2,4,6-トリニトロフェノールのラット新生児における哺育期投与試験

－最終報告書－

2000 年 10 月 11 日

試験委託者　：厚生省生活衛生局
東京都千代田区霞ヶ関 1-2-2 (〒100-0013)

試験施設　　：株式会社パナファーム・ラボラトリーズ 安全性研究所
熊本県宇土市栗崎町 1285 番地 (〒869-0425)

信 頼 性 保 証 書

試験番号:49816

試験表題:2,4,6-トリニトロフェノールのラット新生児における哺育期投与試験

上記の試験の各段階を信頼性保証担当者が調査した．調査の段階，調査実施日，並びに運営管理者及び試験責任者への調査結果の報告日は下記のとおりである．

調査の段階	調査実施日	調査結果の報告日
試験計画書	1999 年 8 月 4 日	1999 年 8 月 4 日
試験計画書の変更書		
PPLPA 4981601	1999 年 8 月 26 日	2000 年 4 月 3 日
PPLPA 4981602	1999 年 10 月 1 日	2000 年 4 月 3 日
PPLPA 4981603	2000 年 3 月 14 日	2000 年 4 月 3 日
PPLPA 4981604	2000 年 10 月 11 日	2000 年 10 月 11 日
動物の受入れ及び検収	1999 年 8 月 17 日	1999 年 8 月 18 日
被験物質の情報，受領，保存及び混合物調製	1999 年 8 月 27 日	1999 年 8 月 30 日
群分け	1999 年 8 月 29 日	1999 年 8 月 30 日
分析成績書(濃度確認)及び試験記録	1999 年 8 月 30 日	1999 年 8 月 30 日
投与及び一般状態観察	1999 年 8 月 30 日	1999 年 8 月 30 日
発育分化検査	1999 年 8 月 30 日	1999 年 8 月 30 日
感覚機能検査	1999 年 8 月 31 日	1999 年 8 月 31 日
採血，血液学検査及び剖検	1999 年 9 月 17 日	1999 年 9 月 17 日
病理組織標本作製	1999 年 10 月 15 日	1999 年 10 月 16 日
尿検査	1999 年 11 月 12 日	1999 年 11 月 12 日
剖検	1999 年 11 月 19 日	1999 年 11 月 19 日
血液生化学検査	1999 年 11 月 22 日	1999 年 11 月 22 日
最終報告書 (案)	2000 年 2 月 9 日～ 2 月 17 日 2000 年 3 月 10 日～ 3 月 13 日	2000 年 3 月 13 日
同上再調査	2000 年 3 月 14 日	2000 年 3 月 14 日
試験記録(最終報告書案作成時)	2000 年 3 月 21 日～ 3 月 22 日	2000 年 3 月 22 日
最終報告書及び保存資料	2000 年 10 月 11 日	2000 年 10 月 11 日

本試験は，OECD-GLP(OECD Principles of GLP,1981)及び厚生省の化学物質 GLP（環保業第 39 号，薬発第 229 号，59 基局第 85 号 1984，一部改正 1988）に従って実施されたことを保証する．また本報告書は，信頼性保証担当者が調査し，試験の方法が正確に記載され，かつ生データが正確に反映されていることを確認した．

信頼性保証部門責任者

2000年 10月 11日 [redacted]

株式会社パナファーム・ラボラトリーズ

陳 述 書

試験の表題：2,4,6-トリニトロ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　：49816

表記試験は，OECD-GLP「OECD Principles of Good Laboratory Practice (1981 年 5 月 OECD 勧告)」及び厚生省の化学物質 GLP「新規化学物質に係る試験及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，薬発第 229 及び 59 基局第 85 号)並びにその改正 (昭和 63 年 11 月 18 日付)」を遵守して実施した.

試験責任者

2000 年 10 月 11 日 [redacted]

株式会社パナファーム・ラボラトリーズ

署 名 欄

試験責任者

2000 年 10 月 11 日 [redacted]

株式会社パナファーム・ラボラトリーズ

試験期間

1. 試験開始日 : 1999 年 8 月 4 日
2. 動物 (母動物)入荷日
   : 1999 年 8 月 17 日
3. 投与開始日 : 1999 年 8 月 30 日
4. 剖検日 : 投与期間終了時 ; 1999 年 9 月 17 日
   検査期間終了時 ; 1999 年 11 月 19 日
5. 試験終了日 : 2000 年 10 月 11 日

試験の実施基準

1. GLP : OECD-GLP ; OECD Principles of Good Laboratory Practice (1981 年 5 月 OECD 勧告)
   化学物質 GLP ; 新規化学物質に係る試験及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, 薬発第 229 号及び 59 基局第 85 号)並びにその改正 (昭和 63 年 11 月 18 日付)

試験の信頼性に悪影響を及ぼす疑いのある予期しえなかった事態及び試験計画書からの逸脱

試験の信頼性に悪影響を及ぼす疑いのある予期しえなかった事態の発生はなく, また, 試験計画書からの逸脱もなかった.

