2.2 (12)	60.4 ± 2.4 (12)	48.5 ± 2.5 (12)
300	9.8 ± 0.7 (12)	11.7 ± 0.8 (12)	15.7 ** ± 1.8 (12)	22.7 ** ± 2.8 (12)	31.0 ** ± 3.5 (12)	38.7 ** ± 3.7 (12)	47.0 ** ± 5.5 (12)	55.4 ** ± 7.2 (12)	43.7 ** ± 7.0 (12)

Each value is mean and SD. (n): Number of animals weighed.
Significantly different from control (** : $p < 0.01$)

Table 5-2 Body weights of male rats treated orally with 4-ethylphenol 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	63 ± 4 (6)	109 ± 7 (6)	172 ± 11 (6)	234 ± 15 (6)	276 ± 53 (6)	345 ± 30 (6)	389 ± 34 (6)	421 ± 35 (6)	447 ± 36 (6)	464 ± 40 (6)	402 ± 38 (6)
30	61 ± 3 (6)	103 ± 5 (6)	164 ± 9 (6)	227 ± 13 (6)	288 ± 21 (6)	345 ± 23 (6)	391 ± 26 (6)	417 ± 28 (6)	445 ± 33 (6)	462 ± 37 (6)	401 ± 36 (6)
100	60 ± 3 (6)	106 ± 5 (6)	170 ± 10 (6)	233 ± 10 (6)	292 ± 17 (6)	347 ± 21 (6)	391 ± 24 (6)	424 ± 27 (6)	455 ± 26 (6)	474 ± 28 (6)	414 ± 29 (6)
300	56 ± 7 (6)	96 ** ± 7 (6)	157 ± 9 (6)	219 ± 11 (6)	284 ± 13 (6)	340 ± 13 (6)	390 ± 16 (6)	423 ± 15 (6)	456 ± 18 (6)	475 ± 18 (6)	420 ± 24 (6)

Each value is mean and SD. (n): Number of animals weighed.
Significantly different from control (** : $p < 0.01$)

Table 6-1 Body weights of female rats treated orally with 4-ethylphenol 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	8.9 ± 0.4 (12)	10.8 ± 0.6 (12)	17.1 ± 1.1 (12)	25.0 ± 1.3 (12)	33.4 ± 1.9 (12)	41.4 + 1.9 (12)	50.2 ± 2.2 (12)	59.0 ± 2.4 (12)	48.2 ± 2.2 (12)
30	8.9 ± 0.4 (12)	10.8 ± 0.6 (12)	17.2 ± 0.8 (12)	25.3 ± 1.1 (12)	33.6 ± 1.7 (12)	41.6 ± 2.2 (12)	50.7 ± 2.3 (12)	59.6 ± 2.7 (12)	48.8 ± 2.6 (12)
100	8.9 ± 0.5 (12)	10.7 ± 0.6 (12)	17.1 ± 1.0 (12)	25.4 ± 1.2 (12)	33.7 ± 2.0 (12)	41.5 ± 2.0 (12)	50.7 ± 2.1 (12)	59.7 ± 2.5 (12)	49.0 ± 2.2 (12)
300	8.9 ± 0.4 (12)	10.8 ± 0.6 (12)	14.4 ** ± 1.7 (12)	20.2 * ± 4.0 (12)	26.4 * ± 6.8 (12)	33.5 * ± 8.0 (10)	41.0 ± 9.4 (10)	48.3 ± 11.1 (10)	37.4 ± 11.2 (10)

Each value is mean and SD. (n): Number of animals weighed.
Significantly different from control (* : $p < 0.05$; ** : $p < 0.01$)

Table 6-2 Body weights of female rats treated orally with 4-ethylphenol 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	59 ± 3 (6)	98 ± 5 (6)	143 ± 10 (6)	176 ± 12 (6)	203 ± 16 (6)	225 ± 21 (6)	239 ± 23 (6)	253 ± 26 (6)	266 ± 28 (6)	277 ± 32 (6)	217 ± 30 (6)
30	60 ± 4 (6)	96 ± 6 (6)	141 ± 10 (6)	176 ± 10 (6)	199 ± 10 (6)	221 ± 10 (6)	237 ± 10 (6)	251 ± 12 (6)	264 ± 11 (6)	271 ± 7 (6)	212 ± 9 (6)
100	60 ± 3 (6)	99 ± 4 (6)	145 ± 9 (6)	180 ± 14 (6)	206 ± 20 (6)	232 ± 29 (6)	250 ± 31 (6)	265 ± 40 (6)	275 ± 40 (6)	286 ± 41 (6)	226 ± 42 (6)
300	45 ± 13 (5)	77 ** ± 14 (5)	122 ± 15 (5)	161 ± 6 (5)	188 ± 6 (5)	210 ± 6 (5)	228 ± 7 (5)	241 ± 11 (5)	253 ± 12 (5)	265 ± 14 (5)	219 ± 9 (5)

Each value is mean and SD. (n): Number of animals weighed.
Significantly different from control (** : $p < 0.01$)

Table 7 Food consumption of male rats treated orally with 4-ethylphenol 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	19 ± 2 (6)	28 ± 3 (6)	30 ± 2 (6)	35 ± 4 (6)	35 ± 4 (6)	38 ± 5 (6)	35 ± 3 (6)	36 ± 4 (6)	33 ± 4 (6)
30	19 ± 3 (6)	26 ± 2 (6)	31 ± 1 (6)	34 ± 3 (6)	35 ± 1 (6)	38 ± 2 (6)	33 ± 4 (6)	35 ± 3 (6)	33 ± 4 (6)
100	19 ± 1 (6)	28 ± 3 (6)	32 ± 2 (6)	35 ± 4 (6)	35 ± 3 (6)	39 ± 4 (6)	35 ± 5 (6)	37 ± 5 (6)	35 ± 4 (6)
300	17 ± 1 (6)	27 ± 2 (6)	31 ± 4 (6)	36 + 4 (6)	37 ± 5 (6)	41 ± 4 (6)	37 ± 3 (6)	39 ± 4 (6)	35 ± 3 (6)

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

Table 8 Food consumption of female rats treated orally with 4-ethylphenol 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	18 ± 2 (6)	23 ± 3 (6)	24 ± 3 (6)	26 ± 3 (6)	25 ± 4 (6)	26 ± 3 (6)	25 ± 2 (6)	27 ± 3 (6)	26 ± 4 (6)
30	18 ± 2 (6)	23 ± 2 (6)	24 ± 2 (6)	26 ± 2 (6)	25 ± 3 (6)	26 ± 2 (6)	25 ± 2 (6)	28 ± 2 (6)	26 ± 4 (6)
100	18 ± 1 (6)	23 ± 2 (6)	24 ± 3 (6)	25 ± 5 (6)	26 ± 4 (6)	27 ± 4 (6)	25 ± 5 (6)	27 ± 4 (6)	26 ± 4 (6)
300	15 ± 0 (5)	22 ± 2 (5)	24 ± 2 (5)	25 ± 1 (5)	26 ± 1 (5)	25 ± 2 (5)	25 ± 2 (5)	25 ± 2 (5)	26 ± 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-ethylphenol 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	Y	B	−	+			5.0	6.0	6.5	7.0	7.5	8.0	8.5	−	±	+	++	+++
0	6	6			2	4	12.9 ± 4.1	1.049 ± 0.016					2	3	1		3	3		
30	6	4	1	1	5	1	10.9 ± 1.7	1.054 ± 0.014					1	4	1		2	4		
100	6	6			5	1	12.8 ± 2.3	1.059 ± 0.006				1	3	2				6		
300	6	5	1		2	4	13.9 ± 3.0	1.055 ± 0.016				1	1	3	1		1	3	2	

Dose (mg/kg)	No. of animals	Glucose					Ketone body					Occult blood					Urobilinogen				Bilirubin			
		−	±	+	++	+++	−	±	+	++	+++	−	±	+	++	+++	0.1	1	2	4	−	+	++	+++
0	6	6					5	1				6					6				6			
30	6	6					3	2	1			4		1		1	6				6			
100	6	6					2	4				4		1		1	6				6			
300	6	6					1	5				6					6				6			

Color : PY(pale yellow), Y(yellow), B(brown)
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-ethylphenol 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				5	1			1	3	1	1	6				6			
30	6	5		1		5		1			1	4	1	6				6			
100	6	5		1		5	1			1	1	4		6				6			
300	6	6				6					3	2	1	6				6			

Dose (mg/kg)	No. of animals	Epithelial cells									Casts						Fat globules		
		Sq				R			S			G		H		W			
		−	+	++	+++	−	+	++	−	+	++	−	+	−	+	−	+	−	+	++
0	6		3	3		5	1		6			6		6		6		6		
30	6		4	2		6			6			6		6		6		6		
100	6		3	3		6			6			6		6		6		6		
300	6		2	4		6			6			6		6		6		6		

− : 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-ethylphenol 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	2	4	8.9 ± 2.3	1.055 ± 0.012						3	3		5	1		
30	6	6	2	4	11.4 ± 6.5	1.044 ± 0.017						4	2		5	1		
100	6	6	3	3	11.6 ± 3.6	1.041 ± 0.013						4	2	1	4	1		
300	5	5	3	2	11.8 ± 5.2	1.052 ± 0.009						3	2		4	1		

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			
30	6	6					6					6					6				6			
100	6	6					6					6					6				6			
300	5	5					5					4	1				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-ethylphenol 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					5	1		6				6			
30	6	6				6					4	2		6				6			
100	6	6				6				1	3	2		6				6			
300	5	5				5				1	1	3		5				5			

Dose (mg/kg)	No. of animals	Epithelial cells									Casts						Fat globules		
		Sq				R			S			G		H		W			
		−	+	++	+++	−	+	++	−	+	++	−	+	−	+	−	+	−	+	++
0	6	6				6			6			6		6		6		6		
30	6	6				6			6			6		6		6		6		
100	6	6				6			6			6		6		6		6		
300	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-ethylphenol 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	456 ± 7	8.9 ± 0.5	28.9 ± 1.1	64 ± 3	19.5 ± 1.3	30.7 ± 0.7	200 ± 18	13.9 ± 0.4	15.7 ± 1.5
30	6	487 * ± 20	9.3 ± 0.7	30.6 ± 1.8	63 ± 5	19.2 ± 1.7	30.5 ± 0.5	206 ± 30	13.8 ± 0.2	15.5 ± 0.5
100	6	497 ** ± 23	9.7 ± 0.2	31.2 * ± 0.6	63 ± 4	19.5 ± 1.0	30.9 ± 0.5	206 ± 37	13.8 ± 0.4	15.9 ± 0.7
300	6	480 ± 20	9.5 ± 0.6	30.4 ± 1.4	63 ± 2	19.7 ± 1.1	31.0 ± 0.7	227 ± 15	13.7 ± 0.4	15.1 ± 0.5

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	19 ± 4	0 ± 0	0 ± 1	0 ± 0	14 ± 3	84 ± 4	2 ± 1	0 ± 0	152 ± 13
30	6	19 ± 3	0 ± 0	0 ± 0	0 ± 0	12 ± 5	88 ± 5	1 ± 1	0 ± 0	159 ± 9
100	6	18 ± 7	0 ± 0	0 ± 1	0 ± 0	11 ± 6	87 ± 6	2 ± 2	0 ± 0	171 ± 20
300	6	18 ± 7	0 ± 0	0 ± 1	0 ± 0	15 ± 5	83 ± 5	1 ± 1	0 ± 0	161 ± 14

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

Table 12 Hematological findings of female rats treated orally with 4-ethylphenol 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	483 ± 21	9.3 ± 0.7	30.0 ± 2.3	62 ± 5	19.2 ± 1.5	30.9 ± 0.5	196 ± 39	13.9 ± 0.2	14.3 ± 0.8
30	6	491 ± 32	10.0 ± 0.6	31.9 ± 1.9	65 ± 3	20.3 ± 1.2	31.3 ± 0.7	231 ± 35	13.9 ± 0.4	15.1 ± 0.5
100	6	499 ± 33	9.7 ± 0.6	30.8 ± 1.5	62 ± 2	19.4 ± 0.6	31.4 ± 0.4	226 ± 32	13.9 ± 0.3	15.0 ± 0.8
300	4	511 ± 21	10.3 ± 0.5	32.7 ± 1.2	64 ± 2	20.2 ± 0.5	31.5 ± 0.6	246 ± 9	13.7 ± 0.4	14.0 ± 0.5

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 ± 8	0 ± 0	0 ± 0	0 ± 0	15 ± 4	84 ± 4	1 ± 1	0 ± 0	158 ± 26
30	6	23 ± 3	0 ± 0	0 ± 0	0 ± 0	10 ± 3	89 ± 4	1 ± 1	0 ± 0	146 ± 7
100	6	24 ± 7	0 ± 0	0 ± 0	0 ± 0	12 ± 6	88 ± 7	1 ± 1	0 ± 0	169 ± 34
300	4	21 ± 5	0 ± 0	0 ± 1	0 ± 0	11 ± 7	89 ± 6	1 ± 1	0 ± 0	173 ± 17

Each value is expressed as mean±S.D.

Table 13 Hematological findings of male rats treated orally with 4-ethylphenol 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	872 ± 56	15.9 ± 0.8	45.5 ± 2.6	52 ± 1	18.3 ± 0.5	35.0 ± 0.5	28 ± 9	12.6 ± 0.2	18.6 ± 1.1
30	6	852 ± 47	16.0 ± 0.6	45.8 ± 1.3	54 ± 2	18.7 ± 0.7	34.9 ± 0.4	31 ± 7	12.6 ± 0.2	17.7 ± 1.0
100	6	840 ± 36	15.8 ± 0.7	45.3 ± 1.7	54 ± 2	18.8 ± 0.7	34.8 ± 0.3	24 ± 8	12.8 ± 0.5	17.8 ± 0.7
300	6	830 ± 44	15.2 ± 0.9	43.8 ± 2.1	53 ± 1	18.3 ± 0.4	34.7 ± 0.5	28 ± 8	12.6 ± 0.3	17.6 ± 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	51 ± 8	0 ± 0	0 ± 1	0 ± 0	15 ± 3	83 ± 3	2 ± 1	0 ± 0	124 ± 14
30	6	60 ± 19	0 ± 0	1 ± 1	0 ± 0	14 ± 7	82 ± 8	3 ± 2	0 ± 0	116 ± 12
100	6	61 ± 14	0 ± 0	1 ± 2	0 ± 0	11 ± 3	87 ± 3	2 ± 1	0 ± 0	123 ± 19
300	6	64 ± 28	0 ± 0	0 ± 1	0 ± 0	14 ± 5	84 ± 6	2 ± 2	0 ± 0	136 ± 14

Each value is expressed as mean±S.D.

Table 14 Hematological findings of female rats treated orally with 4-ethylphenol 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	815 ± 41	15.1 ± 0.7	43.5 ± 1.6	53 ± 1	18.6 ± 0.5	34.7 ± 0.6	19 ± 3	12.6 ± 0.4	15.5 ± 1.0
30	6	800 ± 21	15.2 ± 0.6	43.0 ± 1.3	54 ± 1	19.0 ± 0.4	35.3 ± 0.6	21 ± 5	12.6 ± 0.3	16.1 ± 0.7
100	6	819 ± 20	15.5 ± 0.4	44.1 ± 0.7	54 ± 1	19.0 ± 0.6	35.2 ± 0.7	19 ± 4	12.6 ± 0.1	15.2 ± 0.5
300	5	790 ± 15	14.8 ± 0.2	42.0 ± 0.5	53 ± 0	18.7 ± 0.2	35.2 ± 0.1	20 ± 4	12.8 ± 0.6	15.4 ± 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	34 ± 10	0 ± 0	1 ± 0	0 ± 0	11 ± 4	86 ± 4	2 ± 1	0 ± 0	132 ± 9
30	6	39 ± 8	0 ± 0	1 ± 1	0 ± 0	8 ± 3	90 ± 5	1 ± 1	0 ± 0	128 ± 16
100	6	37 ± 12	0 ± 0	2 ± 1	0 ± 0	12 ± 4	85 ± 5	2 ± 1	0 ± 0	143 ± 21
300	5	41 ± 11	0 ± 0	1 ± 0	0 ± 1	12 ± 3	86 ± 4	1 ± 1	0 ± 0	131 ± 14

Each value is expressed as mean±S.D.

Table 15 Blood biochemical findings of male rats treated orally with 4-ethylphenol 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	648 ± 69	123 ± 12	27 ± 7	1075 ± 125	0.67 ± 0.15	88 ± 14	4.93 ± 0.16	2.98 ± 0.07	1.53 ± 0.10	82 ± 13	25 ± 5
30	6	703 ± 143	119 ± 12	21 ± 5	1013 ± 152	0.73 ± 0.10	94 ± 16	4.97 ± 0.16	3.06 ± 0.15	1.61 ± 0.07	83 ± 14	28 ± 10
100	6	679 ± 116	119 ± 5	23 ± 2	966 ± 66	0.72 ± 0.19	101 ± 29	5.04 ± 0.18	3.06 ± 0.10	1.56 ± 0.15	84 ± 8	25 ± 8
300	6	740 ± 187	118 ± 7	25 ± 4	902 ± 142	0.84 ± 0.42	94 ± 15	5.02 ± 0.26	3.11 ± 0.08	1.64 ± 0.12	91 ± 5	22 ± 7

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	125 ± 15	140 ± 7	11.0 ± 1.9	0.46 ± 0.03	0.40 ± 0.03	10.2 ± 0.2	9.5 ± 0.4	142 ± 2	6.89 ± 0.32	108 ± 2
30	6	125 ± 16	139 ± 8	12.2 ± 2.8	0.46 ± 0.03	0.42 ± 0.03	10.1 ± 0.2	9.5 ± 0.5	141 ± 1	7.19 ± 0.50	108 ± 2
100	6	125 ± 11	136 ± 9	10.4 ± 4.4	0.45 ± 0.02	0.40 ± 0.03	10.1 ± 0.3	9.5 ± 0.5	142 ± 1	7.11 ± 0.44	107 ± 1
300	6	133 ± 7	137 ± 6	11.9 ± 4.4	0.45 ± 0.02	0.40 ± 0.03	10.1 ± 0.2	9.3 ± 0.5	140 ± 1	7.09 ± 0.16	107 ± 1

Each value is expressed as mean±S.D.

Table 16 Blood biochemical findings of female rats treated orally with 4-ethylphenol 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	588 ± 199	124 ± 13	19 ± 3	1034 ± 198	0.87 ± 0.20	97 ± 18	4.95 ± 0.22	3.02 ± 0.15	1.57 ± 0.08	80 ± 11	25 ± 4
30	6	711 ± 234	117 ± 8	20 ± 3	883 ± 103	0.61 ± 0.21	88 ± 6	4.92 ± 0.16	2.98 ± 0.14	1.54 ± 0.09	84 ± 11	26 ± 4
100	6	723 ± 255	119 ± 13	20 ± 2	839 ± 112	0.74 ± 0.17	87 ± 9	5.04 ± 0.13	3.10 ± 0.11	1.61 ± 0.08	85 ± 12	25 ± 11
300	5	853 ± 192	123 ± 13	19 ± 1	927 ± 174	1.01 ± 0.26	86 ± 12	5.03 ± 0.26	3.06 ± 0.17	1.58 ± 0.27	85 ± 23	21 ± 5

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	118 ± 13	144 ± 15	14.3 ± 3.2	0.49 ± 0.07	0.39 ± 0.02	10.2 ± 0.3	9.7 ± 0.8	140 ± 2	7.08 ± 0.68	107 ± 2
30	6	120 ± 14	133 ± 11	13.0 ± 2.1	0.48 ± 0.04	0.42 ± 0.02	10.3 ± 0.1	9.5 ± 0.3	140 ± 1	7.15 ± 0.59	107 ± 2
100	6	122 ± 14	131 ± 7	12.4 ± 2.5	0.47 ± 0.04	0.41 ± 0.04	10.2 ± 0.1	9.8 ± 0.3	140 ± 2	7.33 ± 0.62	107 ± 2
300	5	121 ± 23	128 ± 6	15.3 ± 4.9	0.45 ± 0.03	0.41 ± 0.03	9.9 ± 0.3	9.2 ± 0.5	139 ± 2	7.48 ± 1.15	107 ± 3

Each value is expressed as mean±S.D.