保存物品及び保存場所

1. 試験計画に関する記録
2. 使用動物に関する記録
3. 飼育環境に関する記録
4. 被験物質に関する記録
5. 試験結果に関する記録
6. 保存用被験物質
7. 標本
8. 報告書
9. CD-R
10. そのほかの試験に関係した資料

なお，上記の資料は株式会社パナファーム・ラボラトリーズの資料保管庫に最終報告書提出後 10 年間 (2000 年 10 月 12 日~2010 年 10 月 11 日) 保存する．10 年間経過後の取扱いについては，試験委託者と協議の上決定する．

試験関係者

1. 試験責任者
2. 試験担当責任者
3. 被験物質管理
4. 被験物質混合物調製等
5. 被験物質混合物の濃度分析
6. 動物の受入れ
7. 検疫
8. 飼育管理
9. 群分け

[redacted]

10. 投与

11. 一般状態観察

12. 体重測定

13. 摂餌量測定

14. 尿検査

15. 血液学検査

16. 血液生化学検査

17. 分娩時及び哺育期検査

18. 感覚機能検査

19. 発育分化検査

20. 剖検

21. 器官重量測定

22. 病理組織標本作製

23. 病理組織学検査

24. コンピュータシステム管理

[redacted]

目 次

添付資料

1. 被験物質原体の分析成績書
2. 被験液の安定性試験報告書
3. 被験液の濃度確認成績書

Appendix (個別データ)

要 約

2,4,6-トリニトロフェノールの安全性に関する毒性試験の一環として，1 群雌雄各 6 匹の哺育期間中のラット[Crj:CD(SD)IGS]新生児に 0 (対照)，5，20 及び 80 mg/kg の用量で 18 日間反復経口投与するとともに，63 日間の回復期間を設けて，その毒性及び回復性について検討した．また，成獣ラットの毒性試験成績と比較して相違点を検索し，以下の結果を得た．

試験期間を通して死亡例はなかった．一般状態では，被毛の黄色化が投与期間中に 5 mg/kg 以上の群の雌雄全例で認められた．この被毛の黄色化は，20 及び 80 mg/kg 群では回復期間終了時まで継続して認められたが，5 mg/kg 群では回復期間中にほぼ全例で消失した．

体重では，80 mg/kg 群の雄で投与期間中に，20 mg/kg 以上の群の雌で投与期間終了後に体重の増加抑制が認められた．離乳後 (投与期間終了後) に測定した摂餌量では，雌雄とも被験物質投与の影響は認められなかった．

発育分化検査，感覚機能検査，尿検査，血液学検査及び血液生化学検査では，雌雄とも被験物質投与の影響は認められなかった．

器官重量では，22 日齢剖検例 (投与期間終了時)において 80 mg/kg 群の雌雄で肝臓の重量増加がみられたが，病理組織学検査では雌雄とも被験物質投与に起因した変化は認められなかった．

以上のように，本試験では雌雄とも 5 mg/kg 群から被毛の黄色化が認められたことから，無影響量は，5 mg/kg 未満と考えられた．しかし，被毛の黄色化については，皮膚の組織学的検査において変化がないことから，傷害的意義は乏しく，この変化を除けば，雄では 20 mg/kg，雌では 5 mg/kg で被験物質投与の影響は認められなかった．

被験物質投与によると考えられる変化を，先に実施した成獣ラットの試験成績[1)]と比較すると，ラット新生児では成獣ラットの 100 mg/kg 群にみられなかった体重の増加抑制が 80 mg/kg 群でみられたこと，100 mg/kg 投与した予備試験で死亡が発生していることから，成獣よりも毒性がやや強く発現することが示唆された．

緒 言

2,4,6-トリニトロフェノールの安全性に関する毒性試験の一環として，哺育期間中のラット新生児に 18 日間反復経口投与するとともに，63 日間の回復期間を設けて，その毒性及び回復性について検討した．また，成獣ラットの毒性試験成績と比較し，相違点を検索したので報告する．

試 験 材 料 及 び 方 法

1. 被験物質

[redacted]より提供された 2,4,6-トリニトロフェノール (Lot No. 8802403)を試験に使用した．本被験物質は純度 81.4%，分子量 229.05 の黄色結晶性粉末である (添付資料 1-1)．試験期間中の被験物質の安定性については，投与期間終了後に残余の被験物質を上記の提供先にて分析することにより確認した (添付資料 1-2)．媒体には 0.1%Tween 80(Lot No. M9A9947, ナカライテスク株式会社)添加 0.5%CMC-Na(Lot No. M7T4661, ナカライテスク株式会社)溶液を使用した．なお，被験物質は気密容器に入れ室温，遮光下で被験物質室の保管庫に保存した．0.1%Tween 80 添加 0.5%CMC-Na 溶液は週 1 又は 2 回の頻度で調製し，室温で被験物質室の保管庫に保存した．

2. 使用動物及び飼育条件

Crj:CD(SD)IGS ラット (日本チャールス・リバー株式会社)の妊娠母動物を妊娠 13 日で 20 匹購入し，12 日間の検疫・馴化を行った．この期間中に分娩させ，哺育状況，母動物及び新生児の一般状態の観察を 1 日 1 又は 2 回行い，母動物の体重を入荷後 3 及び 7 日に測定した．この間の観察で健康と思われた新生児雌雄各 48 匹並びに健康状態及び哺育状況の良好な母動物 12 匹を選抜した．投与開始時の新生児は 4 日齢で，体重は雄が 10.0~12.3 g，雌が 9.0~11.2 g であった．動物は温度 24±2°C (許容範囲 21~27°C)，湿度 55±10% (許容範囲 35~75%)，照明 12 時間 (午前 7 時~午後 7 時)及び換気回数 13~15 回/時に設定したバリアーシステム A 区域 (飼育室 04 番)で飼育した．床敷 (ホワイトフレーク，日本チャールス・リバー株式会社)を入れたポリカーボネイト製ケージ (W265 ×H185 ×D425 mm)に母動物 1 匹(新生児を含む)を収容し，離乳後 (生後 22 日以降)はステンレススチール製ケージ (W260