Table 17 Blood biochemical findings of male rats treated orally with 4-ethylphenol 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	280 ± 65	79 ± 5	43 ± 5	633 ± 99	0.79 ± 0.15	45 ± 11	6.17 ± 0.22	3.20 ± 0.20	1.08 ± 0.09	71 ± 12	61 ± 22
30	6	225 ± 84	73 ± 11	44 ± 8	527 ± 56	0.78 ± 0.11	55 ± 24	6.27 ± 0.20	3.23 ± 0.07	1.06 ± 0.04	86 ± 10	66 ± 15
100	6	349 ± 247	76 ± 4	40 ± 1	538 ± 57	0.75 ± 0.29	55 ± 17	6.01 ± 0.18	3.14 ± 0.14	1.11 ± 0.18	76 ± 11	68 ± 13
300	6	295 ± 48	81 ± 14	45 ± 8	587 ± 80	0.92 ± 0.34	54 ± 12	6.18 ± 0.15	3.18 ± 0.09	1.07 ± 0.12	83 ± 9	99* ± 35

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	110 ± 18	155 ± 16	14.6 ± 1.6	0.56 ± 0.03	0.33 ± 0.03	10.0 ± 0.2	7.5 ± 0.6	147 ± 2	4.90 ± 0.17	103 ± 1
30	6	128 ± 12	168 ± 17	16.8 ± 3.2	0.59 ± 0.04	0.31 ± 0.02	10.2 ± 0.4	7.5 ± 0.6	147 ± 1	5.04 ± 0.31	103 ± 2
100	6	113 ± 10	151 ± 12	14.8 ± 2.3	0.55 ± 0.05	0.32 ± 0.03	10.0 ± 0.3	7.4 ± 0.5	147 ± 1	5.03 ± 0.32	104 ± 2
300	6	126 ± 13	161 ± 12	15.5 ± 1.8	0.55 ± 0.04	0.31 ± 0.03	10.2 ± 0.1	7.5 ± 0.3	146 ± 1	5.01 ± 0.13	103 ± 2

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

Table 18 Blood biochemical findings of female rats treated orally with 4-ethylphenol 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	370 ± 46	80 ± 25	35 ± 8	342 ± 91	1.73 ± 0.44	446 ± 124	6.36 ± 0.31	3.51 ± 0.25	1.23 ± 0.12	89 ± 10	24 ± 15
30	6	281 ± 39	70 ± 9	32 ± 4	305 ± 92	1.42 ± 0.40	447 ± 180	6.43 ± 0.34	3.62 ± 0.37	1.29 ± 0.18	99 ± 16	21 ± 6
100	6	275 ± 23	66 ± 4	30 ± 3	283 ± 57	1.19 ± 0.48	449 ± 64	6.47 ± 0.14	3.53 ± 0.14	1.20 ± 0.08	91 ± 21	27 ± 18
300	5	335 ± 98	77 ± 12	33 ± 7	395 ± 43	1.75 ± 0.63	393 ± 82	6.05 ± 0.26	3.39 ± 0.19	1.27 ± 0.09	97 ± 22	20 ± 5

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	142 ± 23	139 ± 12	14.4 ± 2.5	0.64 ± 0.09	0.30 ± 0.02	9.9 ± 0.4	6.6 ± 0.8	145 ± 1	4.57 ± 0.18	105 ± 2
30	6	153 ± 28	143 ± 14	14.6 ± 1.4	0.60 ± 0.03	0.30 ± 0.03	10.1 ± 0.3	6.9 ± 1.6	145 ± 1	4.73 ± 0.28	104 ± 1
100	6	145 ± 33	146 ± 9	14.5 ± 2.5	0.60 ± 0.02	0.30 ± 0.03	10.0 ± 0.3	6.1 ± 0.4	145 ± 1	4.86 ± 0.20	104 ± 2
300	5	151 ± 33	131 ± 15	14.9 ± 3.3	0.59 ± 0.08	0.31 ± 0.03	9.9 ± 0.1	6.4 ± 0.4	144 ± 1	4.67 ± 0.17	105 ± 1

Each value is expressed as mean±S.D.

Table 19 Incidence of necropsy findings of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

				<22 days of age>				<85 days of age>			
			Dose(mg/kg)	0	30	100	300	0	30	100	300
Organ	: Findings	Grade	No. of animals	6	6	6	6	6	6	6	6
Lung	: Red spot	-		6	6	6	6	5	6	6	6
		+		0	0	0	0	1	0	0	0
Thymus	: Red spots	-		6	6	6	6	6	6	6	5
		+		0	0	0	0	0	0	0	1

- : Negative; + : Slight

Table 20 Incidence of necropsy findings of female rats treated orally with 4-ethylphenol 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	30	100	300	0	30	100	300	300
Organ	: Findings	Grade	No. of animals	6	6	6	5	6	6	6	5	2
Lung	: Dark red	−		6	6	6	5	6	6	6	5	1
		+		0	0	0	0	0	0	0	0	1
Gastrointestial tract	: Distention	−		6	6	6	5	6	6	6	5	1
		+−+		0	0	0	0	0	0	0	0	1
Thymus	: Red spots	−		6	6	6	5	6	6	6	4	2
		+		0	0	0	0	0	0	0	1	0

FD : Found dead
− : Negative; + : Slight; +++ : Severe

Table 21 Absolute and relative organ weights of male rats treated orally with 4-ethylphenol 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	57.8 ±2.8	1.57 ±0.03	1.94 ±0.12	0.68 ±0.02	209 ±32	334 ±16	510 ±95	239 ±37	8.9 ±0.7	3.1 ±0.2	22.7 ±3.3	312 ±19	81.9 ±16.7	52.1 ±8.8
	30	6	57.5 ±2.3	1.55 ±0.07	1.95 ±0.17	0.68 ±0.06	223 ±29	323 ±19	502 ±82	255 ±22	9.0 ±1.4	3.2 ±0.2	23.7 ±2.7	327 ±24	91.2 ±11.5	55.2 ±7.6
	100	6	54.8 ±1.8	1.54 ±0.04	1.87 ±0.12	0.64 ±0.04	184 ±23	304 ±19	436 ±27	245 ±24	9.5 ±1.1	2.9 ±0.2	22.8 ±2.7	316 ±24	87.8 ±10.0	49.3 ±3.0
	300	6	50.0 * ±7.6	1.48 ** ±0.06	1.84 ±0.29	0.61 ±0.09	168 ±49	294 ±41	431 ±54	212 ±26	8.8 ±1.7	2.7 ** ±0.3	20.4 ±3.9	283 ±37	82.8 ±14.1	51.1 ±7.3
Relative @	0	6	57.8 ±2.8	2.72 ±0.12	3.37 ±0.14	1.18 ±0.05	361 ±43	579 ±32	883 ±154	413 ±54	15.4 ±1.1	5.5 ±0.6	39.4 ±6.3	540 ±14	142.6 ±33.0	90.4 ±15.9
	30	6	57.5 ±2.3	2.70 ±0.06	3.39 ±0.22	1.17 ±0.08	388 ±57	561 ±13	869 ±108	443 ±35	15.6 ±2.2	5.5 ±0.3	41.3 ±4.9	568 ±21	158.8 ±20.8	95.9 ±12.5
	100	6	54.8 ±1.8	2.81 ±0.08	3.40 ±0.13	1.17 ±0.06	335 ±39	555 ±22	796 ±44	447 ±45	17.4 ±1.8	5.4 ±0.3	41.6 ±4.6	578 ±49	160.5 ±19.5	90.1 ±6.9
	300	6	50.0 * ±7.6	3.00 ±0.42	3.68 ** ±0.16	1.22 ±0.07	331 ±62	591 ±49	867 ±48	427 ±19	17.9 ±3.6	5.3 ±0.5	40.9 ±5.6	569 ±43	165.5 ±11.1	103.8 ±18.8

† : 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-ethylphenol 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	52.9 ±2.1	1.49 ±0.02	1.72 ±0.05	0.64 ±0.06	163 ±23	300 ±14	412 ±19	232 ±25	8.9 ±1.4	3.2 ±0.2	20.2 ±1.2	16.1 ±2.3	41.5 ±3.9
	30	6	53.3 ±1.9	1.47 ±0.04	1.74 ±0.05	0.62 ±0.03	188 ±18	301 ±6	442 ±18	243 ±32	9.9 ±0.8	3.3 ±0.2	21.5 ±2.0	15.3 ±1.7	45.6 ±5.3
	100	6	53.1 ±1.8	1.47 ±0.04	1.79 ±0.10	0.64 ±0.04	179 ±21	307 ±17	440 ±5	250 ±42	9.1 ±1.1	3.2 ±0.4	19.3 ±2.0	17.1 ±2.7	43.5 ±11.7
	300	5	45.3 ±8.0	1.43 ±0.09	1.66 ±0.36	0.57 ±0.09	154 ±44	277 ±66	378 ±68	215 ±56	8.8 ±1.4	2.8 ±0.6	18.5 ±3.4	15.6 ±5.2	40.5 ±11.1
Relative @	0	6	52.9 ±2.1	2.82 ±0.13	3.25 ±0.12	1.21 ±0.11	307 ±33	568 ±28	779 ±22	438 ±42	17.0 ±3.0	6.1 ±0.4	38.2 ±1.6	30.4 ±4.5	78.3 ±5.2
	30	6	53.3 ±1.9	2.77 ±0.14	3.26 ±0.05	1.17 ±0.05	353 ±33	565 ±20	829 ±46	456 ±60	18.7 ±1.7	6.2 ±0.4	40.3 ±3.6	28.6 ±3.4	85.7 ±11.9
	100	6	53.1 ±1.8	2.77 ±0.11	3.37 ±0.11	1.20 ±0.05	337 ±41	578 ±34	830 ±25	469 ±70	17.1 ±2.4	6.1 ±0.9	36.5 ±4.2	32.1 ±4.9	82.2 ±22.7
	300	5	45.3 ±8.0	3.21 ±0.46	3.63 ±0.23	1.26 ±0.07	335 ±45	609 ±66	836 ±33	473 ±91	19.5 ±1.1	6.2 ±0.5	41.0 ±4.0	33.6 ±6.5	89.1 ±17.5

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

Table 23 Absolute and relative organ weights of male rats treated orally with 4-ethylphenol 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	432 ±36	2.12 ±0.05	12.87 ±0.88	2.97 ±0.21	0.80 ±0.12	1.36 ±0.09	1.45 ±0.10	0.42 ±0.07	29.7 ±2.8	13.9 ±1.8	64.3 ±6.6	3.35 ±0.21	0.74 ±0.18	1.71 ±0.31	1.22 ±0.06
	30	6	432 ±33	2.13 ±0.08	12.98 ±1.46	2.94 ±0.15	0.81 ±0.07	1.42 ±0.14	1.46 ±0.12	0.47 ±0.10	30.2 ±3.6	13.3 ±1.3	63.6 ±8.3	3.49 ±0.24	0.63 ±0.12	1.74 ±0.20	1.27 ±0.09
	100	6	442 ±27	2.12 ±0.07	12.74 ±1.68	3.04 ±0.20	0.89 ±0.09	1.39 ±0.04	1.48 ±0.11	0.41 ±0.06	29.6 ±4.0	13.6 ±1.8	63.9 ±8.4	3.51 ±0.30	0.60 ±0.18	1.91 ±0.24	1.20 ±0.15
	300	6	443 ±16	2.01 * ±0.07	13.70 ±1.55	2.97 ±0.26	0.80 ±0.11	1.41 ±0.09	1.38 ±0.10	0.51 ±0.10	31.3 ±1.8	13.0 ±1.3	63.8 ±8.4	3.28 ±0.29	0.57 ±0.12	1.83 ±0.23	1.18 ±0.08
Relative @	0	6	432 ±36	0.49 ±0.04	2.99 ±0.12	0.69 ±0.05	0.19 ±0.03	0.32 ±0.01	0.34 ±0.02	0.10 ±0.02	6.9 ±0.5	3.2 ±0.3	15.0 ±1.6	0.78 ±0.07	0.17 ±0.03	0.40 ±0.06	0.28 ±0.03
	30	6	432 ±33	0.49 ±0.03	3.00 ±0.12	0.68 ±0.03	0.19 ±0.01	0.33 ±0.01	0.34 ±0.02	0.11 ±0.02	7.1 ±1.0	3.1 ±0.2	14.7 ±1.6	0.81 ±0.07	0.15 ±0.03	0.41 ±0.07	0.30 ±0.02
	100	6	442 ±27	0.48 ±0.04	2.87 ±0.23	0.69 ±0.05	0.20 ±0.02	0.32 ±0.02	0.34 ±0.01	0.09 ±0.02	6.7 ±1.2	3.1 ±0.3	14.5 ±2.3	0.80 ±0.07	0.14 ±0.04	0.43 ±0.05	0.27 ±0.03
	300	6	443 ±16	0.45 ±0.02	3.09 ±0.26	0.67 ±0.05	0.18 ±0.02	0.32 ±0.01	0.31 ±0.02	0.12 ±0.02	7.1 ±0.05	2.9 ±0.3	14.4 ±1.9	0.74 ±0.07	0.13 ±0.03	0.42 ±0.07	0.27 ±0.02

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

Table 24 Absolute and relative organ weights of female rats treated orally with 4-ethylphenol 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	253 ±28	1.93 ±0.08	7.03 ±1.02	1.82 ±0.18	0.52 ±0.05	0.90 ±0.07	1.07 ±0.10	0.40 ±0.05	23.4 ±3.4	14.5 ±2.7	71.9 ±5.4	80.9 ±8.6	0.74 ±0.35
	30	6	247 ±5	1.91 ±0.08	6.90 ±0.22	1.83 ±0.08	0.49 ±0.05	0.93 ±0.03	1.04 ±0.08	0.36 ±0.07	23.0 ±3.8	14.9 ±2.2	67.7 ±8.6	77.6 ±11.9	0.71 ±0.23
	100	6	260 ±38	1.92 ±0.04	7.36 ±1.45	1.89 ±0.22	0.49 ±0.08	0.90 ±0.10	1.06 ±0.13	0.38 ±0.07	23.8 ±2.6	15.9 ±1.9	71.7 ±5.8	89.3 ±14.4	0.61 ±0.20
	300	5	245 ±13	1.81 ±0.11	6.50 ±0.55	1.77 ±0.14	0.57 ±0.08	0.86 ±0.02	1.08 ±0.05	0.48 ±0.11	22.0 ±1.9	13.5 ±1.5	63.9 ±7.0	81.4 ±13.6	0.60 ±0.20
Relative @	0	6	253 ±28	0.77 ±0.06	2.77 ±0.11	0.72 ±0.06	0.20 ±0.01	0.36 ±0.02	0.42 ±0.03	0.16 ±0.01	9.3 ±1.2	5.7 ±1.0	28.7 ±3.8	32.1 ±3.4	0.29 ±0.12
	30	6	247 ±5	0.77 ±0.02	2.79 ±0.09	0.74 ±0.03	0.20 ±0.02	0.38 ±0.02	0.42 ±0.03	0.15 ±0.03	9.3 ±1.5	6.0 ±0.9	27.4 ±3.3	31.4 ±4.7	0.29 ±0.10
	100	6	260 ±38	0.75 ±0.10	2.82 ±0.17	0.73 ±0.05	0.19 ±0.01	0.35 ±0.02	0.41 ±0.02	0.15 ±0.03	9.3 ±1.8	6.1 ±0.5	28.1 ±4.8	34.6 ±4.6	0.25 ±0.11
	300	5	245 ±13	0.74 ±0.03	2.65 ±0.12	0.72 ±0.03	0.23 ±0.03	0.35 ±0.02	0.44 ±0.03	0.19 ±0.05	9.0 ±1.1	5.6 ±0.9	26.1 ±2.7	33.1 ±4.2	0.25 ±0.08

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

Table 25 Incidence of histopathological findings of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning <22 days of age>

Organ	: Findings	Dose(mg/kg) / Grade	0 / No. of animals 6	30 / 6	100 / 6	300 / 6
Liver	: Hematopoiesis, extra-medullary	-	0	—	—	0
		+	6	—	—	6
Kidney	: Cyst, solitary	-	5	—	—	6
		+	1	—	—	0
	Cast, hyaline/granular	-	5	—	—	6
		+	1	—	—	0
	Basophilic tubules	-	1	—	—	1
		+	5	—	—	5
Spleen	: Hematopoiesis, extra-medullary	-	0	—	—	0
		+	3	—	—	2
		++	3	—	—	4

- : Negative; + : Slight; ++ : Moderate; — : Not examined

No abnormalities were detected in the organs of the brain, pituitary, thymus, thyroid, parathyroid, trachea, lung, heart, stomach, intestine, pancreas, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, testis, epididymis, prostate and seminal vesicle from control and 300mg/kg groups.

Table 26 Incidence of histopathological findings of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning <22 days of age>

Organ	: Findings	Grade	Dose(mg/kg) No. of animals	Scheduled scrificed 0 6	30 6	100 6	300 5	FD 300 2
Lung	: Congestive edema	-		6	—	—	5	1
		++		0	—	—	0	1
Liver	: Hematopoiesis, extra-medullary	-		0	—	—	0	0
		+		6	—	—	5	2
Kidney	: Cyst, solitary	-		5	—	—	5	2
		+		1	—	—	0	0
	Cast, hyaline, unilateral	-		5	—	—	5	2
		+		1	—	—	0	0
	Basophilic tubules	-		0	—	—	2	1
		+		6	—	—	3	1
	Dilatation, renal pelvis, unilateral	-		4	—	—	5	2
		+		2	—	—	0	0
Thymus	: Atrophy, cortical	-		6	—	—	5	1
		+		0	—	—	0	1
Spleen	: Hematopoiesis, extra-medullary	-		0	—	—	0	0
		+		3	—	—	2	0
		++		3	—	—	3	2

- : Negative; + : Slight; ++ : Moderate; — : Not examined
No abnormalities were detected in the organs of the brain, pituitary, thymus, thyroid, parathyroid, trachea, heart, stomach, intestine, pancreas, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus from control and 300mg/kg groups.

Table 27 Incidence of histopathological findings of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning <85 days of age>

Organ	: Findings	Dose(mg/kg) Grade	0 No. of animals 6	30 6	100 6	300 6
Lung	: Accumulation, foam cell	−	4	—	—	6
		+	2	—	—	0
	Mineralization, artery	−	5	—	—	3
		+	1	—	—	3
	Hemorrhage/inflammation, focal	−	5	—	—	5
		+	1	—	—	1
Liver	: Microgranuloma	−	5	—	—	5
		+	1	—	—	1
	Necrosis, focal	−	6	—	—	5
		+	0	—	—	1
Pancreas	: Atrophy, acinar cell, focal	−	5	—	—	6
		±	1			0
	Cellular infiltration, lymphocyte, focal	−	5	—	—	6
		+	1	—	—	0
	Fibrosis, focal	−	6	—	—	5
		+	0	—	—	1
Kidney	: Basophilic tubules	−	4	—	—	5
		+	2	—	—	1
	Eosinophilic body, proximal tubular epithelium	−	6	—	—	4
		+	0	—	—	2
	Hyaline droplet, proximal tubular epithelium	−	1	—	—	0
		+	5	—	—	6
	Cellular infiltration, lymphocyte, cortex	−	5	—	—	6
		+	1	—	—	0
Prostate	: Cellular infiltration, lymphocyte, interstitium	−	5	—	—	6
		+	1	—	—	0
Thymus	: Hemorrhage	−	6	—	—	5
		+	0	—	—	1
Spleen	: Hematopoiesis, extramedullary	−	0	—	—	0
		+	6	—	—	6
	Deposit, brown pigment	−	0	—	—	0
		+	6	—	—	6

− : Negative; ± : Slight; — : Not examined

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, testis, epididymis and seminal vesicle from control and 300mg/kg groups.

Table 28 Incidence of histopathological findings of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning <85 days of age>

Organ	: Findings	Dose(mg/kg) Grade	0 No. of animals 6	30 6	100 6	300 5
Lung	: Accumulation, foam cell	-	6	—	—	3
		+	0	—	—	2
	Mineralization, artery	-	5	—	—	5
		+	1	—	—	0
Liver	: Microgranuloma	-	2	—	—	4
		+	4	—	—	1
Stomach	: Cyst, epidermal, forestomach	-	6	—	—	4
		+	0	—	—	1
Pituitary	: Cyst, Rathke's pouch, anterior lobe	-	5	—	—	5
		++	1	—	—	0
Thymus	: Hemorrhage	-	6	—	—	3
		+	0	—	—	2
Spleen	: Hematopoiesis, extra-medullary	-	0	—	—	0
		+	6	—	—	5
	Deposit, brown pigment	-	0	—	—	0
		+	6	—	—	5

- : Negative; + : Slight; — : Not examined

No abnormalities were detected in the organs of the brain, thyroid, parathyroid, trachea, heart, intestine, pancreas, kidney, adrenal, lymph node, urinary bladder, spinal cord, bone marrow, sciatic nerve, ovary and uterus from control and 300mg/kg groups

4-エチル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：98-097）

報告書　添付資料B

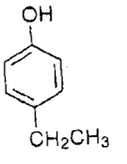
（個体別表等）

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-Ethylphenol (*p*-ethylphenol, *p*-ethylhydroxybenzene)
2. CAS Registry No. : 123-07-9
3. Lot No. : 81107A
4. Purity (impurity) : 98.4% (phenol, 0.198%; 4-methylphenol, 0.206 %; 2-ethylphenol, 0.349%; 3-ethylphenol, 0.588%; *p*-isopropylphenol, 0.162%)
5. Supplier : MARUZEN SEKIYU CHEMICAL Co., Ltd. (2-25-10 Hatthyobori, Tyuo-ku, Tokyo)
6. Day of reception : November 12, 1998
7. Amount : 2.1kg
8. Physico-chemical characterization

Structural formura :



Molecular formura : $C_8H_{10}O$

Molecular weight : 122.16

Appearance at ordinary temperature : Crystalline, white

Melting point : 44.8℃

Boilinng point : 219℃

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 MARUZEN SEKIYU CHEMICAL Co., Ltd. (2-25-10 Hatthyobori, Tyuo-ku, Tokyo)

Test article : 4-Ethylphenol

Lot number : 81107A

Method : GC method

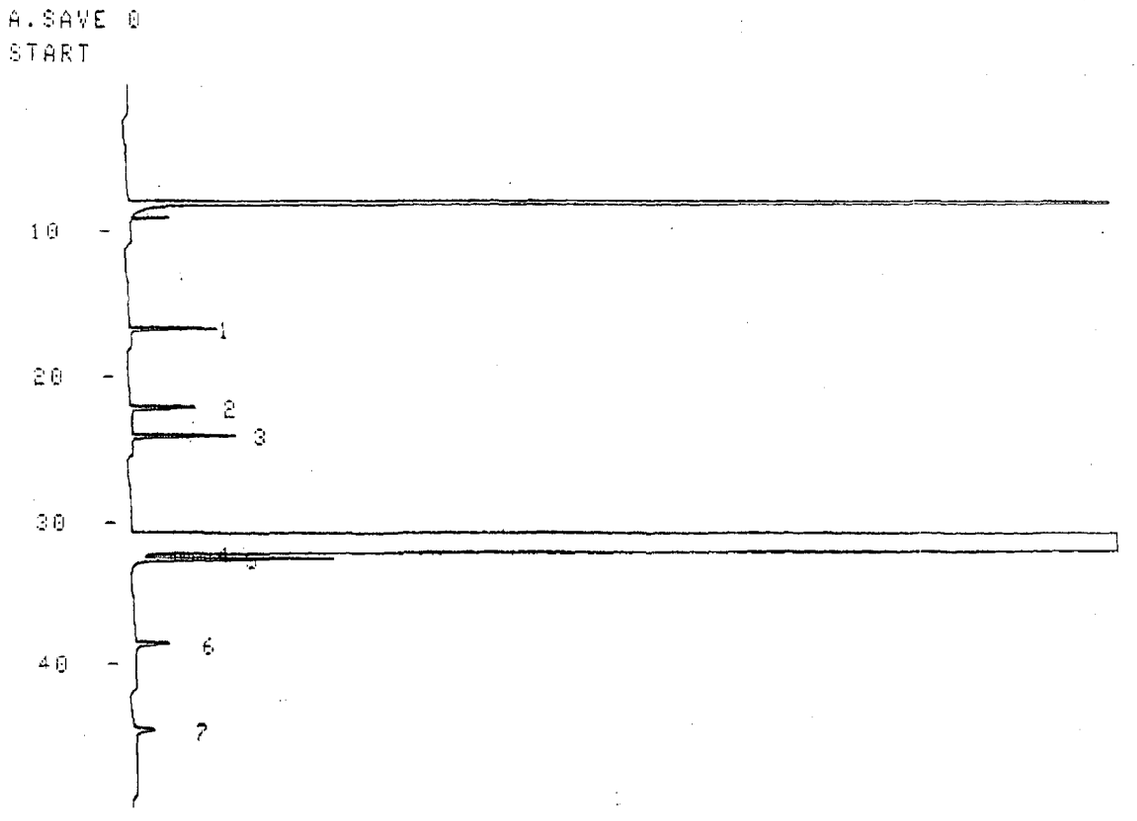
Results :

	Date of analysis	Purity
Before the initiation of the study	November 9, 1998	98.4%
After the termination of the study	November 25, 1999	98.5%

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

4-エチルフェノールのガスクロマトグラム:

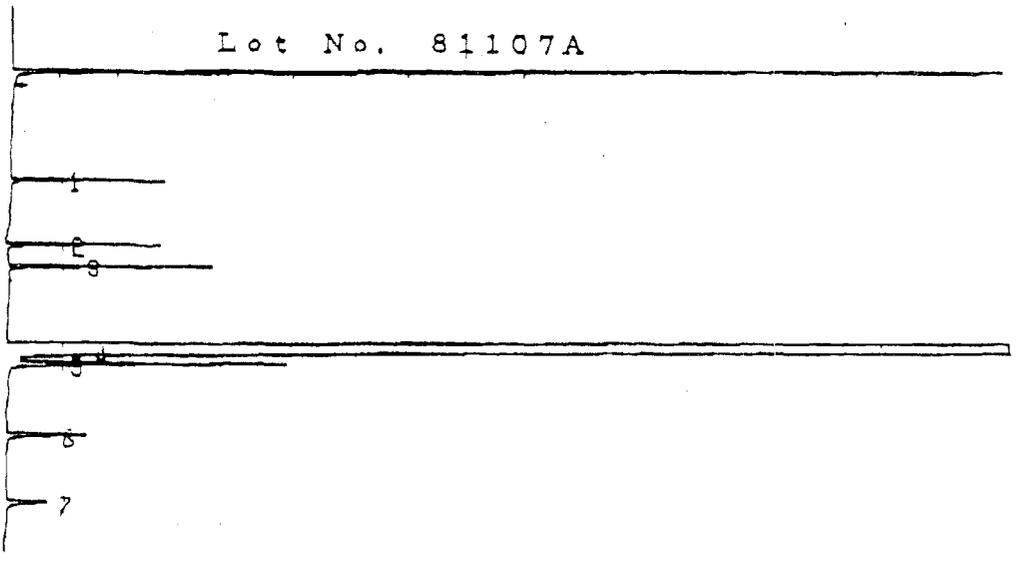
試験開始前（平成10年11月９日）



CHROMATOGRAM 2 MEMORIZED

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	16.712	5127		1	0.1978	PHENOL
2	22.1	5340		2	0.206	P-CRESOL
3	23.985	9041		3	0.3487	O-ETHYL PH.
4	32.147	2550549	S	4	98.3861	P-ETHYL PH.
5	32.588	15243	T	5	0.588	M-ETHYL PH.
6	38.658	4206		6	0.1623	PIPP.
7	44.707	2880		7	0.1111	UNKNOWN
	TOTAL	2592387			100	

4-エチルフェノールのガスクロマトグラム:
投与終了後（平成11年11月25日）



CHROMATOGRAM 64 MEMORIZED

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	13.697	1651			0.1532	PHENOL
2	18.118	2153			0.1999	p-CRESOL
3	19.645	3088			0.2867	o-ETHYL PH.
4	25.888	1061407			98.5422	p-ETHYL PH.
5	26.545	5851	V		0.5432	m-ETHYL PH.
6	31.703	1843			0.1711	PIPP
7	36.525	1117			0.1037	UNKNOWN
	TOTAL	1077109			100	

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

Test article : 4-Ethylphenol (Lot No. 81107A)

Nominal concentrations of the test article in the dose solutions
: 1.0, 3.3 and 10w/v%

Method : GC method

Results :

Date of preparation	Nominal concentrations (w/v%)		
	1.0	3.3	10
May 14, 1998 (Analytical value)	1.0 %	3.3%	9.9%

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.7 Range of temperature(℃)	Range of humidity(%)
May	6, 1999	Arrival of animals	21.8 – 22.2	59
	7,		21.8 – 22.5	58 – 60
	8,		22.0 – 22.3	59 – 60
	9,		22.0 – 22.5	59 – 61
	10,		21.9 – 22.3	59 – 60
	11,		21.9 – 22.1	59 – 60
	12,		21.8 – 22.5	59 – 60
	13,		21.9 – 22.6	59 – 60
	14,		21.9 – 22.5	59 – 60
	15,		21.9 – 22.1	60
	16,	Grouping, beginning of administration	21.9 – 22.0	60
	17,		21.8 – 22.5	59 – 60
	18,		21.9 – 22.4	59 – 60
	19,		21.9 – 22.0	60
	20,		21.9 – 22.6	58 – 60
	21,		21.9 – 22.8	59 – 60
	22,		21.9 – 22.6	59 – 60
	23,		22.1 – 23.0	58 – 60
	24,		22.1 – 22.4	60
	25,		21.9 – 22.9	59 – 60
	26,		22.1 – 22.6	59 – 60
	27,		22.1 – 22.7	60
	28,		22.2	60
	29,		22.1 – 22.5	59 – 60
	30,		22.1 – 22.9	59 – 60
	31,		22.1 – 22.9	59 – 60
June	1,		22.1 – 23.0	59 – 60
	2,		22.1 – 23.1	58 – 60
	3,		22.4 – 22.7	60
	4,	Terminal kill after administration period	22.3 – 22.6	59 – 62
	5,		22.1 – 22.8	59 – 60
	6,		22.1 – 23.0	59 – 60

Appendix 5-2 Environmental condition of animal room

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

Date	Comment	Animal room No.7 Range of temperature(℃)	Range of humidity(%)
June 7, 1999		22.1	60 – 61
8,		22.0 – 22.7	59 – 60
9,		22.0 – 22.7	59 – 60
10,		21.8 – 22.1	60
11,		21.7 – 22.1	60
12,		21.9 – 22.1	60
13,		21.8 – 22.1	60 – 61
14,		21.7 – 22.1	60 – 61
15,		21.7 – 22.1	61
16,		21.7 – 22.1	61
17,		21.7 – 22.0	61
18,		21.6	61
19,		21.7	61
20,		21.7 – 21.8	61
21,		21.6 – 22.0	61
22,		21.9 – 22.1	61
23,		21.8 – 22.1	60 – 61
24,		21.9 – 22.1	61 – 62
25,		21.9	61
26,		21.9 – 22.0	61
27,		21.9 – 22.1	60 – 61
28,		21.8 – 21.9	61 – 62
29,		21.7 – 21.9	61
30,		21.8 – 22.1	61 – 62
July 1,		21.9 – 22.3	61 – 62
2,		21.9 – 22.4	61 – 62
3,		22.0 – 22.1	61
4,		21.9 – 22.7	61
5,		21.9	61
6,		21.8 – 21.9	61 – 62
7,		21.7 – 22.3	61 – 63
8,		21.9 – 22.4	60 – 61
9,		21.7 – 21.9	61
10,		21.9 – 22.5	61

Appendix 5-3 Environmental condition of animal room

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

	Date	Comment	Animal room No.7 Range of temperature(℃)	Range of humidity(%)
July	12, 1999		21.9 – 22.1	61 – 62
	13,		21.7 – 21.9	61 – 62
	14,		21.8 – 22.0	61 – 62
	15,		21.8 – 22.0	61 – 62
	16,		21.7 – 22.0	61
	17,		21.9 – 22.0	61
	18,		21.8 – 22.1	61
	19,		21.6 – 21.9	61 – 62
	20,		21.7 – 21.8	62
	21,		21.7 – 21.9	62
	22,		21.8 – 22.0	61 – 62
	23,		21.7 – 22.2	61 – 62
	24,		21.8 – 22.3	61
	25,		21.9 – 22.4	61
	26,		21.9 – 22.4	61 – 62
	27,		21.9 – 22.1	59 – 61
	28,		21.9 – 22.2	61 – 62
	29,		21.8 – 22.4	61
	30,		21.9 – 22.5	61 – 62
	31,		21.9 – 22.3	61
August	1,		21.9 – 22.3	61
	2,		21.8 – 22.1	61 – 62
	3,		21.8 – 22.2	61
	4,		21.8 – 22.1	61 – 62
	5,		21.7 – 21.9	61 – 62
	6,	Terminal kill after recovery period	21.8 – 21.9	60 – 61

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)9681 FAX:03(3663)9685

Date : March 31 , 1999

CERTIFICATE

Applicant	:	NIHON NOSAN KOGYO K. K
Samples	:	LABO MR-STOCK, Lot No. 990276
Date of Application	:	March 10, 1999
Date of Examination	:	March 10 ～ 31 , 1999
Examination No.	:	3903802

As a result of tests carried out on the sample submitted under the above mentioned name on March 10, 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)	0.14 ppm
Lead (Pb)	0.2 ppm
Cadmium (Cd)	0.11 ppm
Mercury (Hg)	not detected (detection limit 0.01 ppm)
Chromium (Cr)	0.4 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

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

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	0.07 ppm

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

DATE APR 9. 1999

MICROBIOROGICAL INSPECTION

Customer

RESEARCH INSTITUTE FOR ANIMAL SCIENCE
IN BIOCHEMISTRY AND TOXICOLOGY

Sample Designation

LABO MR STOCK
lot No. 990276

S. P. C. ·····3.9×10^3 CFU/g
Coliform Group·····Negative
Salmonella·····Negative
Molds·····< 20 CFU/g

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

[redacted] Director
[redacted]

Appendix 6-2-1 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 bipheny1 (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)9631 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], 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)9635

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 6-3-2 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)9581 FAX:03(3663)9635

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 7-1 Analysis of contaminants in drinking water

Quality Analysis & Certificate for Drinking Water

Certificate No: D－990079

Messrs. Research Institute for Animal in Biochemistry and Toxicology

Date : 1999. FEB. 5th

Tokyo Technic[redacted]o., Ltd.

6chome-7-6 Nakaka[redacted] Tokyo
TEL 03(3688[redacted]

(Tokyo Metropolice Registered M56W327)

Responsible person : [redacted]

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

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

Messrs. Research Institute for Animal in Biochemistry and Toxicology

Date : 1999. Aug. 4th

Tokyo Tech [redacted] e Co., Ltd.

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

(Tokyo Metropolice Registered №56W327)

Responsible person : [redacted]

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

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 No. 69

Japan Food Research Laboratories

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-ethylphenol 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	Straub tail, + (9)[a]
30	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 ; + : Slight
a : Days of age when the sign was observed

Appendix 9-2 Individual clinical signs of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
100	025	KT	22	NAD
	026	KT	22	NAD
	027	KT	22	NAD
	028	KT	22	NAD
	029	KT	22	NAD
	030	KT	22	NAD
	031	KR	85	NAD
	032	KR	85	NAD
	033	KR	85	NAD
	034	KR	85	NAD
	035	KR	85	NAD
	036	KR	85	NAD
300	037	KT	22	Decrease in locomotor activity, + (5, 7)[a] Straub tail, + (8)[a]
	038	KT	22	Decrease in locomotor activity, + (4, 5, 7)[a]
	039	KT	22	Decrease in locomotor activity, + (4, 5, 7)[a] Subnormal temperature, + (8)[a] Emaciation, + (5, 10, 11)[a]
	040	KT	22	NAD
	041	KT	22	NAD
	042	KT	22	Decrease in locomotor activity, + (4-7)[a] Straub tail, + (8)[a]
	043	KR	85	Decrease in locomotor activity, + (4-7)[a] Deep respiration, + (4)[a]

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 ; + : Slight
a : Days of age when the sign was observed

Appendix 9-3 Individual clinical signs of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
300	044	KR	85	Decrease in locomotor activity, + (5)[a]
	045	KR	85	Decrease in locomotor activity, + (5)[a] Deep respiration, + (10)[a]
	046	KR	85	Deep respiration, + (7)[a]
	047	KR	85	Decrease in locomotor activity, + (5)[a] Straub tail, + (8)[a]
	048	KR	85	Decrease in locomotor activity, + (4, 5)[a] Tremor, + (10)/ ++ (7, 8)[a] Straub tail, + (8, 9)[a]

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 ; + : Slight ; ++ : Moderate
a : Days of age when the sign was observed

Appendix 10-1 Individual clinical signs of female rats treated orally with 4-ethylphenol 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	22	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
30	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-days KR : Killed by design after post-administration period of 63-days
NAD : No abnormalities detected
a : Days after initiation of administration ;

Appendix 10-2 Individual clinical signs of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
100	525	KT	22	NAD
	526	KT	22	NAD
	527	KT	22	NAD
	528	KT	22	NAD
	529	KT	22	NAD
	530	KT	22	NAD
	531	KR	85	NAD
	532	KR	85	NAD
	533	KR	85	NAD
	534	KR	85	NAD
	535	KR	85	NAD
	536	KR	85	NAD
300	537	FD	15	Decrease in locomotor activity, + (4, 5, 7)[a] Subnormal temperature, + (5)[a]
	538	KT	22	Decrease in locomotor activity, + (4, 5, 7)[a]
	539	KT	22	Decrease in locomotor activity, + (5, 10)[a] Subnormal temperature, + (5)[a]
	540	KT	22	Decrease in locomotor activity, + (7)[a]
	541	KT	22	Decrease in locomotor activity, + (4, 5, 7, 10) / ++ (9, 11)[a] Subnormal temperature, + (5, 9)[a] Tremor, + (9)[a] Straub tail, + (8)[a] Emaciation, + (5, 6, 10, 13, 14) / ++ (10, 11)[a] Deep respiration, + (9, 11)[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 sign was observed

Appendix 10-3 Individual clinical signs of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

Dose (mg/kg/day)	Animal number	Fate	Age of death (days)	Clinical signs
300	542	KT	22	Decrease in locomotor activity, + (4, 5, 7)[a] Subnormal temperature, + (5)[a] Tremor, + (7, 8, 10)[a] Straub tail, + (9)[a] Emaciation, + (9-13, 15)[a] Deep respiration, + (16, 17)[a]
	543	KR	85	Decrease in locomotor activity, + (5-7)[a] Tremor, + (7)[a] Straub tail, + (8)[a] Deep respiration, + (4)[a]
	544	KR	85	Decrease in locomotor activity, + (4, 5)[a]
	545	KR	85	Decrease in locomotor activity, + (5, 7, 10)[a] Subnormal temperature, + (8)[a] Tremor, + (10)[a] Straub tail, + (10, 11, 16)[a] Deep respiration, + (10, 11, 14)[a] Emaciation, ++ (10)[a]
	546	KR	85	Decrease in locomotor activity, + (5, 7)[a] Tremor, + (7)[a] Straub tail, + (8)[a]
	547	FD	13	Decrease in locomotor activity, + (4, 5)[a] Straub tail, + (8)[a] Emaciation, + (10-13)[a] Deep respiration, + (12, 13)[a]
	548	KR	85	Decrease in locomotor activity, ++ (5)[a] Tremor, + (7, 10)[a] Straub tail, + (9-11, 13), ++(8)[a]

KT : Killed by design after administration period of 18 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 sign was observed

Appendix 11-1 Individual data on sensory functions of male treated orally with 4-ethylphenol 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
30	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-ethylphenol 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
100	025	2	1	1	1	1	1	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
300	037	2	1	1	1	1	2	1	1
	038	2	1	1	1	1	2	1	1
	039	2	1	1	1	1	1	1	1
	040	2	1	1	1	1	2	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	2	1	1
	044	2	1	1	1	1	1	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-ethylphenol 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
30	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-ethylphenol 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
100	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	2	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
300	537	1	1	1	1	1	1	1	1
	538	1	1	1	1	1	2	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	1	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 FD								
	548	1	1	1	1	1	1	1	1

FD : Found dead at 12 days of treatment

Appendix 13-1 Individual external differentiation of male rats treated orally with 4-ethylphenol 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	11	14	
	002	7	10	14	
	003	7	10	14	
	004	7	10	15	
	005	7	10	14	
	006	7	10	14	
	007	7	9	14	20
	008	7	10	14	20
	009	7	10	14	20
	010	7	10	14	20
	011	7	10	13	20
	012	7	10	15	20
	Mean	7.0	10.0	14.1	20.0
30	013	7	10	14	
	014	7	10	14	
	015	7	10	14	
	016	7	10	14	
	017	7	10	14	
	018	7	10	14	
	019	7	10	14	20
	020	7	10	14	20
	021	7	10	14	20
	022	7	10	14	20
	023	7	10	15	21
	024	7	10	15	20
	Mean	7.0	10.0	14.2	20.2

Each value is expressed as days of age.