×H200 ×D380 mm)に出生児 1 匹を収容した．なお，試験期間中の温度の実測値は最高 27°C，最低 22°C，湿度の実測値は最高 72%，最低 49%であった．飼料は高圧蒸気滅菌処理した固型飼料 (MF，オリエンタル酵母工業株式会社)を，飲水は次亜塩素酸ナトリウムを添加 (約 2 ppm)した井戸水を給水瓶又は自動給水装置によりそれぞれ自由に摂取させた．飼料については財団法人日本食品分析センターにて，また飲水については株式会社鶴城南九科研センターにて分析を行い，いずれも許容基準に適合していることを確認した．なお，飼育器材は高圧蒸気滅菌したものを使用し，ケージ架台及びポリカーボネイト製ケージ用上蓋は 4 週間に 1 回以上，ステンレススチール製ケージは 2 週間に 1 回以上，ポリカーボネイト製ケージ及び給水瓶は週 1 回以上，受皿は週 3 回以上の頻度で交換するとともに，飼育室は毎日清掃し，消毒薬を浸したモップで清拭した．

3. 試験群構成，投与量設定の根拠及び群分け

試験群構成を下表に示した．

試験群	投与量 (mg/kg)	投与液濃度 (%)	投与容量 (mL/kg)	性別	使用動物数		動物番号
					22 日齢剖検 (投与期間終了時)	85 日齢剖検 (回復期間終了時)	
対照群	0	0	5	♂	6	6	901~906, 907*~912*
				♀	6	6	951~956, 957*~962*
低用量群	5	0.1	5	♂	6	6	913~918, 919*~924*
				♀	6	6	963~968, 969*~974*
中間用量群	20	0.4	5	♂	6	6	925~930, 931*~936*
				♀	6	6	975~980, 981*~986*
高用量群	80	1.6	5	♂	6	6	937~942, 943*~948*
				♀	6	6	987~992, 993*~998*

*: 85 日齢で剖検した動物.

投与量は，2,4,6-トリニトロフェノールのラットを用いた特殊生殖毒性予備試験 (投与量: 0, 20, 100 及び 500 mg/kg)の結果から設定した．すなわち，当該試験では 100 mg/kg 以上の群の雌雄で自発運動の低下，緩徐呼吸，体温低下などがみられ 100 mg/kg 群の雄 1 例及び雌 2 例，500 mg/kg 群の雌雄全例が死亡した．また，100 mg/kg 雄で腎臓重量の減少が認められた．したがって，本試験では，80 mg/kg を高用量とし，以下公比 4 をもって 20 及び 5 mg/kg を設定した．

群分けは，新生児が 3 日齢 (分娩日を 0 日齢として起算)になった時点で群分けを行った．

すなわち，3 日齢の新生児に雌雄別に仮の連続番号を付けて体重を測定し，この際，1 腹当たりの新生児数が極端に少ないものは母動物ごと除外した．次に，測定した体重を基に層別連続無作為化法で各群に振り分けた．また，分娩後，健康状態及び哺育状況の良好な母動物を 12 匹選び，群分け後の新生児の哺育に使用した．母動物への新生児の割り当ては下表のように行った．なお，残余の新生児及び母動物は試験から除外した．

試験群	性別	母動物番号及び割当て児数											
		22 日齢剖検分						85 日齢剖検分					
		161	162	163	164	165	166	167	168	169	170	171	172
対照群	♂	1	1	1	1	1	1	1	1	1	1	1	1
	♀	1	1	1	1	1	1	1	1	1	1	1	1
低用量群	♂	1	1	1	1	1	1	1	1	1	1	1	1
	♀	1	1	1	1	1	1	1	1	1	1	1	1
中間用量群	♂	1	1	1	1	1	1	1	1	1	1	1	1
	♀	1	1	1	1	1	1	1	1	1	1	1	1
高用量群	♂	1	1	1	1	1	1	1	1	1	1	1	1
	♀	1	1	1	1	1	1	1	1	1	1	1	1

4. 投与経路及び投与方法

投与経路は，OECD 試験法ガイドラインに準じ，また予想されるヒトへの曝露経路の一つである経口投与とした．4 日齢から 21 日齢まで 1 日 1 回，18 日間反復投与し，その後，回復群は生後 84 日 (回復 63 日)まで飼育・観察を行った．投与量は 5，20 及び 80 mg/kg とした．投与容量は 5 mL/kg とし，投与液量は最新の体重を基に算出し，対照群には同容量の媒体を投与した．

5. 被験物質及び対照物質の調製法及び調製頻度

被験物質を所定の濃度 (純度換算せず)となるように 0.1%Tween 80 添加 0.5%CMC-Na 溶液に懸濁し，週 2 又は 3 回の頻度で調製した．調製した被験物質は，飼育区域内の検体保管室に設置した冷蔵庫に冷蔵保存した．本被験物質の 0.1 mg/mL 懸濁液は室温で 8 日間，200 mg/mL 懸濁液は室温で 4 日間安定であり，均一性に問題がないことが確認されている (添付資料 2)．また，初回に調製した各濃度の投与液について濃度測定を行い，設定濃度の許容範囲 (±10%以内)にあることを確認した (添付資料 3)．

6. 観察，検査及び測定の頻度並びに方法

1) 一般状態観察並びに体重及び摂餌量測定

投与期間中(離乳時まで)は毎日投与前，投与後の 2 回，出生児及び母動物の一般状態の観察及び生死の確認を行った．なお，離乳後は出生児について一般状態の観察及び生死の確認を 1 日 1 回行った．体重は投与開始日及びその後は週 2 回の割合で午前中に，出生児並びに離乳時までの母動物の体重を測定した．摂餌量は離乳後の出生児について週 2 回の割合で午前中に測定した．すなわち，午前中に飼料を入れた給餌器を秤量してケージにセットし，翌日の午前中に給餌器をケージから取り出し，残量を秤量した．この差し引きを 1 日当たりの摂餌量とした．なお，摂餌量の表示日は，残量の測定日とした．

2) 発育分化検査

出生児の全例について耳介展開 [生後 4 日 (投与 1 日)]，毛生 [生後 8 日 (投与 5 日)]，切歯萠出 [生後 10 日 (投与 7 日)]，四足歩行及び眼瞼開裂 [生後 15 日 (投与 12 日)]，精巣下降 [生後 21 日 (投与 18 日)]，陰茎亀頭包皮分泌腺開裂 [生後 42 日 (回復 21 日)]及び膣開口 [生後 42 日 (回復 21 日)]を検査した．いずれの場合も陰性であった動物は以後陽性になるまで毎日検査した．なお，精巣下降，陰茎亀頭包皮分泌腺開裂及び膣開口については完了日に体重の測定を行った．

3) 感覚機能検査

面上正向反射及び同側屈筋反射 [生後 5 日 (投与 2 日)]，視覚性踏み直り反射 [生後 16 日 (投与 13 日)]及び耳介反射 [生後 28 日 (回復 7 日)]について検査した．陰性であった動物は以後陽性になるまで毎日検査した．

4) 尿検査

11 週齢時に実施し，代謝ケージを用いて午前 8~12 時の時間帯の新鮮尿を採取したのち，引き続き 24 時間蓄積尿を採取した．なお，採尿日の給餌は新鮮尿採取後に行い，飲水は通常通り与えた．検査を行った項目及び方法を以下に示した．

項 目	方　法		単位又は表示
尿量	メスシリンダー測定		mL
色調	肉眼的観察		
浸透圧	氷点降下法	OSMOMETER OM801，VOGEL 社	Osm/kg
比重	屈折率法	尿屈折計，株式会社アタゴ	
以上の 4 項目は 24 時間蓄積尿を用いて検査した．			
pH	試験紙法		5~9
蛋白質	試験紙法		−~++++
ブドウ糖	試験紙法		−~++++
ケトン体	試験紙法		−~+++
ビリルビン	試験紙法		−~+++
潜血	試験紙法		−~+++
ウロビリノーゲン	試験紙法		<1，1，4，8，12 mg/dL
以上の 7 項目は新鮮尿を用いてプレテスト 8a(和光純薬工業株式会社)により検査した．			

尿沈渣: 採取した新鮮尿を 1500 回転/分で 5 分間遠心分離し，得られた沈渣を鏡検し，以下の基準で判定した．

	−	+	++	+++
上皮細胞	1 視野に 3 個未満	1 視野に 3 個以上 10 個未満	1 視野に 10 個以上 20 個未満	1 視野に 20 個以上
赤血球	1 視野に 10 個未満	1 視野に 10 個以上 30 個未満	1 視野に 30 個以上 100 個未満	1 視野に赤血球が重なり合ったり，過密状態で数の確認が不可能な場合
白血球	1 視野に 3 個未満	1 視野に 3 個以上 20 個未満	1 視野に 20 個以上 40 個未満	1 視野に 40 個以上
円柱	すべての視野に皆無	すべての視野で 1 個以上	−	−
非細胞沈渣*	1 視野に 10 個未満	1 視野に 10 個以上 20 個未満	1 視野に 20 個以上 30 個未満	1 視野に結晶が重なり合ったり過密状態で数の確認が不可能な場合

倍率:×400　　*:主に燐酸塩，蓚酸塩結晶

5) 血液学検査

生後 22 及び生後 85 日に実施し，ペントバルビタール・ナトリウム 30 mg/kg を腹腔内に投与して麻酔したのち，後大静脈腹部より血液約 0.5~1 mL を採取した．血球系の検査には，血液を EDTA-2K 2 mg 加採血ビン (SB-41 又は SB-44，シスメックス株式会社)に分注したものを用いた．また，生後 85 日の動物については血球系検査の採血の前に，血液 0.9 mL を採取し，3.8%クエン酸ナトリウム 0.1 mL を入れた試験管に分注し，3000 回転/分で 15 分間遠心分離して得られた血漿を血液凝固系検査に用いた．動物は，採血前日から 18 時間以上絶食させた．検査を行った項目及び方法を以下に示した．