Appendix 13-2 Individual external differentiation of male rats treated orally with 4-ethylphenol 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
100	025	7	10	15	
	026	7	10	14	
	027	7	10	14	
	028	7	10	15	
	029	7	10	15	
	030	7	10	14	
	031	7	10	14	20
	032	7	10	14	20
	033	7	10	14	20
	034	7	10	14	20
	035	7	11	15	21
	036	7	11	15	20
	Mean	7.0	10.2	14.4	20.2
300	037	7	9	13	
	038	7	10	14	
	039	7	10	15	
	040	7	10	15	
	041	7	9	14	
	042	7	10	14	
	043	7	9	14	20
	044	7	10	14	20
	045	7	10	14	20
	046	7	10	14	21
	047	7	9	15	21
	048	7	10	13	20
	Mean	7.0	9.7	14.1	20.3

Each value is expressed as days of age.

Appendix 14-1 Individual external differentiation of female rats treated orally with 4-ethylphenol 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	10	14	
	502	7	10	14	
	503	7	11	14	
	504	7	10	14	
	505	7	10	14	
	506	7	10	14	
	507	7	10	14	33
	508	7	10	14	41
	509	7	10	14	33
	510	7	10	14	34
	511	7	10	14	34
	512	7	10	15	32
	Mean	7.0	10.1	14.1	34.5
30	513	7	10	14	
	514	7	9	14	
	515	7	10	14	
	516	7	10	14	
	517	7	10	14	
	518	7	10	15	
	519	7	10	14	34
	520	7	10	14	32
	521	7	10	14	33
	522	7	10	14	32
	523	7	10	14	33
	524	7	10	15	33
	Mean	7.0	9.9	14.2	32.8

Each value is expressed as days of age.

Appendix 14-2 Individual external differentiation of female rats treated orally with 4-ethylphenol 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
100	525	7	10	14	
	526	7	11	14	
	527	7	10	14	
	528	7	10	14	
	529	7	10	14	
	530	7	10	14	
	531	7	10	14	34
	532	7	10	14	33
	533	7	10	14	32
	534	7	10	14	33
	535	7	10	14	33
	536	7	10	15	33
	Mean	7.0	10.1	14.1	33.0
300	537	7	10	14	
	538	7	10	14	
	539	7	10	13	
	540	7	10	14	
	541	7	9	14	
	542	7	9	14	
	543	7	10	14	35
	544	7	10	14	32
	545	7	10	14	35
	546	7	10	14	41
	547	7	10	13	
	548	7	10	13	34
	Mean	7.0	9.8	13.8	35.4

Each value is expressed as days of age.

Appendix 15-1 Individual body weights of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

(g)

Dose	Animal	Days of age								Gain										Gain
(mg/kg/day)	number	3	4	7	10	13	16	19	21	4-21	21	28	35	42	49	56	63	70	77	84	21-84
0	001	9.4	11.3	17.2	24.6	31.4	38.6	49.4	61.1	49.8											
	002	10.3	11.7	18.8	26.7	36.2	45.7	55.3	65.9	54.2											
	003	9.1	11.0	17.6	26.1	36.9	46.8	57.0	66.2	55.2											
	004	9.3	11.5	18.6	28.1	38.2	45.9	56.0	64.9	53.4											
	005	10.5	12.3	19.0	27.4	36.8	46.2	56.0	65.6	53.3											
	006	8.9	10.7	17.5	26.7	34.7	42.5	51.1	61.4	50.7											
	007	10.7	12.2	19.0	27.3	36.0	45.2	55.0	66.1	53.9	66	109	170	233	281	323	364	402	430	445	379
	008	10.2	12.7	20.4	28.1	36.9	44.6	53.3	60.9	48.2	61	100	160	224	176	332	379	413	436	450	389
	009	8.6	10.0	16.0	22.9	31.1	39.3	48.6	58.6	48.6	59	102	160	214	268	312	349	375	399	410	351
	010	9.9	11.8	18.3	25.0	32.2	39.5	50.3	59.0	47.2	59	109	177	240	301	358	399	429	459	485	426
	011	10.1	11.8	18.2	27.0	35.0	43.1	52.9	63.3	51.5	63	111	173	233	295	352	394	425	451	468	405
	012	10.5	12.7	19.7	28.1	36.7	46.6	55.3	68.0	55.3	68	120	189	259	332	395	448	480	508	527	459
	Mean	9.8	11.6	18.4	26.5	35.2	43.7	53.4	63.4	51.8	63	109	172	234	276	345	389	421	447	464	402
30	013	10.4	12.5	19.2	26.7	33.5	42.2	53.3	61.9	49.4											
	014	9.9	12.0	18.9	27.6	36.5	45.5	55.1	65.9	53.9											
	015	10.5	12.5	20.1	27.6	37.4	47.8	58.8	68.3	55.8											
	016	9.0	10.3	16.7	25.8	35.2	42.7	52.3	61.3	51.0											
	017	10.2	12.1	19.9	28.5	36.6	45.8	55.6	65.2	53.1											
	018	8.6	10.4	17.3	26.8	35.7	43.0	52.7	62.1	51.7											
	019	10.5	12.2	19.2	27.5	34.1	42.1	52.3	60.9	48.7	61	103	168	228	292	354	395	409	427	441	380
	020	9.7	12.1	18.8	27.7	36.8	45.6	54.9	64.0	51.9	64	105	162	227	282	337	390	427	458	485	421
	021	10.8	12.6	19.7	27.8	36.3	42.1	52.6	62.4	49.8	62	106	172	242	320	383	433	459	493	511	449
	022	10.1	11.8	18.0	24.6	32.7	40.9	50.1	59.8	48.0	60	104	167	231	285	332	361	380	398	404	344
	023	9.2	10.8	17.4	26.4	34.2	42.7	49.9	57.4	46.6	57	93	146	203	256	314	365	398	434	456	399
	024	9.3	11.7	17.9	25.9	34.6	44.4	53.7	64.2	52.5	64	105	166	232	294	351	399	431	461	476	412
	Mean	9.9	11.8	18.6	26.9	35.3	43.7	53.4	62.8	51.0	61	103	164	227	288	345	391	417	445	462	401

Appendix 15-2 Individual body weights of male rats treated orally with 4-ethylphenol 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
100	025	10.9	13.3	19.8	26.9	33.6	41.2	51.9	61.1	47.8											
	026	9.9	11.8	18.6	26.1	32.9	42.3	50.0	58.8	47.0											
	027	9.9	11.7	18.9	26.9	36.1	45.3	52.2	59.6	47.9											
	028	9.1	11.2	17.9	26.6	35.6	42.9	52.8	61.8	50.6											
	029	8.9	10.5	16.1	24.3	32.9	41.2	49.5	58.3	47.8											
	030	10.1	12.3	18.9	28.6	36.7	45.6	53.2	63.0	50.7											
	031	10.5	12.6	19.7	27.5	34.3	41.3	49.9	58.3	45.7	58	99	155	218	268	317	359	388	418	432	374
	032	10.6	12.8	20.3	28.7	38.2	46.3	55.5	64.8	52.0	65	111	182	244	309	362	403	440	469	482	417
	033	9.6	11.6	18.4	26.0	33.6	41.9	49.4	59.0	47.4	59	110	179	246	314	378	420	457	483	507	448
	034	10.4	12.3	19.0	26.3	34.1	42.0	49.5	57.4	45.1	57	100	168	231	294	350	405	442	477	496	439
	035	9.2	10.9	17.3	26.3	35.3	43.9	54.3	63.8	52.9	64	108	169	230	284	334	367	396	430	452	388
	036	9.3	11.3	17.2	23.9	31.9	40.5	48.7	58.8	47.5	59	105	166	229	285	341	393	420	452	475	416
	Mean	9.9	11.9	18.5	26.5	34.6	42.9	51.4	60.4	48.5	60	106	170	233	292	347	391	424	455	474	414
300	037	10.3	12.1	15.1	22.5	30.5	38.7	48.1	58.7	46.6											
	038	10.9	13.0	16.7	24.2	32.2	41.3	50.1	60.3	47.3											
	039	9.0	11.0	11.5	17.1	23.5	31.7	37.9	40.9	29.9											
	040	9.2	11.1	18.4	27.3	37.6	44.7	54.0	64.2	53.1											
	041	10.1	11.9	16.2	20.9	29.4	37.5	46.0	55.0	43.1											
	042	8.8	10.8	15.5	23.6	32.2	38.7	44.7	53.3	42.5											
	043	9.6	11.6	15.7	22.7	30.5	38.6	49.0	57.6	46.0	58	102	163	224	288	338	381	418	449	473	415
	044	9.7	11.6	18.5	27.0	35.6	42.0	52.6	60.9	49.3	61	102	163	226	290	349	398	435	459	480	419
	045	10.0	11.2	15.3	20.7	29.5	33.0	36.2	42.3	31.1	42	83	150	220	290	352	415	445	490	508	466
	046	10.4	12.2	15.6	22.0	29.7	36.8	44.2	53.2	41.0	53	97	164	226	295	345	396	422	452	462	409
	047	9.2	10.8	14.7	23.7	32.0	41.4	51.3	59.9	49.1	60	98	157	221	281	340	380	409	440	457	397
	048	10.5	13.3	14.8	21.1	29.7	39.9	49.5	58.7	45.4	59	94	143	197	259	315	371	408	445	471	412
	Mean	9.8	11.7	15.7	22.7	31.0	38.7	47.0	55.4	43.7	56	96	157	219	284	340	390	423	456	475	420

Appendix 16-1 Individual body weights of female rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

(g)

Dose	Animal	Days of age								Gain										Gain
(mg/kg/day)	number	3	4	7	10	13	16	19	21	4-21	21	28	35	42	49	56	63	70	77	84	21-84
0	501	8.8	10.6	16.3	24.3	31.3	39.0	48.2	57.6	47.0											
	502	9.2	11.0	17.6	25.2	33.5	41.1	50.3	56.9	45.9											
	503	9.0	11.0	17.1	24.6	34.2	43.5	52.6	61.4	50.4											
	504	9.3	11.4	18.4	27.0	35.5	43.0	51.5	57.2	45.8											
	505	8.7	10.5	16.1	24.9	33.8	42.5	50.3	60.6	50.1											
	506	9.1	11.2	17.8	26.6	36.0	42.3	49.7	57.9	46.7											
	507	8.5	10.4	16.5	24.6	32.6	41.2	50.4	60.4	50.0	60	96	141	173	199	214	227	239	255	260	200
	508	9.4	11.6	18.9	26.9	36.3	44.8	53.9	63.7	52.1	64	104	153	195	227	260	279	299	317	334	270
	509	8.4	9.7	15.8	23.2	30.3	38.2	48.6	57.0	47.3	57	96	142	177	206	227	238	257	261	275	218
	510	8.8	10.5	16.7	23.3	31.7	39.3	45.5	55.9	45.4	56	89	124	157	177	197	209	220	232	241	185
	511	8.3	9.9	15.8	24.0	31.9	40.6	50.4	58.1	48.2	58	101	148	180	208	231	244	252	266	286	228
	512	9.6	11.5	18.5	25.9	34.0	41.6	51.2	60.9	49.4	61	102	147	176	203	220	236	251	262	263	202
	Mean	8.9	10.8	17.1	25.0	33.4	41.4	50.2	59.0	48.2	59	98	143	176	203	225	239	253	266	277	217
30	513	8.9	10.6	16.9	24.2	32.2	40.4	50.5	60.7	50.1											
	514	9.0	10.6	16.6	25.2	31.6	39.0	48.3	57.0	46.4											
	515	8.4	9.9	15.9	23.6	34.4	42.3	52.0	59.4	49.5											
	516	8.7	10.5	17.4	26.2	36.0	44.0	53.4	61.8	51.3											
	517	8.5	10.1	15.8	23.8	32.0	39.3	48.8	58.1	48.0											
	518	9.3	11.3	18.2	27.0	35.5	44.7	52.9	62.0	50.7											
	519	9.4	11.5	17.9	25.4	32.3	41.0	49.8	58.6	47.1	59	97	147	184	205	226	242	255	270	272	213
	520	9.6	11.8	18.2	26.7	35.7	44.2	53.5	63.6	51.8	64	107	155	185	205	225	240	250	267	274	210
	521	9.2	11.1	17.3	26.1	34.1	41.1	51.4	59.6	48.5	60	95	142	182	206	226	242	259	266	267	207
	522	9.3	10.9	17.5	24.2	31.2	37.9	45.9	53.2	42.3	53	93	142	176	204	228	245	263	274	277	224
	523	8.6	10.7	17.3	25.4	33.3	41.5	50.3	60.1	49.4	60	89	131	167	193	220	234	248	263	277	217
	524	8.3	10.4	16.9	25.4	34.3	43.7	51.7	60.5	50.1	61	94	129	160	182	202	218	229	242	259	198
	Mean	8.9	10.8	17.2	25.3	33.6	41.6	50.7	59.6	48.8	60	96	141	176	199	221	237	251	264	271	212

Appendix 16-2 Individual body weights of female rats treated orally with 4-ethylphenol 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
100	525	9.4	11.2	18.1	25.6	32.6	40.7	49.9	60.1	48.9											
	526	9.1	11.1	17.0	24.8	32.5	40.5	49.2	57.8	46.7											
	527	8.6	10.2	16.5	24.6	33.9	42.7	50.1	58.7	48.5											
	528	8.7	10.4	16.9	25.6	33.2	40.8	50.5	57.8	47.4											
	529	8.8	10.4	16.2	24.5	33.2	40.3	49.0	57.3	46.9											
	530	9.7	11.9	19.2	28.7	39.0	45.7	54.5	63.1	51.2											
	531	9.2	11.0	17.0	25.3	33.9	40.9	49.7	58.4	47.4	58	94	142	180	205	227	245	257	265	276	218
	532	8.3	10.2	16.1	25.2	33.8	42.5	53.4	63.6	53.4	64	104	156	195	223	255	283	298	307	320	256
	533	8.5	9.9	16.2	25.1	31.7	38.8	49.0	57.9	48.0	58	95	145	179	209	238	256	267	282	291	233
	534	8.9	10.5	16.5	24.0	31.8	39.7	48.5	57.8	47.3	58	100	155	198	230	269	284	320	328	342	284
	535	8.4	10.3	16.9	25.4	33.4	41.4	50.5	59.7	49.4	60	95	135	160	175	192	205	210	219	228	168
	536	9.5	11.6	18.7	26.5	35.5	44.4	54.4	64.1	52.5	64	103	139	170	191	208	225	237	248	260	196
	Mean	8.9	10.7	17.1	25.4	33.7	41.5	50.7	59.7	49.0	60	99	145	180	206	232	250	265	275	286	226
300	537	8.9	10.9	14.3	21.8	29.1															
	538	9.0	11.1	16.6	25.1	33.8	41.5	49.9	59.2	48.1											
	539	8.5	10.3	12.8	19.9	27.8	35.3	43.3	50.7	40.4											
	540	9.2	10.9	16.8	26.1	34.1	41.0	50.1	58.9	48.0											
	541	8.5	10.6	12.3	16.3	17.5	23.2	30.0	35.0	24.4											
	542	9.6	10.6	14.3	21.4	28.8	35.4	42.3	52.6	42.0											
	543	8.7	10.6	13.9	21.0	29.1	36.5	44.8	51.2	40.6	51	81	124	162	189	212	236	251	265	273	222
	544	9.3	11.1	17.2	21.5	29.7	37.0	45.4	53.5	42.4	54	92	142	169	197	218	234	249	255	272	218
	545	8.3	10.3	13.2	16.4	21.9	23.1	27.9	34.6	24.3	35	70	116	160	183	202	219	225	234	242	207
	546	9.2	12.1	13.1	14.2	16.0	20.8	26.0	29.3	17.2	29	56	101	152	181	207	222	235	252	261	232
	547	8.4	9.8	13.0	14.7	16.0															
	548	9.4	10.8	15.2	24.0	33.2	40.9	50.1	57.6	46.8	58	87	129	164	189	212	228	243	260	275	217
	Mean	8.9	10.8	14.4	20.2	26.4	33.5	41.0	48.3	37.4	45	77	122	161	188	210	228	241	253	265	219

Appendix 17 Individual food consumption of male rats treated orally with 4-ethylphenol 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	20	28	30	32	33	35	34	34	32
	008	15	25	28	31	30	33	34	32	30
	009	16	24	28	30	34	34	32	33	30
	010	20	28	31	38	38	41	37	38	37
	011	19	30	30	36	36	37	33	36	31
	012	21	31	34	41	41	45	39	43	39
	Mean	19	28	30	35	35	38	35	36	33
30	019	18	26	30	34	36	36	26	32	29
	020	24	25	31	35	34	39	37	37	38
	021	17	28	31	37	36	41	35	39	36
	022	18	27	32	35	35	35	32	31	28
	023	18	22	28	29	34	36	32	34	29
	024	19	28	31	34	36	39	35	38	36
	Mean	19	26	31	34	35	38	33	35	33
100	031	18	23	30	31	30	33	28	32	29
	032	18	31	31	38	36	39	36	37	33
	033	19	31	33	39	37	40	38	39	34
	034	18	28	32	39	37	45	43	45	42
	035	20	28	34	35	37	36	36	38	36
	036	18	25	30	30	33	38	31	33	34
	Mean	19	28	32	35	35	39	35	37	35
300	043	19	28	32	35	39	38	36	37	35
	044	17	26	29	34	37	40	37	37	34
	045	17	29	36	42	43	49	43	46	38
	046	18	28	33	38	33	40	37	36	30
	047	17	26	29	35	40	42	35	39	36
	048	16	23	25	31	30	36	33	36	36
	Mean	17	27	31	36	37	41	37	39	35

Appendix 18 Individual food consumption of female rats treated orally with 4-ethylphenol 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	19	24	21	25	22	21	23	27	26
	508	20	25	27	28	29	29	29	30	30
	509	16	22	23	25	24	25	25	25	26
	510	16	19	22	23	23	25	22	24	23
	511	22	27	28	29	29	29	24	31	32
	512	17	22	23	23	20	24	24	25	20
	Mean	18	23	24	26	25	26	25	27	26
30	519	18	22	23	23	23	24	23	29	21
	520	21	25	24	25	22	24	23	26	27
	521	16	21	23	26	24	26	26	26	23
	522	18	26	28	29	28	28	28	29	29
	523	16	22	24	27	29	29	25	30	31
	524	17	20	22	24	22	25	24	25	25
	Mean	18	23	24	26	25	26	25	28	26
100	531	17	23	24	24	25	24	23	26	21
	532	18	24	25	27	29	32	27	28	28
	533	19	22	24	23	26	29	24	29	26
	534	19	26	29	34	33	31	33	32	32
	535	18	23	21	22	24	23	19	23	25
	536	18	20	21	21	21	23	22	21	22
	Mean	18	23	24	25	26	27	25	27	26
300	543	15	21	23	24	26	27	26	23	26
	544	16	24	23	27	25	26	25	25	30
	545	15	24	26	24	25	26	24	25	24
	546	15	20	25	26	28	23	26	28	25
	547									
	548	15	21	21	24	25	25	22	25	27
	Mean	15	22	24	25	26	25	25	25	26