項　目	方　法	単　位
白血球数	電気抵抗検出方式	$\times 10^2/\mu L$
赤血球数 (RBC)	電気抵抗検出方式	$\times 10^4/\mu L$
ヘモグロビン量 (Hgb)	Oxyhemoglobin 法	g/dL
ヘマトクリット値 (Hct)	血球 pulse 波高値検出方式	%
血小板数	電気抵抗検出方式	$\times 10^4/\mu L$
以上の 5 項目は多項目自動血球計数装置 (Sysmex CC-780，シスメックス株式会社)を用いて測定した．		
平均赤血球容積	$\frac{Hct(\%)}{RBC(10^4/\mu L)} \times 10^3$	fL
平均赤血球血色素量	$\frac{Hgb(g/dL)}{RBC(10^4/\mu L)} \times 10^3$	pg
平均赤血球血色素濃度	$\frac{Hgb(g/dL)}{Hct(\%)} \times 10^2$	%
以上の Wintrobe の赤血球恒数を RBC，Hgb 及び Hct より算出した．		
白血球形態検査 (白血球百分比)	May-Grünwald-Giemsa 染色	%
網状赤血球率	New methylene blue 超生体染色	‰
白血球形態検査は光学顕微鏡 (オリンパス光学株式会社)を用いて検査した． ただし，網状赤血球率の検査は塗抹標本の作製まで実施し，検査は行わなかった．		
プロトロンビン時間	散乱光検出方式	秒
活性化部分トロンボプラスチン時間	散乱光検出方式	秒
以上の 2 項目は全自動血液凝固測定装置 (Sysmex CA-5000，シスメックス株式会社)を用いて測定した．なお，生後 22 日の動物については実施しなかった．		

6) 血液生化学検査

生後 22 日及び生後 85 日に実施し，血液学検査用の採血に引き続き，後大静脈腹部より全採血 (最大 3 mL)した血液を，室温で約 60 分間放置後，3000 回転/分で 10 分間遠心分離して得られた血清を用いた．検査を行った項目及び方法を以下に示した

項 目	方　法	単位
総蛋白質量	Biuret 法	g/dL
アルブミン	BCG 法	g/dL
A/G 比	総蛋白質量及びアルブミン量より算出	
総ビリルビン	Vanadate oxidation 法	mg/dL
GOT	UV-rate 法	IU/L
GPT	UV-rate 法	IU/L
γ-グルタミルトランスペプチダーゼ	L-γ-Glutamyl-3-hydroxymethyl-4-nitroanilide 基質法	IU/L
アルカリ性フォスファターゼ	p-Nitrophenylphosphate acid 基質法	IU/L
総コレステロール	COD-HDAOS 法	mg/dL
トリグリセライド	GPO-HDAOS 法，glycerol blanking 法	mg/dL
リン脂質	Choline oxidase-DAOS 法	mg/dL
グルコース	Hexokinase-G-6-PDH 法	mg/dL
尿素窒素	Urease-GLDH 法	mg/dL
クレアチニン	Jaffé 法	mg/dL
無機リン	PNP-XOD 法	mg/dL
カルシウム	MXB 法	mg/dL
以上の 16 項目は自動分析装置 (7170，株式会社日立製作所)を用いて測定した．		
ナトリウム	電極法	mEq/L
カリウム	電極法	mEq/L
クロール	電量滴定法	mEq/L
以上の 3 項目は電解質分析装置 (PVA-αIII，株式会社アナリティカル・インスツルメンツ)を用いて測定した．		

7) 剖検

生後 22 日及び生後 85 日に，採血終了後，放血致死せしめ，速やかに解剖してすべての器官及び組織について異常の有無を綿密に検査した．

8) 器官重量

生後 22 日及び生後 85 日の剖検時に脳，心臓，肺(気管支を含む)，甲状腺，下垂体，胸腺，肝臓，脾臓，腎臓，副腎，精巣，精巣上体及び卵巣を摘出して器官重量(絶対重量)を測定するとともに，剖検日の体重を基に体重比器官重量(相対重量)を算出した．

9) 病理組織学検査

下記の各器官・組織並びに肉眼的異常部位を 10%中性緩衝ホルマリン溶液 (ただし，眼球は 2.5%グルタールアルデヒド溶液で，精巣及び精巣上体はブアン液で前固定)で固定して保存した．対照群及び高用量群についてはパラフィン切片としたのち，ヘマトキシリン・エオジン (HE)染色を施して鏡検した．また，肉眼的異常部位についても検査した．

脳	脾臓
下垂体	腎臓
甲状腺	副腎
心臓	精巣
肺 (気管支を含む)	精巣上体
胸腺	卵巣
肝臓	肉眼的異常器官・組織

7. 統計学処理

体重，摂餌量，尿検査 (定性反応を除く)，血液学検査，血液生化学検査，器官重量及び体重比器官重量については，各群ごとに平均値と標準偏差を求め，まず，分散の均一性を Bartlett 法により検定した．分散が均一な場合は Dunnett の多重比較検定を用いて，異なる場合は Steel の多重比較検定を用いて対照群との比較を行った．発育分化検査成績[(分化児数/検査児数)×100]と感覚機能検査成績[(反応児数/検査児数)×100]についてはχ^2 検定により，病理組織学検査については，Mann-Whitney の U 検定により解析した．いずれの検定においても有意水準を 1 及び 5%とした．

試 験 成 績

1. 一般状態

一般状態の観察結果を Table 1 及び Appendix 1，2 に示した．

各群とも死亡の発生はなかった．一般状態では，被毛の黄色化が 5 mg/kg 以上の群の雌雄全例で認められた．被毛の黄色化は，20 及び 80 mg/kg 群では，それぞれ投与 5 及び 3 日から発現し，回復期間終了時まで継続して認められた．5 mg/kg 群では，投与 10 日から被毛の黄色化が発現したが，回復期間中にほぼ全例で消失した．

このほか，歯の異常が 5 mg/kg 群の雄 1 例で投与期間終了後 31～38 日に認められた.

2. 体重

体重推移を Fig. 1 及び Fig. 2 並びに Table 2 及び Appendix 3，4 に示した.

投与期間中では，80 mg/kg 群の雄で投与 4 及び 8 日に対照群と比較して有意な低値が認められた.

離乳後 (投与期間終了後)では，20 mg/kg 以上の群の雌で増加抑制傾向がみられ，20 mg/kg 群の投与期間終了後 21，25 及び 32～63 日では対照群と比較して有意な低値が認められた.

3. 摂餌量

離乳後 (投与期間終了後)の摂餌量の推移を Fig. 3 及び Fig. 4 並びに Table 3 及び Appendix 5，6 に示した.

20 mg/kg 群の雌で投与期間終了後 14，35，39 日及び 56 日に有意な低値がみられたが，一過性の散発的な変化であり，80 mg/kg 群に同様の変動は認められなかったことからいずれも偶発的変化と考えられた.

4. 発育分化検査

検査結果を Table 4 及び Appendix 7 に示した.

5 mg/kg 群の雄で切歯萌出の分化率が 100%であったため，対照群との間に有意な高値が認められたが，20 mg/kg 以上の群では同様な変化はみられなかったことから，被験物質投与との関連はないと判断した．各群の雌雄とも，耳介展開，毛生，眼瞼開裂，四足歩行，精巣下降，陰茎亀頭包皮分泌腺開裂又は膣開口の分化率に対照群との間の差は認められなかった.

5. 感覚機能検査

検査結果を Table 5 及び Appendix 8 に示した.

各群の雌雄とも，面上正向反射，同側屈筋反射，視覚性踏み直り反射及び耳介反射の反射率に対照群との間の差は認められなかった.

6. 尿検査

検査結果を Table 6 及び Appendix 9, 10 に示した.

各群の雌雄ともすべての検査項目で変化は認められなかった.

7. 血液学検査

22 日齢 (投与期間終了時)の検査結果を Table 7 及び Appendix 11, 12 に示し, 85 日齢(回復期間終了時)の検査結果を Table 8 及び Appendix 13, 14 に示した.

22 日齢では, 各群の雌雄ともすべての項目で変化は認められなかった.

85 日齢では, 5 及び 80 mg/kg 群の雄で赤血球数の減少及び 80 mg/kg 群の雄で活性化部分トロンボプラスチン時間の短縮が認められた. このほか, 5 及び 20 mg/kg 群の雄で MCH の増加がみられたが, 80 mg/kg 群では同様の変動がなかったことから, 被験物質投与との関連はないと判断した.

8. 血液生化学検査

22 日齢 (投与期間終了時)の検査結果を Table 9 及び Appendix 15, 16 に示し, 85 日齢剖(回復期間終了時)の検査結果を Table 10 及び Appendix 17, 18 に示した.

22 日齢では, 各群の雌雄ともすべての項目で変化は認められなかった.

85 日齢では, 80 mg/kg 群の雄で総蛋白質及びカルシウムの減少が認められた. このほか, 20 mg/kg 群の雌で無機リンの増加が認められたが, 80 mg/kg 群では同様の変動がみられてないことから, 被験物質投与との関連はないと判断した.

9. 剖検

22 日齢 (投与期間終了時)の検査結果を Table 11 及び Appendix 19, 20 に示し, 85 日齢(回復期間終了時)の検査結果を Table 12 及び Appendix 21, 22 に示した.

22 日齢剖検例では, 5 mg/kg 以上の群の雌雄全例で被毛の黄色化が認められた.

85 日齢剖検例では, 5 mg/kg 群の雄 1 例並びに 20 mg/kg 以上の群の雌雄全例で被毛の黄色化, 80 mg/kg 群の雄 1 例で精巣上体に黄白色斑がみられた. このほか, 5 mg/kg 群の雌 1 例で腎盂拡張, 20 mg/kg 群の雄 2 及び 1 例で精巣又は精巣上体の小型化, 対照群の雄 1 例で精巣の肥大がみられたが, これらの変化は低頻度で軽微な変化であり, 投与期間及び回復期間

終了時の 80 mg/kg 群では同様の変化はみられてないことから，いずれも自然発生の変化と考えられた.

10. 器官重量

22 日齢 (投与期間終了時)の測定結果を Table 13 及び Appendix 23，24 に，85 日齢(回復期間終了時)の測定結果を Table 14 及び Appendix 25，26 に示した.

22 日齢では，80 mg/kg 群の雌雄で肝臓において絶対及び相対重量の増加又は増加傾向が認められた．このほか，20 mg/kg 群の雌で卵巣において絶対及び相対重量の減少が認められたが，80 mg/kg 群では同様な変化がみられていないことから，被験物質投与との関連性はないと判断した.

85 日齢では，5 mg/kg 群の雄で副腎において相対重量の増加及び 20 mg/kg 群の雌で脳及び心臓において相対重量の増加が認められたが，80 mg/kg 群では同様の変化がみられてないことから，被験物質投与との関連はないと判断した.