Appendix 19 - 1 Individual urinary findings of male rats treated orally with 4-ethylphenol 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	+	10.6	1.056	7.5	±	−	−	−	0.1	−
	008	PY	−	13.2	1.020	8.0	±	−	−	−	0.1	−
	009	PY	+	7.3	1.044	8.0	+	−	−	−	0.1	−
	010	PY	+	19.5	1.062	8.5	+	−	±	−	0.1	−
	011	PY	+	11.9	1.050	8.0	±	−	−	−	0.1	−
	012	PY	−	14.9	1.062	7.5	+	−	−	−	0.1	−
30	019	PY	+	9.9	1.068	8.0	+	−	±	−	0.1	−
	020	PY	−	12.9	1.048	8.0	+	−	−	−	0.1	−
	021	PY	+	12.4	1.052	8.5	±	−	−	+	0.1	−
	022	Y	+	8.8	1.070	7.5	+	−	±	−	0.1	−
	023	B	+	9.6	1.052	8.0	+	−	+	+++	0.1	−
	024	PY	+	11.6	1.032	8.0	±	−	−	−	0.1	−

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

Appendix 19 - 2 Individual urinary findings of male rats treated orally with 4-ethylphenol 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
100	031	PY	−	13.8	1.062	7.0	+	−	−	+	0.1	−
	032	PY	+	12.1	1.060	8.0	+	−	−	+++	0.1	−
	033	PY	+	15.6	1.052	8.0	+	−	±	−	0.1	−
	034	PY	+	14.8	1.064	7.5	+	−	±	−	0.1	−
	035	PY	+	9.6	1.064	7.5	+	−	±	−	0.1	−
	036	PY	+	10.8	1.050	7.5	+	−	±	−	0.1	−
300	043	PY	+	11.5	1.064	8.0	+	−	±	−	0.1	−
	044	PY	+	12.0	1.070	7.0	++	−	−	−	0.1	−
	045	Y	−	19.6	1.044	7.5	±	−	±	−	0.1	−
	046	PY	−	12.2	1.028	8.5	+	−	±	−	0.1	−
	047	PY	+	13.7	1.064	8.0	++	−	±	−	0.1	−
	048	PY	+	14.1	1.058	8.0	+	−	±	−	0.1	−

Appendix 19 - 3 Individual urinary findings of male rats treated orally with 4-ethylphenol 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	−	−	+	−	−	++	−	−	−	−	−	−
30	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-ethylphenol 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	
100	031	−	−	−	−	−	+	−	−	−	−	−	−
	032	+++	+	++	−	−	++	−	−	−	−	−	−
	033	−	−	+	−	−	+	−	−	−	−	−	−
	034	−	−	++	−	−	+	−	−	−	−	−	−
	035	−	−	++	−	−	++	−	−	−	−	−	−
	036	−	−	++	−	−	++	−	−	−	−	−	−
300	043	−	−	++	−	−	++	−	−	−	−	−	−
	044	−	−	+	−	−	+	−	−	−	−	−	−
	045	−	−	+	−	−	++	−	−	−	−	−	−
	046	−	−	+	−	−	+	−	−	−	−	−	−
	047	−	−	+++	−	−	++	−	−	−	−	−	−
	048	−	−	++	−	−	++	−	−	−	−	−	−

Appendix 20 - 1 Individual urinary findings of female rats treated orally with 4-ethylphenol 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	+	6.1	1.040	8.5	±	−	−	−	0.1	−
	508	PY	−	11.4	1.050	8.5	±	−	−	−	0.1	−
	509	PY	+	6.4	1.068	8.0	±	−	−	−	0.1	−
	510	PY	+	9.1	1.056	8.0	±	−	−	−	0.1	−
	511	PY	−	8.8	1.044	8.0	±	−	−	−	0.1	−
	512	PY	+	11.3	1.070	8.5	+	−	−	−	0.1	−
30	519	PY	+	9.8	1.018	8.5	±	−	−	−	0.1	−
	520	PY	−	5.5	1.038	8.5	±	−	−	−	0.1	−
	521	PY	+	8.4	1.034	8.0	±	−	−	−	0.1	−
	522	PY	+	24.1	1.052	8.0	+	−	−	−	0.1	−
	523	PY	+	9.4	1.062	8.0	±	−	−	−	0.1	−
	524	PY	−	11.3	1.060	8.0	±	−	−	−	0.1	−

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

Appendix 20 - 2 Individual urinary findings of female rats treated orally with 4-ethylphenol 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
100	531	PY	+	10.2	1.022	8.0	±	−	−	−	0.1	−
	532	PY	−	10.3	1.060	8.0	+	−	−	−	0.1	−
	533	PY	+	6.7	1.036	8.0	±	−	−	−	0.1	−
	534	PY	+	15.9	1.046	8.0	±	−	−	−	0.1	−
	535	PY	−	10.8	1.046	8.5	±	−	−	−	0.1	−
	536	PY	−	15.7	1.036	8.5	−	−	−	−	0.1	−
300	543	PY	+	9.8	1.066	8.0	+	−	−	−	0.1	−
	544	PY	+	20.5	1.046	8.0	±	−	−	−	0.1	−
	545	PY	−	8.6	1.052	8.5	±	−	−	−	0.1	−
	546	PY	−	12.4	1.042	8.5	±	−	−	−	0.1	−
	547	----	----	----	----	----	----	----	----	----	----	----
	548	PY	−	7.8	1.056	8.0	±	−	−	±	0.1	−

----: Not available

Appendix 20 - 3 Individual urinary findings of female rats treated orally with 4-ethylphenol 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	507	−	−	+	−	−	+	−	−	−	−	−	−
	508	−	−	+	−	−	+	−	−	−	−	−	−
	509	−	−	++	−	−	+	−	−	−	−	−	−
	510	−	−	+	−	−	+	−	−	−	−	−	−
	511	−	−	+	−	−	+	−	−	−	−	−	−
	512	−	−	+	−	−	+	−	−	−	−	−	−
30	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-ethylphenol 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	
100	531	−	−	+	−	−	+	−	−	−	−	−	−
	532	−	−	+	−	−	+	−	−	−	−	−	−
	533	−	−	++	−	−	+	−	−	−	−	−	−
	534	−	−	+	−	−	+	−	−	−	−	−	−
	535	−	−	−	−	−	+	−	−	−	−	−	−
	536	−	−	++	−	−	+	−	−	−	−	−	−
300	543	−	−	++	−	−	+	−	−	−	−	−	−
	544	−	−	−	−	−	+	−	−	−	−	−	−
	545	−	−	+	−	−	+	−	−	−	−	−	−
	546	−	−	++	−	−	+	−	−	−	−	−	−
	547	----	----	----	----	----	----	----	----	----	----	----	----
	548	−	−	++	−	−	+	−	−	−	−	−	−

---- : Not available

Appendix 21 - 1 Individual hematological findings of male rats treated orally with 4-ethylphenol 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	444	9.3	29.4	66	20.9	31.6	222	14.6	14.9
	002	455	8.6	28.3	62	18.9	30.4	181	14.0	18.6
	003	453	9.6	30.6	68	21.2	31.4	202	13.8	15.7
	004	457	8.8	29.1	64	19.3	30.2	216	13.8	15.0
	005	463	8.2	27.3	59	17.7	30.0	178	13.8	15.6
	006	461	8.7	28.4	62	18.9	30.6	202	13.3	14.2
	Mean	456	8.9	28.9	64	19.5	30.7	200	13.9	15.7
30	013	500	10.1	32.6	65	20.2	31.0	223	13.5	16.0
	014	454	9.9	32.1	71	21.8	30.8	243	14.1	15.8
	015	472	8.6	28.5	60	18.2	30.2	220	13.8	15.7
	016	493	9.1	29.7	60	18.5	30.6	204	13.9	14.6
	017	498	9.8	32.0	64	19.7	30.6	187	13.6	15.9
	018	504	8.5	28.8	57	16.9	29.5	158	13.9	15.1
	Mean	487	9.3	30.6	63	19.2	30.5	206	13.8	15.5
100	025	471	9.7	31.3	66	20.6	31.0	240	13.4	16.2
	026	514	9.8	31.1	61	19.1	31.5	166	13.9	16.7
	027	498	9.9	31.6	63	19.9	31.3	191	14.3	16.4
	028	469	9.6	32.0	68	20.5	30.0	217	14.3	15.0
	029	504	9.3	30.2	60	18.5	30.8	168	13.6	15.3
	030	525	9.6	31.2	59	18.3	30.8	253	13.3	15.5
	Mean	497	9.7	31.2	63	19.5	30.9	206	13.8	15.9
300	037	452	8.7	28.5	63	19.2	30.5	237	13.7	15.1
	038	466	9.9	31.3	67	21.2	31.6	237	13.9	15.5
	039	487	10.0	31.4	64	20.5	31.8	204	13.2	15.2
	040	497	9.4	30.7	62	18.9	30.6	214	13.7	15.8
	041	504	10.0	31.9	63	19.8	31.3	241	14.4	15.0
	042	476	8.7	28.8	61	18.3	30.2	228	13.4	14.2
	Mean	480	9.5	30.4	63	19.7	31.0	227	13.7	15.1

Appendix 21 - 2 Individual hematological findings of male rats treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

< 22 days of age >

Dose (mg/kg)	Animal number	WBC ($10^3/\mu L$)	Differential leukocyte counts (%)							Plat. ($10^4/\mu L$)
			Baso.	Eosin.	Neutro. Stab	Neutro. Seg.	Lymph.	Mono.	Other	
0	001	13	0	1	0	17	79	3	0	138
	002	20	0	0	0	12	86	2	0	152
	003	23	0	0	0	19	79	2	0	138
	004	21	0	0	0	11	86	3	0	173
	005	15	0	0	0	11	89	0	0	158
	006	22	0	1	0	12	85	2	0	151
	Mean	19	0	0	0	14	84	2	0	152
30	013	21	0	0	0	10	89	1	0	151
	014	21	0	0	0	11	87	2	0	173
	015	21	0	0	0	20	80	0	0	165
	016	16	0	0	0	6	94	0	0	161
	017	15	0	0	0	11	89	0	0	150
	018	17	0	0	0	11	88	1	0	153
	Mean	19	0	0	0	12	88	1	0	159
100	025	28	0	0	0	5	95	0	0	182
	026	10	0	0	0	18	78	4	0	174
	027	11	0	0	0	9	87	4	0	158
	028	19	0	2	0	7	90	1	0	192
	029	18	0	0	1	8	90	1	0	136
	030	21	0	0	0	18	81	1	0	181
	Mean	18	0	0	0	11	87	2	0	171
300	037	18	0	1	0	15	84	0	0	142
	038	13	0	0	0	12	86	2	0	147
	039	10	0	0	0	13	85	2	0	166
	040	17	0	0	0	20	79	1	0	171
	041	17	0	1	0	22	77	0	0	177
	042	30	0	0	0	9	89	2	0	160
	Mean	18	0	0	0	15	83	1	0	161

Appendix 22 - 1 Individual hematological findings of female rats treated orally with 4-ethylphenol 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	515	9.4	29.8	58	18.3	31.5	166	14.1	14.2
	502	497	9.1	30.4	61	18.3	29.9	211	14.0	15.3
	503	484	10.1	32.5	67	20.9	31.1	196	13.9	14.3
	504	455	8.2	26.5	58	18.0	30.9	149	14.2	14.3
	505	467	10.0	32.1	69	21.4	31.2	196	13.9	14.6
	506	480	8.8	28.4	59	18.3	31.0	260	13.5	12.8
	Mean	483	9.3	30.0	62	19.2	30.9	196	13.9	14.3
30	513	495	9.3	29.9	60	18.8	31.1	231	14.4	15.6
	514	459	10.2	31.3	68	22.2	32.6	187	14.2	15.0
	515	527	10.6	34.6	66	20.1	30.6	248	13.4	14.2
	516	530	10.4	33.5	63	19.6	31.0	242	14.1	15.2
	517	464	9.3	29.9	64	20.0	31.1	195	13.5	15.1
	518	469	10.0	32.0	68	21.3	31.3	282	13.9	15.5
	Mean	491	10.0	31.9	65	20.3	31.3	231	13.9	15.1
100	525	522	9.5	30.5	58	18.2	31.1	207	13.8	14.8
	526	510	10.1	31.9	63	19.8	31.7	203	14.1	15.2
	527	484	9.4	30.2	62	19.4	31.1	285	14.0	16.3
	528	516	10.1	31.8	62	19.6	31.8	240	14.1	13.7
	529	438	8.7	28.1	64	19.9	31.0	217	13.8	14.7
	530	524	10.1	32.0	61	19.3	31.6	202	13.4	15.2
	Mean	499	9.7	30.8	62	19.4	31.4	226	13.9	15.0
300	537	----	----	----	----	----	----	----	----	----
	538	479	9.6	31.2	65	20.0	30.8	235	14.0	14.5
	539	522	10.5	32.8	63	20.1	32.0	255	13.5	14.2
	540	519	10.2	32.7	63	19.7	31.2	243	13.2	13.3
	541	----	----	----	----	----	----	----	----	----
	542	522	10.9	34.2	66	20.9	31.9	250	13.9	13.9
	Mean	511	10.3	32.7	64	20.2	31.5	246	13.7	14.0

---- : Not available

Appendix 22 - 2 Individual hematological findings of female rats treated orally with 4-ethylphenol 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	20	0	0	0	11	89	0	0	193
	502	18	0	0	0	10	89	1	0	186
	503	12	0	0	0	15	83	2	0	128
	504	34	0	0	0	21	78	1	0	152
	505	28	0	0	0	15	85	0	0	137
	506	27	0	0	0	17	82	1	0	153
	Mean	23	0	0	0	15	84	1	0	158
30	513	23	0	0	0	7	93	0	0	155
	514	23	0	0	0	12	85	3	0	137
	515	18	0	0	0	13	86	1	0	153
	516	21	0	0	0	12	88	0	0	143
	517	25	0	0	0	5	94	1	0	141
	518	25	0	1	0	8	89	2	0	149
	Mean	23	0	0	0	10	89	1	0	146
100	525	35	0	0	0	22	76	2	0	200
	526	17	0	0	0	12	88	0	0	135
	527	17	0	0	1	12	85	2	0	174
	528	22	0	0	0	10	89	1	0	143
	529	25	0	0	0	8	92	0	0	219
	530	27	0	0	0	5	95	0	0	145
	Mean	24	0	0	0	12	88	1	0	169
300	537	----	----	----	----	----	----	----	----	----	----
	538	28	0	0	0	16	84	0	0	195
	539	16	0	0	0	5	93	2	0	174
	540	18	0	1	0	4	95	0	0	167
	541	----	----	----	----	----	----	----	----	----	----
	542	20	0	0	0	17	83	0	0	155
	Mean	21	0	0	0	11	89	1	0	173

---- : Not available

Appendix 23 - 1 Individual hematological findings of male rats treated orally with 4-ethylphenol 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	892	16.4	46.4	52	18.4	35.3	24	12.8	19.9
	008	945	16.6	48.2	51	17.6	34.4	17	12.8	18.1
	009	800	14.5	41.9	52	18.1	34.6	32	12.5	17.2
	010	838	15.3	43.0	51	18.3	35.6	30	12.4	18.7
	011	835	16.0	45.5	54	19.2	35.2	42	12.6	19.9
	012	920	16.6	47.9	52	18.0	34.7	24	12.5	17.9
	Mean	872	15.9	45.5	52	18.3	35.0	28	12.6	18.6
30	019	915	16.5	46.7	51	18.0	35.3	26	12.5	19.3
	020	794	14.8	43.3	55	18.6	34.2	36	12.7	16.7
	021	857	16.4	46.7	54	19.1	35.1	29	12.8	17.2
	022	892	16.1	46.0	52	18.0	35.0	22	12.7	17.9
	023	809	15.9	46.2	57	19.7	34.4	40	12.8	18.2
	024	846	16.1	45.9	54	19.0	35.1	33	12.2	16.9
	Mean	852	16.0	45.8	54	18.7	34.9	31	12.6	17.7
100	031	878	15.9	45.5	52	18.1	34.9	18	13.4	17.9
	032	856	15.3	44.4	52	17.9	34.5	36	12.4	18.5
	033	814	15.7	45.2	56	19.3	34.7	19	12.5	18.6
	034	800	14.9	43.0	54	18.6	34.7	22	12.4	17.2
	035	881	17.0	48.2	55	19.3	35.3	17	13.3	17.9
	036	811	15.7	45.2	56	19.4	34.7	31	12.8	16.8
	Mean	840	15.8	45.3	54	18.8	34.8	24	12.8	17.8
300	043	858	15.9	45.5	53	18.5	34.9	24	12.3	18.0
	044	819	15.6	45.2	55	19.0	34.5	15	12.3	16.7
	045	756	13.7	40.3	53	18.1	34.0	39	12.6	17.3
	046	879	15.8	44.7	51	18.0	35.3	28	12.9	18.8
	047	854	15.8	44.9	53	18.5	35.2	32	12.9	17.7
	048	813	14.5	42.0	52	17.8	34.5	29	12.8	17.0
	Mean	830	15.2	43.8	53	18.3	34.7	28	12.6	17.6

Appendix 23 - 2 Individual hematological findings of male rats treated orally with 4-ethylphenol 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	65	0	0	0	15	81	4	0	134
	008	53	0	0	0	9	89	2	0	126
	009	42	0	1	0	17	80	2	0	135
	010	51	0	1	0	18	81	0	0	114
	011	53	0	0	0	12	85	3	0	132
	012	44	0	0	1	16	82	1	0	101
	Mean	51	0	0	0	15	83	2	0	124
30	019	57	0	3	0	6	90	1	0	116
	020	90	0	0	0	10	88	2	0	134
	021	52	0	3	0	13	83	1	0	104
	022	33	0	0	0	15	83	2	0	126
	023	70	0	1	0	15	78	6	0	113
	024	55	0	1	0	27	69	3	0	104
	Mean	60	0	1	0	14	82	3	0	116
100	031	88	0	0	0	12	87	1	0	98
	032	52	0	1	0	6	90	3	0	132
	033	56	0	0	0	12	86	2	0	126
	034	50	0	0	0	9	90	1	0	142
	035	64	0	0	0	12	86	2	0	138
	036	56	0	4	0	12	81	3	0	101
	Mean	61	0	1	0	11	87	2	0	123
300	043	45	0	0	0	12	88	0	0	148
	044	55	0	0	0	13	86	1	0	123
	045	66	0	0	0	19	80	1	0	155
	046	65	0	1	0	17	76	6	0	131
	047	37	0	1	0	18	79	2	0	121
	048	117	0	0	0	5	92	3	0	137
	Mean	64	0	0	0	14	84	2	0	136

Appendix 24 - 1 Individual hematological findings of female rats treated orally with 4-ethylphenol 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	892	16.3	46.1	52	18.3	35.4	22	12.7	15.7
	508	805	14.9	42.9	53	18.5	34.7	18	12.3	14.4
	509	778	14.1	41.3	53	18.1	34.1	19	12.5	14.3
	510	801	15.6	44.1	55	19.5	35.4	14	13.3	16.6
	511	789	14.9	42.9	54	18.9	34.7	19	12.1	16.2
	512	824	14.9	43.9	53	18.1	33.9	23	12.5	15.9
	Mean	815	15.1	43.5	53	18.6	34.7	19	12.6	15.5
30	519	814	15.5	43.1	53	19.0	36.0	16	12.7	16.6
	520	778	14.2	40.9	53	18.3	34.7	24	12.8	16.6
	521	809	15.8	43.9	54	19.5	36.0	15	12.8	16.9
	522	799	15.0	42.8	54	18.8	35.0	20	12.6	15.5
	523	773	15.0	42.3	55	19.4	35.5	23	12.0	15.7
	524	826	15.6	44.8	54	18.9	34.8	29	12.7	15.2
	Mean	800	15.2	43.0	54	19.0	35.3	21	12.6	16.1
100	531	815	15.8	44.2	54	19.4	35.7	17	12.8	14.8
	532	804	16.1	44.6	55	20.0	36.1	16	12.5	15.3
	533	813	15.0	43.9	54	18.5	34.2	19	12.6	14.6
	534	835	15.5	44.5	53	18.6	34.8	21	12.6	14.8
	535	850	15.7	44.7	53	18.5	35.1	24	12.7	15.7
	536	795	15.0	42.8	54	18.9	35.0	14	12.6	15.7
	Mean	819	15.5	44.1	54	19.0	35.2	19	12.6	15.2
300	543	793	14.9	42.4	53	18.8	35.1	26	12.8	15.5
	544	789	14.7	41.6	53	18.6	35.3	18	12.8	16.0
	545	768	14.6	41.3	54	19.0	35.4	18	12.2	15.0
	546	789	14.8	42.1	53	18.8	35.2	15	13.7	16.5
	547	----	----	----	----	----	----	----	----	----
	548	809	15.0	42.6	53	18.5	35.2	23	12.5	14.2
	Mean	790	14.8	42.0	53	18.7	35.2	20	12.8	15.4