11. 病理組織学検査

22 日齢 (投与期間終了時)の検査結果を Table 15 及び Appendix 27，28 に示し，85 日齢(回復期間終了時)の検査結果を Table 16 及び Appendix 29，30 に示した.

22 日齢では，対照群の雄 1 例，雌 2 例及び 80 mg/kg 群の雄 2 例，雌 1 例で腎臓において軽度の尿細管拡張がみられたが，出現例数及び程度において対照群と 80 mg/kg 群で差は認められなかったことから，被験物質投与との関連のない偶発的変化と判断した.

85 日齢では，80 mg/kg 群の雄 1 例で精巣上体に軽度の精子肉芽腫がみられた．このほか，肉眼でみられた自然発生の変化に対応する組織所見として 5 mg/kg 群の雌 1 例で腎臓に軽度の腎盂拡張，対照群の雌 3 例で腎臓に軽度の鉱質沈着，20 mg/kg 群の雄 2 例で精巣に重度の精細管の萎縮，対照群の雄 1 例で精巣に軽度の精細管の拡張，20 mg/kg 群の雄 2 例で精巣上体に重度の管腔内の精子の減少又は軽度の細胞粥，対照群の雄 1 例で大脳に軽度の側脳室の拡張が認められた.

考 察

2,4,6-トリニトロフェノールの安全性に関する毒性試験の一環として，哺育期間中のラット新生児に 4 日齢から 18 日間反復経口投与するとともに，63 日間の回復期間を設けて，その毒性及び回復性について検討した．また，成獣ラットの毒性発現状況と比較し，相違点を検索した．

試験期間を通して死亡例はなかった．一般状態では，被毛の黄色化が投与期間中に 5 mg/kg 以上の群の雌雄全例で認められた．被毛の黄色化は，20 及び 80 mg/kg 群では回復期間終了時まで継続して認められたが，5 mg/kg 群では回復期間中にほぼ全例で消失した．体重では，80 mg/kg 群の雄で投与期間中に，20 mg/kg 以上の群の雌で投与期間終了後に体重の増加抑制が認められた．離乳後（投与期間終了後）に測定した摂餌量では，雌雄とも被験物質投与の影響は認められなかった．

発育分化及び感覚機能検査並びに尿検査では，雌雄とも被験物質投与の影響は認められなかった．

血液学検査及び血液生化学検査では，85 日齢(回復期間終了時)の検査において 5 及び 80 mg/kg 群の雄で赤血球数の減少，80 mg/kg 群の雄で活性化部分トロンボプラスチン時間の短縮並びに総蛋白質及びカルシウムの減少が認められたが，いずれも生理的変動範囲内の軽微な変動であり，22 日齢（投与期間終了時）の検査において同様な変動はなかったことから，毒性学的な意義はないと考えられた．

病理学検査では，一般状態でみられた被毛の黄色化が 22 日齢剖検例において 5 mg/kg 以上の群の雌雄全例，85 日齢剖検例において 5 mg/kg の雄 1 例及び 20 mg/kg 以上の群の雌雄全例で認められた．この被毛の黄色化については発生機序を明らかにすることはできなかったが，皮膚の病理組織学検査で器質的変化がみられなかったことから，傷害的な意義は乏しいものと考えられた．器官重量では，22 日齢剖検例において 80 mg/kg 群の雌雄で肝臓の重量増加が認められ，本被験物質投与による肝臓への影響が示唆されたが，血液生化学検査において肝機能関連パラメータの変動はなく，病理組織学検査でも対応する器質的変化がなかったことから，重篤な変化ではないと考えられた． このほか，85 日齢剖検例において 80 mg/kg 群の雄で精巣上体の黄白色斑がみられ，組織学的に精子肉芽腫が認められたが，1 例のみの軽微な変化であり，投与期間終了時の 80 mg/kg 群では同様の変化はなかったことから，自然発生的の変化と考えられた．

以上のように，本試験では雌雄とも 5 mg/kg 群から被毛の黄色化が認められたことから，無影

響量は，5 mg/kg 未満と考えられた．しかし，被毛の黄色化については，皮膚の組織学検査において変化がないことから，傷害的意義は乏しく，この変化を除けば，雄では 20 mg/kg，雌では 5 mg/kg で被験物質投与の影響は認められなかった．