---- : Not available

Appendix 24 - 2 Individual hematological findings of female rats treated orally with 4-ethylphenol 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	52	0	0	0	9	89	2	0	136
	508	34	0	1	0	7	90	2	0	121
	509	30	0	1	0	13	85	1	0	145
	510	31	0	1	0	8	89	2	0	126
	511	33	0	1	0	18	81	0	0	126
	512	23	0	1	0	13	84	2	0	137
	Mean	34	0	1	0	11	86	2	0	132
30	519	48	0	0	0	5	95	0	0	126
	520	33	0	0	0	5	95	0	0	116
	521	39	0	0	0	9	90	1	0	133
	522	30	0	2	0	7	90	1	0	121
	523	33	0	1	0	13	83	3	0	115
	524	49	0	3	0	9	87	1	0	157
	Mean	39	0	1	0	8	90	1	0	128
100	531	46	0	1	0	9	88	2	0	146
	532	55	0	0	0	8	90	2	0	129
	533	38	0	2	0	7	90	1	0	163
	534	31	0	3	0	17	77	3	0	144
	535	26	0	1	0	15	83	1	0	165
	536	26	0	2	0	14	82	2	0	110
	Mean	37	0	2	0	12	85	2	0	143
300	543	50	0	1	0	9	89	1	0	129
	544	26	0	1	1	13	85	0	0	109
	545	33	0	1	1	12	86	0	0	136
	546	52	0	0	0	9	89	2	0	140
	547	----	----	----	----	----	----	----	----	----
	548	45	0	1	0	17	79	3	0	143
	Mean	41	0	1	0	12	86	1	0	131

---- : Not available

Appendix 25 - 1 Individual blood biochemical findings of male rats treated orally with 4-ethylphenol 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	678	125	39	1075	0.72	108	4.72	2.88	1.57	75	17
	002	742	118	27	1165	0.52	72	4.80	3.01	1.68	77	26
	003	603	111	26	1063	0.64	92	4.88	2.96	1.54	80	23
	004	704	120	17	987	0.88	75	5.01	3.01	1.51	75	23
	005	581	116	29	902	0.49	98	5.06	2.94	1.39	78	32
	006	580	145	25	1255	0.78	84	5.13	3.07	1.49	108	30
	Mean	648	123	27	1075	0.67	88	4.93	2.98	1.53	82	25
30	013	585	100	15	811	0.66	99	4.82	2.95	1.58	74	30
	014	677	125	27	1134	0.74	80	4.91	2.99	1.56	70	13
	015	581	132	26	1122	0.73	82	5.10	3.22	1.71	78	35
	016	955	130	21	829	0.66	86	4.82	2.91	1.52	95	22
	017	778	114	16	1059	0.64	122	4.94	3.04	1.60	73	28
	018	643	113	23	1124	0.92	97	5.23	3.27	1.67	105	40
	Mean	703	119	21	1013	0.73	94	4.97	3.06	1.61	83	28
100	025	645	121	25	945	0.98	148	4.83	3.00	1.64	69	26
	026	628	116	23	1042	0.74	81	4.98	3.04	1.57	86	14
	027	651	119	23	886	0.81	68	4.97	3.17	1.76	88	34
	028	913	126	20	976	0.77	88	5.10	3.13	1.59	80	18
	029	602	113	22	906	0.50	99	5.00	2.91	1.39	88	23
	030	632	117	25	1040	0.50	119	5.37	3.12	1.39	92	33
	Mean	679	119	23	966	0.72	101	5.04	3.06	1.56	84	25
300	037	700	115	30	720	0.43	89	4.73	3.02	1.77	85	33
	038	563	112	27	992	0.57	107	4.91	3.04	1.63	94	21
	039	596	128	21	1073	1.63	73	4.93	3.14	1.75	89	11
	040	643	112	20	877	0.91	88	5.29	3.19	1.52	94	23
	041	902	119	26	996	0.75	114	4.88	3.06	1.68	87	23
	042	1033	124	23	756	0.77	91	5.39	3.21	1.47	98	21
	Mean	740	118	25	902	0.84	94	5.02	3.11	1.64	91	22

Appendix 25 - 2 Individual blood biochemical findings of male rats treated orally with 4-ethylphenol 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	116	151	9.8	0.43	0.38	9.8	8.9	143	6.81	106
	002	117	135	9.6	0.44	0.38	10.3	9.4	140	7.05	108
	003	116	145	9.2	0.44	0.39	10.3	9.8	142	6.78	107
	004	120	138	14.0	0.49	0.44	10.1	9.3	143	6.83	110
	005	127	141	10.8	0.50	0.38	10.2	10.0	143	6.46	108
	006	155	131	12.5	0.46	0.42	10.4	9.4	139	7.43	106
	Mean	125	140	11.0	0.46	0.40	10.2	9.5	142	6.89	108
30	013	111	131	7.3	0.43	0.47	9.9	8.6	140	8.04	107
	014	110	131	15.5	0.50	0.42	10.0	9.5	143	6.82	110
	015	122	147	12.5	0.46	0.40	10.2	9.8	143	6.77	107
	016	136	135	11.1	0.47	0.44	9.9	9.7	140	7.53	107
	017	116	139	12.9	0.42	0.39	10.3	9.5	141	6.88	105
	018	152	151	14.1	0.45	0.41	10.3	9.9	140	7.12	109
	Mean	125	139	12.2	0.46	0.42	10.1	9.5	141	7.19	108
100	025	108	143	4.0	0.46	0.42	9.6	8.9	141	7.22	108
	026	120	127	8.8	0.42	0.43	10.1	10.2	141	7.15	107
	027	128	140	7.9	0.45	0.39	10.1	9.3	141	6.89	108
	028	122	122	16.3	0.45	0.44	10.3	9.9	143	7.62	108
	029	129	137	11.8	0.47	0.39	10.1	9.0	141	7.42	106
	030	141	146	13.7	0.47	0.35	10.4	9.4	143	6.36	106
	Mean	125	136	10.4	0.45	0.40	10.1	9.5	142	7.11	107
300	037	130	141	5.7	0.45	0.37	10.1	9.6	139	7.13	106
	038	132	131	9.8	0.46	0.38	10.1	9.4	140	6.91	107
	039	122	147	18.0	0.43	0.44	9.7	8.3	140	7.15	109
	040	139	137	14.2	0.49	0.41	10.2	9.2	142	7.13	108
	041	136	131	9.4	0.43	0.42	10.1	9.6	139	7.32	107
	042	141	137	14.5	0.45	0.39	10.4	9.7	141	6.89	107
	Mean	133	137	11.9	0.45	0.40	10.1	9.3	140	7.09	107

Appendix 26 - 1 Individual blood biochemical findings of female rats treated orally with 4-ethylphenol 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	641	142	23	1279	1.00	88	5.09	3.06	1.51	84	22
	502	690	116	19	932	0.70	87	5.26	3.19	1.54	100	28
	503	694	127	19	1080	0.78	118	4.68	2.92	1.66	78	19
	504	340	106	16	698	0.75	79	4.72	2.80	1.46	66	30
	505	818	120	16	1117	0.77	120	5.05	3.16	1.67	74	23
	506	344	131	19	1095	1.22	87	4.91	3.00	1.57	78	29
	Mean	588	124	19	1034	0.87	97	4.95	3.02	1.57	80	25
30	513	1004	113	20	851	0.47	88	4.87	2.97	1.56	69	24
	514	1017	115	21	940	0.34	78	4.95	3.08	1.65	90	26
	515	556	121	17	692	0.91	89	4.83	2.92	1.53	98	28
	516	544	112	18	928	0.78	96	5.18	3.20	1.62	78	22
	517	620	131	25	907	0.64	85	4.69	2.80	1.48	76	24
	518	525	110	18	982	0.50	89	4.98	2.92	1.42	93	33
	Mean	711	117	20	883	0.61	88	4.92	2.98	1.54	84	26
100	525	446	105	20	717	0.47	93	5.10	3.09	1.54	82	36
	526	701	111	23	1031	0.79	89	4.81	3.00	1.66	99	17
	527	1206	138	18	814	0.82	80	5.14	3.19	1.64	67	20
	528	700	127	19	762	0.60	98	5.06	3.09	1.57	82	16
	529	640	124	19	898	0.78	72	4.97	2.98	1.50	79	20
	530	645	109	20	810	0.96	87	5.16	3.26	1.72	98	42
	Mean	723	119	20	839	0.74	87	5.04	3.10	1.61	85	25
300	537	----	----	----	----	----	----	----	----	----	----	----
	538	1015	108	19	769	0.99	68	5.17	2.86	1.24	109	24
	539	979	134	20	845	0.94	99	5.08	3.10	1.57	77	19
	540	584	118	18	873	0.63	81	5.38	3.26	1.54	82	25
	541	970	138	20	928	1.32	92	4.76	3.17	1.99	53	14
	542	716	117	20	1220	1.19	88	4.78	2.93	1.58	105	23
	Mean	853	123	19	927	1.01	86	5.03	3.06	1.58	85	21

---- : Not available

Appendix 26 - 2 Individual blood biochemical findings of female rats treated orally with 4-ethylphenol 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	124	168	17.0	0.61	0.40	10.5	11.2	143	7.43	110
	502	140	157	13.3	0.50	0.40	10.3	9.6	141	6.40	107
	503	103	135	11.5	0.46	0.38	10.0	9.0	141	6.64	108
	504	110	138	10.3	0.46	0.36	10.1	9.2	139	6.40	106
	505	113	132	14.7	0.45	0.39	10.6	9.8	139	7.74	107
	506	116	136	18.7	0.43	0.39	9.9	9.2	138	7.87	105
	Mean	118	144	14.3	0.49	0.39	10.2	9.7	140	7.08	107
30	513	101	147	15.9	0.48	0.44	10.3	9.8	138	7.40	106
	514	118	137	13.3	0.48	0.40	10.4	9.3	140	6.17	109
	515	130	133	11.9	0.53	0.42	10.1	9.6	139	7.80	110
	516	115	139	14.8	0.48	0.43	10.4	9.0	141	7.32	106
	517	115	123	10.6	0.40	0.40	10.1	9.9	141	6.74	106
	518	142	116	11.2	0.49	0.45	10.3	9.5	140	7.44	105
	Mean	120	133	13.0	0.48	0.42	10.3	9.5	140	7.15	107
100	525	123	143	12.0	0.52	0.35	10.3	9.9	139	7.12	106
	526	123	120	9.1	0.41	0.47	10.2	9.5	139	8.30	107
	527	105	130	12.6	0.48	0.45	9.9	9.3	140	7.14	110
	528	116	132	16.8	0.49	0.41	10.3	9.8	141	7.26	108
	529	118	131	12.1	0.47	0.40	10.2	10.2	143	6.47	109
	530	147	132	11.5	0.46	0.40	10.2	9.9	138	7.70	104
	Mean	122	131	12.4	0.47	0.41	10.2	9.8	140	7.33	107
300	537	----	----	----	----	----	----	----	----	----	----
	538	140	133	11.5	0.48	0.40	10.0	8.8	139	7.76	106
	539	113	130	12.7	0.46	0.41	9.9	9.4	139	7.64	109
	540	125	132	11.9	0.46	0.38	10.0	8.8	140	7.55	109
	541	86	129	23.0	0.42	0.46	9.4	8.9	142	5.63	110
	542	141	117	17.6	0.41	0.40	10.3	10.0	137	8.80	102
	Mean	121	128	15.3	0.45	0.41	9.9	9.2	139	7.48	107

---- : Not available

Appendix 27 - 1 Individual blood biochemical findings of male rats treated orally with 4-ethylphenol 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	366	81	51	779	0.72	49	5.99	3.14	1.10	66	84
	008	308	75	36	621	0.98	53	6.52	3.61	1.24	91	85
	009	321	71	39	495	0.97	61	5.98	3.08	1.06	54	40
	010	256	78	44	562	0.76	36	6.09	3.09	1.03	73	60
	011	184	82	44	685	0.75	32	6.09	3.14	1.06	74	32
	012	242	85	41	658	0.58	39	6.34	3.15	0.99	68	66
	Mean	280	79	43	633	0.79	45	6.17	3.20	1.08	71	61
30	019	356	69	38	462	0.82	43	6.10	3.22	1.12	73	78
	020	247	59	36	524	0.74	46	6.27	3.21	1.05	89	73
	021	158	87	57	559	0.87	100	6.46	3.26	1.02	86	84
	022	116	70	43	614	0.79	34	6.09	3.13	1.06	76	60
	023	261	66	40	475	0.86	44	6.12	3.19	1.09	100	44
	024	209	85	51	525	0.57	63	6.57	3.34	1.03	91	58
	Mean	225	73	44	527	0.78	55	6.27	3.23	1.06	86	66
100	031	346	82	41	491	1.27	81	5.66	3.37	1.47	73	66
	032	248	74	39	564	0.57	40	6.08	3.11	1.05	71	66
	033	192	75	39	601	0.45	40	6.09	3.07	1.02	90	75
	034	840	80	41	597	0.83	44	6.10	3.05	1.00	75	61
	035	263	73	40	472	0.58	56	6.13	3.22	1.11	61	87
	036	204	71	42	501	0.81	69	5.98	3.00	1.01	88	50
	Mean	349	76	40	538	0.75	55	6.01	3.14	1.11	76	68
300	043	381	99	48	685	0.79	44	6.23	3.17	1.04	78	67
	044	240	65	37	516	0.64	50	6.04	3.14	1.08	89	158
	045	284	72	41	660	0.95	75	6.29	3.09	0.97	95	110
	046	288	79	40	590	0.87	54	5.96	3.36	1.29	80	74
	047	308	74	43	478	0.67	41	6.24	3.19	1.05	69	110
	048	268	96	60	593	1.57	61	6.33	3.15	0.99	86	73
	Mean	295	81	45	587	0.92	54	6.18	3.18	1.07	83	99

Appendix 27 - 2 Individual blood biochemical findings of male rats treated orally with 4-ethylphenol 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	116	185	17.4	0.61	0.34	9.9	8.0	147	4.92	103
	008	138	145	14.9	0.55	0.32	10.2	6.8	148	4.84	104
	009	85	154	13.7	0.58	0.36	9.6	6.7	144	5.03	102
	010	113	143	15.0	0.57	0.36	9.8	7.4	147	5.05	102
	011	101	145	13.1	0.55	0.31	10.1	7.9	148	4.59	103
	012	104	158	13.4	0.52	0.30	10.2	7.9	148	4.95	104
	Mean	110	155	14.6	0.56	0.33	10.0	7.5	147	4.90	103
30	019	122	164	12.4	0.57	0.30	9.5	6.8	146	5.38	106
	020	132	180	18.8	0.61	0.30	10.5	8.1	148	5.25	101
	021	127	154	17.0	0.58	0.29	10.4	6.9	147	4.82	101
	022	108	145	13.4	0.52	0.34	10.0	7.4	148	4.66	102
	023	140	187	19.2	0.64	0.32	10.3	8.1	146	4.83	102
	024	137	180	20.0	0.63	0.33	10.3	7.4	146	5.32	103
	Mean	128	168	16.8	0.59	0.31	10.2	7.5	147	5.04	103
100	031	108	155	11.7	0.57	0.27	9.8	6.9	146	4.76	105
	032	110	158	15.6	0.63	0.32	9.9	7.3	148	5.15	103
	033	127	148	13.4	0.50	0.31	10.1	7.7	146	5.33	101
	034	111	167	13.9	0.56	0.33	10.1	8.2	145	5.42	104
	035	98	142	16.1	0.52	0.36	10.5	7.6	147	4.86	103
	036	122	133	18.2	0.54	0.32	9.8	6.9	147	4.63	105
	Mean	113	151	14.8	0.55	0.32	10.0	7.4	147	5.03	104
300	043	122	161	15.9	0.60	0.32	10.1	7.3	147	4.99	104
	044	145	165	15.3	0.56	0.34	10.1	7.2	145	4.96	101
	045	137	155	12.7	0.52	0.29	10.3	7.5	146	4.97	102
	046	119	139	14.5	0.49	0.32	10.0	8.0	145	4.90	105
	047	110	171	16.9	0.57	0.31	10.3	7.5	146	5.26	102
	048	123	172	17.8	0.58	0.25	10.2	7.2	146	5.00	102
	Mean	126	161	15.5	0.55	0.31	10.2	7.5	146	5.01	103

Appendix 28 - 1 Individual blood biochemical findings of female rats treated orally with 4-ethylphenol 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	434	60	28	384	1.07	553	6.85	3.86	1.29	92	28
	508	344	65	35	436	1.97	436	6.31	3.38	1.15	94	51
	509	358	76	29	226	1.49	414	6.22	3.19	1.05	68	11
	510	304	70	30	398	1.86	306	5.91	3.34	1.30	90	24
	511	373	82	45	230	2.36	628	6.43	3.73	1.38	94	13
	512	409	128	45	380	1.62	340	6.42	3.53	1.22	96	18
	Mean	370	80	35	342	1.73	446	6.36	3.51	1.23	89	24
30	519	340	65	26	230	1.75	566	6.69	4.15	1.63	99	20
	520	264	66	37	444	1.11	229	5.98	3.23	1.17	93	24
	521	282	64	32	246	1.53	530	6.66	3.75	1.29	121	28
	522	234	78	35	345	1.69	349	6.37	3.39	1.14	74	10
	523	257	65	29	207	0.75	699	6.78	3.87	1.33	110	21
	524	311	84	33	358	1.70	306	6.08	3.30	1.19	96	22
	Mean	281	70	32	305	1.42	447	6.43	3.62	1.29	99	21
100	531	280	69	30	222	0.79	476	6.54	3.46	1.12	112	27
	532	305	63	32	245	0.71	501	6.66	3.70	1.25	118	61
	533	276	69	31	301	1.47	484	6.42	3.49	1.19	91	16
	534	260	61	31	282	1.97	393	6.51	3.51	1.17	89	26
	535	291	61	24	260	0.91	493	6.44	3.68	1.33	68	21
	536	239	70	31	385	1.29	345	6.24	3.33	1.14	67	8
	Mean	275	66	30	283	1.19	449	6.47	3.53	1.20	91	27
300	543	315	74	30	461	1.41	307	5.92	3.34	1.29	93	27
	544	343	93	46	411	1.41	470	6.08	3.36	1.24	100	19
	545	273	65	29	350	1.69	490	6.15	3.27	1.14	113	13
	546	498	85	32	371	2.86	341	5.71	3.24	1.31	62	24
	547	----	----	----	----	----	----	----	----	----	----	----
	548	247	68	29	382	1.38	357	6.40	3.72	1.39	117	19
	Mean	335	77	33	395	1.75	393	6.05	3.39	1.27	97	20

---- : Not available

Appendix 28 - 2 Individual blood biochemical findings of female rats treated orally with 4-ethylphenol 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	147	155	15.2	0.66	0.28	10.6	6.9	146	4.35	104
	508	139	151	11.7	0.59	0.31	9.8	6.0	144	4.59	106
	509	99	128	13.6	0.59	0.31	9.5	6.2	145	4.73	103
	510	147	136	17.9	0.55	0.33	9.8	6.8	143	4.37	101
	511	164	124	11.7	0.63	0.31	9.7	5.8	144	4.79	107
	512	155	140	16.3	0.80	0.27	10.1	8.0	146	4.56	106
	Mean	142	139	14.4	0.64	0.30	9.9	6.6	145	4.57	105
30	519	156	148	14.1	0.57	0.27	10.3	7.1	145	4.85	105
	520	135	136	13.7	0.57	0.32	9.6	6.5	145	5.02	105
	521	187	141	16.6	0.60	0.32	10.0	5.7	144	4.98	105
	522	113	129	13.5	0.59	0.34	10.0	6.4	146	4.75	102
	523	181	134	13.7	0.64	0.27	10.3	5.8	145	4.34	104
	524	143	169	16.1	0.64	0.29	10.2	10.1	146	4.43	104
	Mean	153	143	14.6	0.60	0.30	10.1	6.9	145	4.73	104
100	531	173	143	13.5	0.63	0.33	10.1	6.0	146	4.55	105
	532	190	138	15.7	0.62	0.33	10.3	6.0	146	4.77	102
	533	130	162	11.9	0.58	0.27	9.9	6.4	145	5.16	103
	534	148	151	13.0	0.60	0.27	10.3	6.8	145	4.81	102
	535	130	144	19.0	0.60	0.31	9.6	5.9	145	4.93	104
	536	100	137	13.7	0.57	0.30	9.6	5.7	145	4.93	108
	Mean	145	146	14.5	0.60	0.30	10.0	6.1	145	4.86	104
300	543	135	143	13.6	0.55	0.33	9.9	6.7	143	4.52	103
	544	151	119	13.2	0.55	0.30	9.8	6.3	145	4.96	106
	545	178	143	12.7	0.55	0.32	10.0	5.9	145	4.64	105
	546	106	110	20.7	0.73	0.34	9.8	6.8	143	4.57	105
	547	----	----	----	----	----	----	----	----	----	----
	548	187	138	14.3	0.58	0.27	10.1	6.1	145	4.66	106
	Mean	151	131	14.9	0.59	0.31	9.9	6.4	144	4.67	105

---- : Not available

Appendix 29-1 Individual pathological findings of male rats treated orally with 4-ethylphenol 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 Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	002	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Spleen	: Hematopoiesis, extramedullary +
	003	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cyst, solitary +
				Basophilic tubules, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++
	004	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary +
	005	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cast, granular, unilateral +
				Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	006	NAD	a Liver	: Hematopoiesis, extramedullary +
			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-ethylphenol 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
30	013	NAD	Not examined	
	014	NAD	Not examined	
	015	NAD	Not examined	
	016	NAD	Not examined	
	017	NAD	Not examined	
	018	NAD	Not examined	

NAD : No abnormalities detected

Appendix 29-3 Individual pathological findings of male rats treated orally with 4-ethylphenol 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
100	025	NAD	Not examined	
	026	NAD	Not examined	
	027	NAD	Not examined	
	028	NAD	Not examined	
	029	NAD	Not examined	
	030	NAD	Not examined	

NAD : No abnormalities detected

Appendix 29-4 Individual pathological findings of male rats treated orally with 4-ethylphenol 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
300	037	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	038	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	039	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Spleen	: Hematopoiesis, extramedullary +
	040	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary +
	041	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	042	NAD	a Liver	: Hematopoiesis, extramedullary +
			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 30-1 Individual pathological findings of female rats treated orally with 4-ethylphenol 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	: Cyst, solitary, unilateral +
				Basophilic tubules +
				Dilatation, renal pelvis, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++
	502	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Cast, hyaline, unilateral +
				Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary +
	503	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Parathyroid	: Not in section
			Spleen	Hematopoiesis, extramedullary ++
	504	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Spleen	: Hematopoiesis, extramedullary +
	505	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Spleen	: Hematopoiesis, extramedullary ++
	506	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
				Dilatation, renal pelvis, unilateral +
			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 30-2 Individual pathological findings of female rats treated orally with 4-ethylphenol 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
30	513	NAD	Not examined	
	514	NAD	Not examined	
	515	NAD	Not examined	
	516	NAD	Not examined	
	517	NAD	Not examined	
	518	NAD	Not examined	

NAD : No abnormalities detected

Appendix 30-3 Individual pathological findings of female rats treated orally with 4-ethylphenol 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
100	525	NAD	Not examined	
	526	NAD	Not examined	
	527	NAD	Not examined	
	528	NAD	Not examined	
	529	NAD	Not examined	
	530	NAD	Not examined	

NAD : No abnormalities detected

Appendix 30-4 Individual pathological findings of female rats treated orally with 4-ethylphenol 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
300	537	FD Lung : Dark red +	a Lung	: Congestive edema ++
			Liver	: Hematopoiesis, extramedullary +
			Spleen	: Hematopoiesis, extramedullary ++
	538	NAD	a Liver	: Hematopoiesis, extramedullary +
			Spleen	: Hematopoiesis, extramedullary ++
	539	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary ++
	540	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules +
			Spleen	: Hematopoiesis, extramedullary +
	541	NAD	a Liver	: Hematopoiesis, extramedullary +
			Kidney	: Basophilic tubules, unilateral +
			Parathyroid	: Not in section
			Spleen	: Hematopoiesis, extramedullary ++
	542	NAD	a Liver	: Hematopoiesis, extramedullary +
			Spleen	: Hematopoiesis, extramedullary +

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

FD : Found dead

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-ethylphenol 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	Lung	: Accumulation, foam cell +
				Liver	: Microgranuloma +
				Pancreas	: Atrophy, acinar cell, focal +
					Cellular infiltration, lymphocyte, focal +
				Kidney	: Basophilic tubules, unilateral +
					Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	008	NAD	a	Kidney	: Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	009	NAD	a	Kidney	: Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	010	Lung : Red spot +	a	Lung	: Hemorrhage/inflammation, focal +
					Accumulation, foam cell +
				Kidney	: Hyaline droplet, proximal tubular epithelium +
				Prostate	: Cellular infiltration, lymphocyte, interstitium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	011	NAD	a	Kidney	: Hyaline droplet, proximal tubular epithelium +
				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 31-1-2 Individual pathological findings of male rats treated orally with 4-ethylphenol 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)	012	NAD	a Lung	:	Mineralization, artery +
			Kidney	:	Basophilic tubules, unilateral +
					Cellular infiltration, lymphocyte, cortex, unilateral +
			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-ethylphenol 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
30	019	NAD	Not examined	
	020	NAD	Not examined	
	021	NAD	Not examined	
	022	NAD	Not examined	
	023	NAD	Not examined	
	024	NAD	Not examined	

NAD : No abnormalities detected

Appendix 31-3 Individual pathological findings of male rats treated orally with 4-ethylphenol 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
100	031	NAD	Not examined	
	032	NAD	Not examined	
	033	NAD	Not examined	
	034	NAD	Not examined	
	035	NAD	Not examined	
	036	NAD	Not examined	

NAD : No abnormalities detected

Appendix 31-4-1 Individual pathological findings of male rats treated orally with 4-ethylphenol 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
300	043	NAD	a	Kidney	: Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	044	NAD	a	Lung	: Mineralization, artery +
				Kidney	: Eosinophilic body, proximal tubular epithelium +
					Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	045	NAD	a	Kidney	: Hyaline droplet, proximal tubular epithelium +
				Spleen	: Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	046	NAD	a	Lung	: Mineralization, artery +
				Liver	: Necrosis, focal +
				Pancreas	: Fibrosis, focal +
				Kidney	: Basophilic tubules, unilateral +
					Hyaline droplet, proximal tubular epithelium +
				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 31-4-2 Individual pathological findings of male rats treated orally with 4-ethylphenol 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
300 (Continued)	047	NAD	a Lung	:	Hemorrhage/inflammation, focal +
					Mineralization, artery +
			Liver	:	Microgranuloma +
			Kidney	:	Hyaline droplet, proximal tubular epithelium +
			Spleen	:	Hematopoiesis, extramedullary +
					Deposit, brown pigment +
	048	Thymus : Red spots +	a Kidney	:	Eosinophilic body, proximal tubular epithelium +
					Hyaline droplet, proximal tubular epithelium +
			Thymus	:	Hemorrhage +
			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 32-1 Individual pathological findings of female rats treated orally with 4-ethylphenol 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 Liver	: Microgranuloma +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	508	NAD	a Lung	: Mineralization, artery +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	509	NAD	a Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	510	NAD	a Liver	: Microgranuloma +
			Pituitary	: Cyst, Rathke's pouch, anterior lobe ++
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	511	NAD	a Liver	: Microgranuloma +
			Spleen	: Hematopoiesis, extramedullary +
				Deposit, brown pigment +
	512	NAD	a Liver	: Microgranuloma +
			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 32-2 Individual pathological findings of female rats treated orally with 4-ethylphenol 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
30	519	NAD	Not examined	
	520	NAD	Not examined	
	521	NAD	Not examined	
	522	NAD	Not examined	
	523	NAD	Not examined	
	524	NAD	Not examined	

NAD : No abnormalities detected

Appendix 32-3 Individual pathological findings of female rats treated orally with 4-ethylphenol 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
100	531	NAD	Not examined	
	532	NAD	Not examined	
	533	NAD	Not examined	
	534	NAD	Not examined	
	535	NAD	Not examined	
	536	NAD	Not examined	

NAD : No abnormalities detected

Appendix 32-4 Individual pathological findings of female rats treated orally with 4-ethylphenol 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
300	543	NAD	a Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	544	NAD	a Thymus	: Hemorrhage +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	545	Thymus : Red spots +	a Lung	: Accumulation, foam cell +
			Liver	: Microgranuloma +
			Stomach	: Cyst, epidermal, forestomach +
			Thymus	: Hemorrhage +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	546	NAD	a Lung	: Accumulation, foam cell +
			Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +
	547	FD Gastro- : Distention +++ intestinal tract	a Liver	: Hematopoiesis, extramedullary +
			Stomach	: NAD
			Intestine	: NAD
			Kidney	: Basophilic tubules -
			Thymus	: Atrophy, cortical +
			Spleen	: Hematopoiesis, extramedullary ++
	548	NAD	a Spleen	: Hematopoiesis, extramedullary + Deposit, brown pigment +

NAD : No abnormalities detected; + : Slight; ++ : Moderate; +++ : Severe
FD : Found dead
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-ethylphenol 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	54.7	1.54	1.89	0.65	206	304	429	227	7.5	3.2	20.8	286	80.4	58.2
	002	59.5	1.60	2.03	0.68	210	326	455	297	9.2	2.9	18.4	318	68.2	57.4
	003	60.6	1.54	2.05	0.68	245	344	639	219	9.2	3.0	22.9	329	95.5	59.9
	004	57.1	1.59	2.02	0.71	202	338	625	229	9.7	3.4	28.3	301	68.7	36.9
	005	60.3	1.59	1.95	0.70	236	345	448	268	8.9	3.0	22.3	337	70.2	46.7
	006	54.3	1.56	1.72	0.67	154	345	466	194	8.8	3.3	23.4	300	108.4	53.6
	Mean	57.8	1.57	1.94	0.68	209	334	510	239	8.9	3.1	22.7	312	81.9	52.1
30	013	55.8	1.50	2.08	0.65	275	305	476	252	7.3	3.1	20.9	300	86.6	43.8
	014	57.4	1.61	1.88	0.71	236	315	509	266	8.0	3.5	26.7	336	89.8	64.7
	015	61.2	1.65	2.16	0.74	212	357	657	288	10.9	3.2	20.7	365	80.1	53.1
	016	55.5	1.51	1.76	0.67	206	311	434	244	10.4	3.0	25.0	309	101.6	55.5
	017	59.4	1.57	2.05	0.71	210	332	496	223	9.1	3.4	26.3	341	108.5	62.5
	018	55.8	1.48	1.77	0.57	196	318	437	255	8.1	2.9	22.7	312	80.7	51.5
	Mean	57.5	1.55	1.95	0.68	223	323	502	255	9.0	3.2	23.7	327	91.2	55.2
100	025	57.3	1.56	2.02	0.67	197	314	425	257	10.5	2.8	20.9	316	83.9	49.7
	026	53.8	1.51	1.82	0.68	174	292	439	253	9.9	2.8	20.6	362	105.1	54.4
	027	54.8	1.59	1.81	0.67	219	296	450	249	10.0	2.9	21.9	295	78.8	46.3
	028	54.6	1.56	1.93	0.61	189	309	466	272	10.2	3.2	23.9	314	93.2	46.2
	029	52.0	1.47	1.67	0.59	163	279	389	233	7.4	2.8	21.6	301	79.4	49.9
	030	56.0	1.52	1.94	0.62	159	333	446	203	9.2	3.1	27.7	310	86.1	49.0
	Mean	54.8	1.54	1.87	0.64	184	304	436	245	9.5	2.9	22.8	316	87.8	49.3
300	037	54.3	1.51	2.00	0.60	236	307	483	230	10.0	2.6	18.7	271	94.6	57.8
	038	54.0	1.50	2.01	0.70	163	307	464	223	9.8	3.0	23.5	306	80.8	53.7
	039	35.9	1.37	1.39	0.45	89	220	342	162	7.8	2.2	15.9	213	58.9	45.1
	040	56.9	1.55	2.17	0.66	188	334	470	227	9.7	3.0	22.9	309	99.2	50.5
	041	51.4	1.45	1.81	0.63	183	274	429	223	5.9	2.8	24.9	301	79.7	40.4
	042	47.5	1.47	1.64	0.60	150	321	397	208	9.8	2.3	16.5	296	83.3	58.9
	Mean	50.0	1.48	1.84	0.61	168	294	431	212	8.8	2.7	20.4	283	82.8	51.1

† : Total weights of the prostate and seminal vesicle

Appendix 34 Individual absolute organ weights of female rats treated orally with 4-ethylphenol 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	51.6	1.51	1.65	0.58	139	291	412	251	7.8	3.0	20.2	12.0	36.3
	502	51.7	1.47	1.77	0.61	140	301	384	228	9.5	3.5	19.5	19.2	40.5
	503	56.5	1.47	1.76	0.68	188	316	443	271	7.4	3.4	22.3	16.3	48.4
	504	52.0	1.48	1.75	0.58	169	282	405	212	8.8	2.9	18.6	16.5	41.7
	505	54.3	1.48	1.72	0.66	189	295	416	204	8.9	3.4	20.1	16.7	41.0
	506	51.4	1.52	1.66	0.73	152	316	412	224	11.2	3.1	20.6	15.6	41.1
	Mean	52.9	1.49	1.72	0.64	163	300	412	232	8.9	3.2	20.2	16.1	41.5
30	513	53.3	1.42	1.76	0.58	170	302	458	224	10.2	3.2	19.8	17.7	47.9
	514	50.6	1.49	1.67	0.62	173	304	451	213	10.4	3.4	19.1	15.2	45.2
	515	53.2	1.47	1.70	0.60	218	296	451	221	8.6	2.9	20.8	12.9	42.8
	516	54.6	1.43	1.77	0.64	195	297	447	276	10.8	3.4	23.0	13.8	42.3
	517	52.1	1.52	1.72	0.62	191	295	409	289	10.0	3.3	24.3	15.9	54.9
	518	56.1	1.51	1.80	0.67	182	311	433	235	9.6	3.5	21.8	16.0	40.3
	Mean	53.3	1.47	1.74	0.62	188	301	442	243	9.9	3.3	21.5	15.3	45.6
100	525	53.3	1.40	1.80	0.59	205	279	444	195	8.5	3.0	19.0	20.1	55.5
	526	52.5	1.44	1.67	0.62	180	304	439	271	9.4	3.6	15.8	13.8	60.7
	527	52.4	1.48	1.76	0.64	163	323	431	216	8.5	3.8	21.4	16.5	38.7
	528	51.9	1.48	1.73	0.61	201	317	439	236	11.2	3.2	20.3	14.3	33.4
	529	51.9	1.51	1.82	0.65	154	298	444	271	8.4	2.7	20.7	19.6	39.7
	530	56.6	1.52	1.96	0.71	170	321	444	308	8.5	3.0	18.8	18.0	33.2
	Mean	53.1	1.47	1.79	0.64	179	307	440	250	9.1	3.2	19.3	17.1	43.5
300	537	(33.2)	(1.27)	(1.44)	(0.50)	(119)	(211)	(403)	(161)	(7.1)	(2.5)	(10.3)	(8.9)	(35.9)
	538	52.3	1.48	2.05	0.65	206	375	449	231	9.2	3.4	21.0	19.2	33.8
	539	45.0	1.40	1.65	0.59	157	244	353	274	9.0	3.0	21.5	13.5	46.8
	540	51.0	1.48	1.92	0.64	179	300	431	208	10.0	3.3	19.4	21.5	52.9
	541	32.2	1.28	1.12	0.43	91	199	279	125	6.4	1.9	13.2	8.1	24.9
	542	46.1	1.50	1.54	0.54	137	267	380	239	9.4	2.6	17.5	15.7	44.2
	Mean	45.3	1.43	1.66	0.57	154	277	378	215	8.8	2.8	18.5	15.6	40.5

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

Appendix 35 Individual relative organ weights of male rats treated orally with 4-ethylphenol 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	54.7	2.82	3.46	1.19	377	556	784	415	13.7	5.9	38.0	523	147.0	106.4
	002	59.5	2.69	3.41	1.14	353	548	765	499	15.5	4.9	30.9	534	114.6	96.5
	003	60.6	2.54	3.38	1.12	404	568	1054	361	15.2	5.0	37.8	543	157.6	98.8
	004	57.1	2.78	3.54	1.24	354	592	1095	401	17.0	6.0	49.6	527	120.3	64.6
	005	60.3	2.64	3.23	1.16	391	572	743	444	14.8	5.0	37.0	559	116.4	77.4
	006	54.3	2.87	3.17	1.23	284	635	858	357	16.2	6.1	43.1	552	199.6	98.7
	Mean	57.8	2.72	3.37	1.18	361	579	883	413	15.4	5.5	39.4	540	142.6	90.4
30	013	55.8	2.69	3.73	1.16	493	547	853	452	13.1	5.6	37.5	538	155.2	78.5
	014	57.4	2.80	3.28	1.24	411	549	887	463	13.9	6.1	46.5	585	156.4	112.7
	015	61.2	2.70	3.53	1.21	346	583	1074	471	17.8	5.2	33.8	596	130.9	86.8
	016	55.5	2.72	3.17	1.21	371	560	782	440	18.7	5.4	45.0	557	183.1	100.0
	017	59.4	2.64	3.45	1.20	354	559	835	375	15.3	5.7	44.3	574	182.7	105.2
	018	55.8	2.65	3.17	1.02	351	570	783	457	14.5	5.2	40.7	559	144.6	92.3
	Mean	57.5	2.70	3.39	1.17	388	561	869	443	15.6	5.5	41.3	568	158.8	95.9
100	025	57.3	2.72	3.53	1.17	344	548	742	449	18.3	4.9	36.5	551	146.4	86.7
	026	53.8	2.81	3.38	1.26	323	543	816	470	18.4	5.2	38.3	673	195.4	101.1
	027	54.8	2.90	3.30	1.22	400	540	821	454	18.2	5.3	40.0	538	143.8	84.5
	028	54.6	2.86	3.53	1.12	346	566	853	498	18.7	5.9	43.8	575	170.7	84.6
	029	52.0	2.83	3.21	1.13	313	537	748	448	14.2	5.4	41.5	579	152.7	96.0
	030	56.0	2.71	3.46	1.11	284	595	796	363	16.4	5.5	49.5	554	153.8	87.5
	Mean	54.8	2.81	3.40	1.17	335	555	796	447	17.4	5.4	41.6	578	160.5	90.1
300	037	54.3	2.78	3.68	1.10	435	565	890	424	18.4	4.8	34.4	499	174.2	106.4
	038	54.0	2.78	3.72	1.30	302	569	859	413	18.1	5.6	43.5	567	149.6	99.4
	039	35.9	3.82	3.87	1.25	248	613	953	451	21.7	6.1	44.3	593	164.1	125.6
	040	56.9	2.72	3.81	1.16	330	587	826	399	17.0	5.3	40.2	543	174.3	88.8
	041	51.4	2.82	3.52	1.23	356	533	835	434	11.5	5.4	48.4	586	155.1	78.6
	042	47.5	3.09	3.45	1.26	316	676	836	438	20.6	4.8	34.7	623	175.4	124.0
	Mean	50.0	3.00	3.68	1.22	331	591	867	427	17.9	5.3	40.9	569	165.5	103.8

† : Total weights of the prostate and seminal vesicle

Appendix 36 Individual relative organ weights of female rats treated orally with 4-ethylphenol 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	51.6	2.93	3.20	1.12	269	564	798	486	15.1	5.8	39.1	23.3	70.3
	502	51.7	2.84	3.42	1.18	271	582	743	441	18.4	6.8	37.7	37.1	78.3
	503	56.5	2.60	3.12	1.20	333	559	784	480	13.1	6.0	39.5	28.8	85.7
	504	52.0	2.85	3.37	1.12	325	542	779	408	16.9	5.6	35.8	31.7	80.2
	505	54.3	2.73	3.17	1.22	348	543	766	376	16.4	6.3	37.0	30.8	75.5
	506	51.4	2.96	3.23	1.42	296	615	802	436	21.8	6.0	40.1	30.4	80.0
	Mean	52.9	2.82	3.25	1.21	307	568	779	438	17.0	6.1	38.2	30.4	78.3
30	513	53.3	2.66	3.30	1.09	319	567	859	420	19.1	6.0	37.1	33.2	89.9
	514	50.6	2.94	3.30	1.23	342	601	891	421	20.6	6.7	37.7	30.0	89.3
	515	53.2	2.76	3.20	1.13	410	556	848	415	16.2	5.5	39.1	24.2	80.5
	516	54.6	2.62	3.24	1.17	357	544	819	505	19.8	6.2	42.1	25.3	77.5
	517	52.1	2.92	3.30	1.19	367	566	785	555	19.2	6.3	46.6	30.5	105.4
	518	56.1	2.69	3.21	1.19	324	554	772	419	17.1	6.2	38.9	28.5	71.8
	Mean	53.3	2.77	3.26	1.17	353	565	829	456	18.7	6.2	40.3	28.6	85.7
100	525	53.3	2.63	3.38	1.11	385	523	833	366	15.9	5.6	35.6	37.7	104.1
	526	52.5	2.74	3.18	1.18	343	579	836	516	17.9	6.9	30.1	26.3	115.6
	527	52.4	2.82	3.36	1.22	311	616	823	412	16.2	7.3	40.8	31.5	73.9
	528	51.9	2.85	3.33	1.18	387	611	846	455	21.6	6.2	39.1	27.6	64.4
	529	51.9	2.91	3.51	1.25	297	574	855	522	16.2	5.2	39.9	37.8	76.5
	530	56.6	2.69	3.46	1.25	300	567	784	544	15.0	5.3	33.2	31.8	58.7
	Mean	53.1	2.77	3.37	1.20	337	578	830	469	17.1	6.1	36.5	32.1	82.2
	537	(33.2)	(3.83)	(4.34)	(1.51)	(358)	(636)	(1214)	(485)	(21.4)	(7.5)	(31.0)	(26.8)	(108.1)
300	538	52.3	2.83	3.92	1.24	394	717	859	442	17.6	6.5	40.2	36.7	64.6
	539	45.0	3.11	3.67	1.31	349	542	784	609	20.0	6.7	47.8	30.0	104.0
	540	51.0	2.90	3.76	1.25	351	588	845	408	19.6	6.5	38.0	42.2	103.7
	541	32.2	3.98	3.48	1.34	283	618	866	388	19.9	5.9	41.0	25.2	77.3
	542	46.1	3.25	3.34	1.17	297	579	824	518	20.4	5.6	38.0	34.1	95.9
	Mean	45.3	3.21	3.63	1.26	335	609	836	473	19.5	6.2	41.0	33.6	89.1

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

Appendix 37 Individual absolute organ weights of male rats treated orally with 4-ethylphenol 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	420	2.15	12.11	2.65	0.58	1.32	1.48	0.34	31.6	11.9	69.9	3.64	0.66	1.85	1.20
	008	413	2.05	12.83	2.98	0.75	1.37	1.41	0.51	29.0	13.2	63.2	3.04	0.82	1.17	1.19
	009	384	2.10	12.14	2.89	0.88	1.27	1.29	0.39	24.5	13.2	63.9	3.25	0.44	1.51	1.28
	010	452	2.16	13.40	2.94	0.91	1.41	1.60	0.49	32.2	15.3	62.3	3.50	0.80	1.96	1.23
	011	431	2.09	12.36	3.11	0.88	1.28	1.44	0.43	30.9	12.7	53.8	3.26	0.76	1.88	1.13
	012	490	2.18	14.37	3.27	0.82	1.51	1.46	0.35	30.0	16.8	72.8	3.39	0.96	1.91	1.29
	Mean	432	2.12	12.87	2.97	0.80	1.36	1.45	0.42	29.7	13.9	64.3	3.35	0.74	1.71	1.22
30	019	416	2.02	11.80	2.72	0.82	1.38	1.32	0.52	29.0	11.7	67.9	3.02	0.81	1.88	1.27
	020	452	2.19	14.30	3.09	0.80	1.60	1.48	0.56	36.0	13.0	57.4	3.67	0.53	1.56	1.17
	021	477	2.23	14.66	3.09	0.94	1.58	1.67	0.53	27.5	15.0	78.1	3.55	0.73	1.80	1.43
	022	380	2.08	10.85	2.81	0.76	1.22	1.45	0.35	31.2	12.3	59.2	3.52	0.63	1.99	1.19
	023	429	2.16	12.96	2.95	0.79	1.39	1.40	0.53	31.8	13.0	56.1	3.61	0.51	1.44	1.28
	024	440	2.07	13.31	2.95	0.76	1.37	1.42	0.35	25.8	14.6	63.0	3.59	0.58	1.75	1.28
	Mean	432	2.13	12.98	2.94	0.81	1.42	1.46	0.47	30.2	13.3	63.6	3.49	0.63	1.74	1.27
100	031	403	2.23	10.15	3.15	0.89	1.40	1.31	0.37	35.1	11.2	65.7	3.00	0.32	1.51	0.98
	032	449	2.16	12.72	3.04	0.96	1.35	1.46	0.41	29.3	16.3	70.0	3.74	0.79	1.95	1.38
	033	471	2.11	13.57	3.21	0.97	1.39	1.53	0.35	28.3	14.8	55.3	3.51	0.72	2.03	1.16
	034	465	2.12	15.07	3.20	0.88	1.42	1.63	0.42	31.9	12.7	72.4	3.48	0.73	2.10	1.28
	035	417	2.05	11.73	2.68	0.72	1.35	1.41	0.52	29.6	12.5	68.2	3.87	0.46	2.14	1.28
	036	447	2.05	13.18	2.94	0.90	1.45	1.52	0.38	23.2	13.8	51.7	3.43	0.60	1.73	1.09
	Mean	442	2.12	12.74	3.04	0.89	1.39	1.48	0.41	29.6	13.6	63.9	3.51	0.60	1.91	1.20
300	043	439	2.04	11.98	2.87	0.72	1.34	1.43	0.37	32.4	15.5	63.2	3.49	0.78	2.09	1.29
	044	447	2.13	15.01	3.31	0.72	1.46	1.37	0.58	32.7	12.9	59.8	3.70	0.58	1.62	1.20
	045	471	2.02	15.95	3.16	0.94	1.56	1.54	0.50	30.8	12.8	66.1	3.16	0.53	1.57	1.12
	046	437	1.93	12.62	3.05	0.87	1.36	1.28	0.56	32.5	12.4	79.4	2.86	0.52	1.91	1.18
	047	424	1.96	12.66	2.57	0.69	1.38	1.27	0.42	31.4	12.9	57.8	3.20	0.60	2.07	1.07
	048	438	1.99	13.95	2.86	0.88	1.35	1.37	0.62	28.0	11.5	56.4	3.24	0.43	1.69	1.21
	Mean	443	2.01	13.70	2.97	0.80	1.41	1.38	0.51	31.3	13.0	63.8	3.28	0.57	1.83	1.18

Appendix 38 Individual absolute organ weights of female rats treated orally with 4-ethylphenol 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	235	1.90	6.58	1.56	0.47	0.82	1.05	0.42	23.9	13.5	72.7	89.1	0.42
	508	304	2.06	8.82	2.05	0.59	1.01	1.23	0.46	28.9	15.3	71.1	94.2	0.84
	509	250	1.83	7.01	1.82	0.55	0.96	1.14	0.34	20.3	18.5	78.2	78.1	0.76
	510	222	1.91	5.71	1.80	0.48	0.84	0.96	0.36	24.2	10.7	73.7	76.1	0.48
	511	261	1.94	7.12	1.99	0.53	0.86	0.98	0.42	23.8	13.1	73.6	75.1	1.37
	512	248	1.95	6.91	1.70	0.47	0.90	1.05	0.37	19.4	16.0	62.1	72.9	0.59
	Mean	253	1.93	7.03	1.82	0.52	0.90	1.07	0.40	23.4	14.5	71.9	80.9	0.74
30	519	249	1.88	6.78	1.86	0.50	0.90	0.97	0.39	24.2	12.7	69.0	64.4	0.53
	520	248	1.97	6.72	1.93	0.55	0.91	1.06	0.31	26.1	16.3	69.3	69.3	0.82
	521	246	1.87	6.73	1.69	0.48	0.89	1.02	0.41	16.5	16.7	53.7	78.9	0.53
	522	252	2.05	7.30	1.85	0.55	0.92	1.13	0.24	27.0	15.1	80.6	99.1	0.47
	523	250	1.85	6.91	1.85	0.42	0.97	1.14	0.44	22.7	17.1	65.7	75.5	0.89
	524	239	1.84	6.94	1.79	0.46	0.96	0.93	0.34	21.2	11.7	67.8	78.6	1.02
	Mean	247	1.91	6.90	1.83	0.49	0.93	1.04	0.36	23.0	14.9	67.7	77.6	0.71
100	531	253	1.92	6.54	1.71	0.47	0.93	1.04	0.48	25.1	15.5	67.3	70.6	0.48
	532	288	1.91	8.62	2.09	0.60	0.99	1.23	0.36	19.2	17.4	68.4	99.9	0.49
	533	263	1.95	7.42	1.86	0.51	0.90	1.04	0.46	26.8	18.0	82.5	95.0	0.63
	534	313	1.96	9.47	2.22	0.56	1.01	1.17	0.37	23.9	16.8	71.9	100.2	0.36
	535	204	1.86	5.67	1.65	0.38	0.75	0.88	0.28	23.1	13.1	72.6	71.1	0.83
	536	237	1.92	6.41	1.79	0.44	0.80	0.99	0.35	24.4	14.5	67.3	98.9	0.86
	Mean	260	1.92	7.36	1.89	0.49	0.90	1.06	0.38	23.8	15.9	71.7	89.3	0.61
300	543	253	1.87	7.16	1.90	0.70	0.86	1.12	0.61	21.7	13.1	71.1	92.8	0.50
	544	252	1.96	6.78	1.85	0.50	0.83	1.10	0.31	19.3	14.6	59.0	89.3	0.49
	545	223	1.70	5.75	1.54	0.50	0.87	1.08	0.43	24.1	15.5	57.5	58.3	0.55
	546	244	1.70	6.16	1.81	0.59	0.86	1.08	0.53	21.4	12.3	72.0	84.9	0.52
	547	(16)	(0.93)	(0.66)	(0.29)	(0.06)	(0.14)	(0.30)	(0.03)	(4.1)	(1.5)	(6.0)	(2.2)	(0.02)
	548	252	1.81	6.63	1.76	0.56	0.86	1.00	0.50	23.3	12.1	60.1	81.6	0.95
	Mean	245	1.81	6.50	1.77	0.57	0.86	1.08	0.48	22.0	13.5	63.9	81.4	0.60

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

Appendix 39 Individual relative organ weights of male rats treated orally with 4-ethylphenol 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	420	0.51	2.88	0.63	0.14	0.31	0.35	0.08	7.5	2.8	16.6	0.87	0.16	0.44	0.29
	008	413	0.50	3.11	0.72	0.18	0.33	0.34	0.12	7.0	3.2	15.3	0.74	0.20	0.28	0.29
	009	384	0.55	3.16	0.75	0.23	0.33	0.34	0.10	6.4	3.4	16.6	0.85	0.11	0.39	0.33
	010	452	0.48	2.96	0.65	0.20	0.31	0.35	0.11	7.1	3.4	13.8	0.77	0.18	0.43	0.27
	011	431	0.48	2.87	0.72	0.20	0.30	0.33	0.10	7.2	2.9	12.5	0.76	0.18	0.44	0.26
	012	490	0.44	2.93	0.67	0.17	0.31	0.30	0.07	6.1	3.4	14.9	0.69	0.20	0.39	0.26
	Mean	432	0.49	2.99	0.69	0.19	0.32	0.34	0.10	6.9	3.2	15.0	0.78	0.17	0.40	0.28
30	019	416	0.49	2.84	0.65	0.20	0.33	0.32	0.13	7.0	2.8	16.3	0.73	0.19	0.45	0.31
	020	452	0.48	3.16	0.68	0.18	0.35	0.33	0.12	8.0	2.9	12.7	0.81	0.12	0.35	0.26
	021	477	0.47	3.07	0.65	0.20	0.33	0.35	0.11	5.8	3.1	16.4	0.74	0.15	0.38	0.30
	022	380	0.55	2.86	0.74	0.20	0.32	0.38	0.09	8.2	3.2	15.6	0.93	0.17	0.52	0.31
	023	429	0.50	3.02	0.69	0.18	0.32	0.33	0.12	7.4	3.0	13.1	0.84	0.12	0.34	0.30
	024	440	0.47	3.03	0.67	0.17	0.31	0.32	0.08	5.9	3.3	14.3	0.82	0.13	0.40	0.29
	Mean	432	0.49	3.00	0.68	0.19	0.33	0.34	0.11	7.1	3.1	14.7	0.81	0.15	0.41	0.30
100	031	403	0.55	2.52	0.78	0.22	0.35	0.33	0.09	8.7	2.8	16.3	0.74	0.08	0.37	0.24
	032	449	0.48	2.83	0.68	0.21	0.30	0.33	0.09	6.5	3.6	15.6	0.83	0.18	0.43	0.31
	033	471	0.45	2.88	0.68	0.21	0.30	0.32	0.07	6.0	3.1	11.7	0.75	0.15	0.43	0.25
	034	465	0.46	3.24	0.69	0.19	0.31	0.35	0.09	6.9	2.7	15.6	0.75	0.16	0.45	0.28
	035	417	0.49	2.81	0.64	0.17	0.32	0.34	0.12	7.1	3.0	16.4	0.93	0.11	0.51	0.31
	036	447	0.46	2.95	0.66	0.20	0.32	0.34	0.09	5.2	3.1	11.6	0.77	0.13	0.39	0.24
	Mean	442	0.48	2.87	0.69	0.20	0.32	0.34	0.09	6.7	3.1	14.5	0.80	0.14	0.43	0.27
300	043	439	0.46	2.73	0.65	0.16	0.31	0.33	0.08	7.4	3.5	14.4	0.79	0.18	0.48	0.29
	044	447	0.48	3.36	0.74	0.16	0.33	0.31	0.13	7.3	2.9	13.4	0.83	0.13	0.36	0.27
	045	471	0.43	3.39	0.67	0.20	0.33	0.33	0.11	6.5	2.7	14.0	0.67	0.11	0.33	0.24
	046	437	0.44	2.89	0.70	0.20	0.31	0.29	0.13	7.4	2.8	18.2	0.65	0.12	0.44	0.27
	047	424	0.46	2.99	0.61	0.16	0.33	0.30	0.10	7.4	3.0	13.6	0.75	0.14	0.49	0.25
	048	438	0.45	3.18	0.65	0.20	0.31	0.31	0.14	6.4	2.6	12.9	0.74	0.10	0.39	0.28
	Mean	443	0.45	3.09	0.67	0.18	0.32	0.31	0.12	7.1	2.9	14.4	0.74	0.13	0.42	0.27

Appendix 40 Individual relative organ weights of female rats treated orally with 4-ethylphenol 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	235	0.81	2.80	0.66	0.20	0.35	0.45	0.18	10.2	5.7	30.9	37.9	0.18
	508	304	0.68	2.90	0.67	0.19	0.33	0.40	0.15	9.5	5.0	23.4	31.0	0.28
	509	250	0.73	2.80	0.73	0.22	0.38	0.46	0.14	8.1	7.4	31.3	31.2	0.30
	510	222	0.86	2.57	0.81	0.22	0.38	0.43	0.16	10.9	4.8	33.2	34.3	0.22
	511	261	0.74	2.73	0.76	0.20	0.33	0.38	0.16	9.1	5.0	28.2	28.8	0.52
	512	248	0.79	2.79	0.69	0.19	0.36	0.42	0.15	7.8	6.5	25.0	29.4	0.24
	Mean	253	0.77	2.77	0.72	0.20	0.36	0.42	0.16	9.3	5.7	28.7	32.1	0.29
30	519	249	0.76	2.72	0.75	0.20	0.36	0.39	0.16	9.7	5.1	27.7	25.9	0.21
	520	248	0.79	2.71	0.78	0.22	0.37	0.43	0.13	10.5	6.6	27.9	27.9	0.33
	521	246	0.76	2.74	0.69	0.20	0.36	0.41	0.17	6.7	6.8	21.8	32.1	0.22
	522	252	0.81	2.90	0.73	0.22	0.37	0.45	0.10	10.7	6.0	32.0	39.3	0.19
	523	250	0.74	2.76	0.74	0.17	0.39	0.46	0.18	9.1	6.8	26.3	30.2	0.36
	524	239	0.77	2.90	0.75	0.19	0.40	0.39	0.14	8.9	4.9	28.4	32.9	0.43
	Mean	247	0.77	2.79	0.74	0.20	0.38	0.42	0.15	9.3	6.0	27.4	31.4	0.29
100	531	253	0.76	2.58	0.68	0.19	0.37	0.41	0.19	9.9	6.1	26.6	27.9	0.19
	532	288	0.66	2.99	0.73	0.21	0.34	0.43	0.13	6.7	6.0	23.8	34.7	0.17
	533	263	0.74	2.82	0.71	0.19	0.34	0.40	0.17	10.2	6.8	31.4	36.1	0.24
	534	313	0.63	3.03	0.71	0.18	0.32	0.37	0.12	7.6	5.4	23.0	32.0	0.12
	535	204	0.91	2.78	0.81	0.19	0.37	0.43	0.14	11.3	6.4	35.6	34.9	0.41
	536	237	0.81	2.70	0.76	0.19	0.34	0.42	0.15	10.3	6.1	28.4	41.7	0.36
	Mean	260	0.75	2.82	0.73	0.19	0.35	0.41	0.15	9.3	6.1	28.1	34.6	0.25
300	543	253	0.74	2.83	0.75	0.28	0.34	0.44	0.24	8.6	5.2	28.1	36.7	0.20
	544	252	0.78	2.69	0.73	0.20	0.33	0.44	0.12	7.7	5.8	23.4	35.4	0.19
	545	223	0.76	2.58	0.69	0.22	0.39	0.48	0.19	10.8	7.0	25.8	26.1	0.25
	546	244	0.70	2.52	0.74	0.24	0.35	0.44	0.22	8.8	5.0	29.5	34.8	0.21
	547	(16)	(5.81)	(4.12)	(1.81)	(0.37)	(0.87)	(1.88)	(0.19)	(25.6)	(9.4)	(37.5)	(13.8)	(0.12)
	548	252	0.72	2.63	0.70	0.22	0.34	0.40	0.20	9.2	4.8	23.8	32.4	0.38
	Mean	245	0.74	2.65	0.72	0.23	0.35	0.44	0.19	9.0	5.6	26.1	33.1	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-ethylphenol during 18 days from 4 days of age to weaning

(g)

Animal number	Days of age 4	10	16	21	Gain 4-21
601	289	310	334	320	31
602	295	327	341	333	38
603	314	352	350	320	6
604	329	349	382	344	15
605	279	318	339	307	28
606	306	349	352	356	50
607	267	319	336	325	58
608	278	322	340	324	46
609	264	301	311	303	39
610	226	269	270	256	30
611	246	290	307	292	46
612	285	315	332	328	43
Mean	282	318	333	317	36

Appendix 42 Individual food consumption of foster mother rats that reared pups treated orally with 4-ethylphenol during 18 days from 4 days of age to weaning

(g)

Animal number	Days of age 7	13	19
601	53	66	81
602	55	72	84
603	52	66	86
604	58	76	83
605	52	67	84
606	57	72	84
607	57	63	79
608	61	76	84
609	55	59	77
610	50	61	74
611	56	70	80
612	51	71	85
Mean	55	68	82

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