上記の結果を，先に実施した成獣ラット(投与量：4，20 及び 100 mg/kg)の試験成績[1]と比較すると，成獣ラットの 20 及び 100 mg/kg 群で本試験でみられたと同様な被毛の黄色化が観察されており，その発現パターンも幼若ラットの 20 及び 80 mg/kg 群とほぼ同様であった．しかし，成獣ラットの 4 mg/kg 群では被毛の黄色化はみられなかったのに対し，幼若ラットでは 5 mg/kg 群の雌雄で回復期間中にほぼ全例消失したものの，投与期間中から被毛の黄色化が認められた．また，成獣ではみられなかった体重の増加抑制が本試験において認められた．病理学検査では，成獣の 100 mg/kg 群で肝臓の重量増加がみられ，組織学的に小葉中心性の肝細胞肥大が認められた．本試験においては，22 日齢 (投与期間終了時) の 80 mg/kg 群で肝臓の重量増加はみられたものの，組織学的には変化は認められなかった．一般に小葉中心性の肝細胞肥大は解毒のための生体の適応反応である代謝機能亢進を示唆していることが多い．幼若ラットでは，肝細胞の代謝機能が未だ確立しておらず，そのために適応性の変化が顕著に現れなかったと考えられた．このほか，成獣ラットでは，100 mg/kg 群で貧血様変化，精巣毒性，盲腸の潰瘍などがみられたが，幼若ラットの 80 mg/kg 群では同様の変化は認められなかった．しかし，これらの変化については投与量の相違に起因した可能性があり，幼若動物と成獣との差を表すものとは言い難かった．すなわち，幼若ラットの予備試験では 100 mg/kg 群の雌雄で自発運動の低下，緩徐呼吸，体温低下などがみられ，100 mg/kg 群の雄 1/4 例及び雌 2/4 例が死亡しており，幼若ラットに対し 100 mg/kg は致死量と考えられることから，逆に 100 mg/kg 投与の場合，成獣に比べ幼若ラットの方が毒性は強く現れると推察された．以上より，ラットでは 2,4,6-トリニトロフェノールを新生児に投与すると成獣に比較して毒性がやや強く発現することが示唆された．

文 献

1) [redacted] (1999): 2,4,6-トリニトロフェノールのラットを用いた経口投与による 28 日間の反復投与毒性試験，株式会社三菱化学安全科学研究所(試験番号: 8L660).

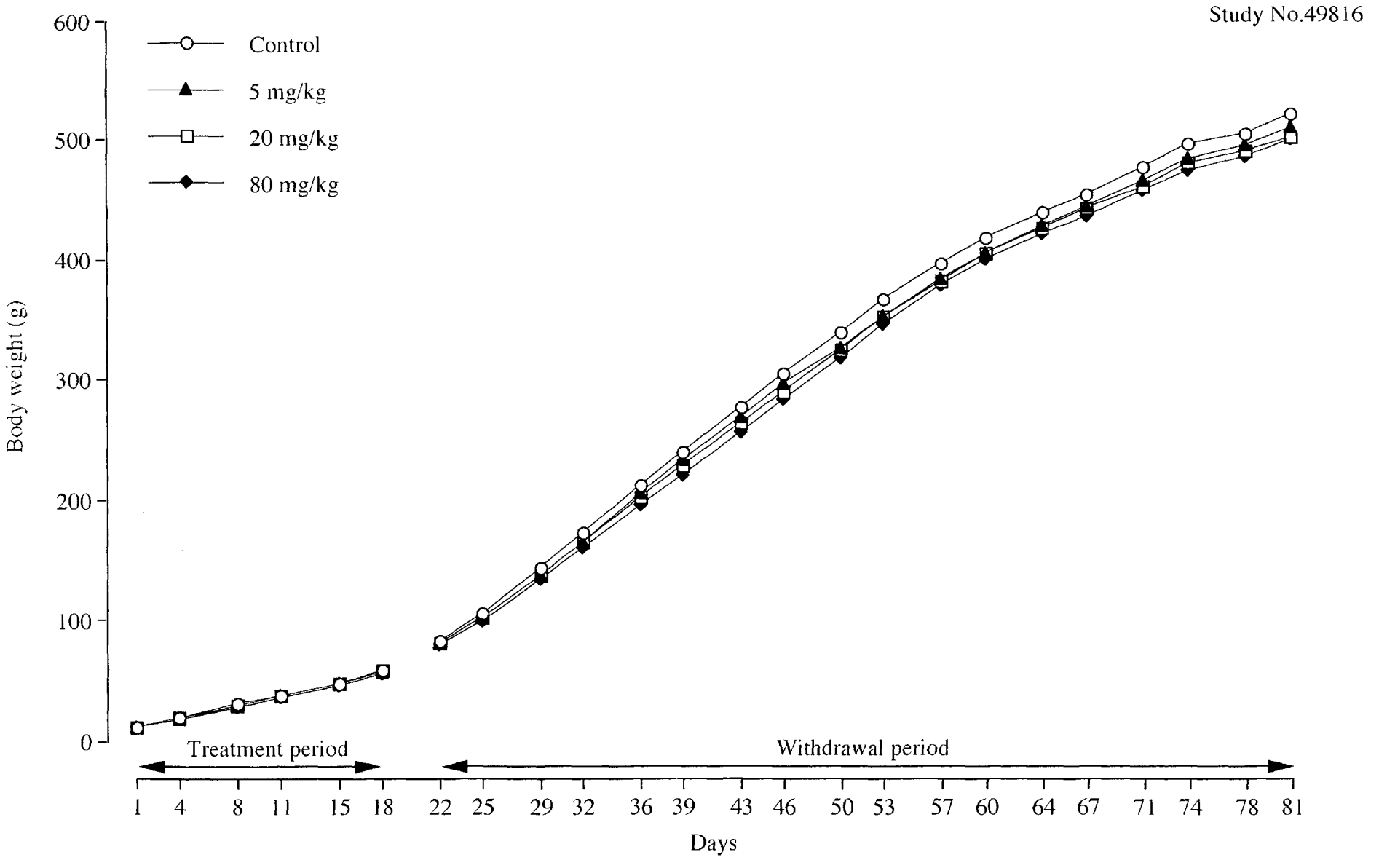


Fig. 1 Body weight changes in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period.

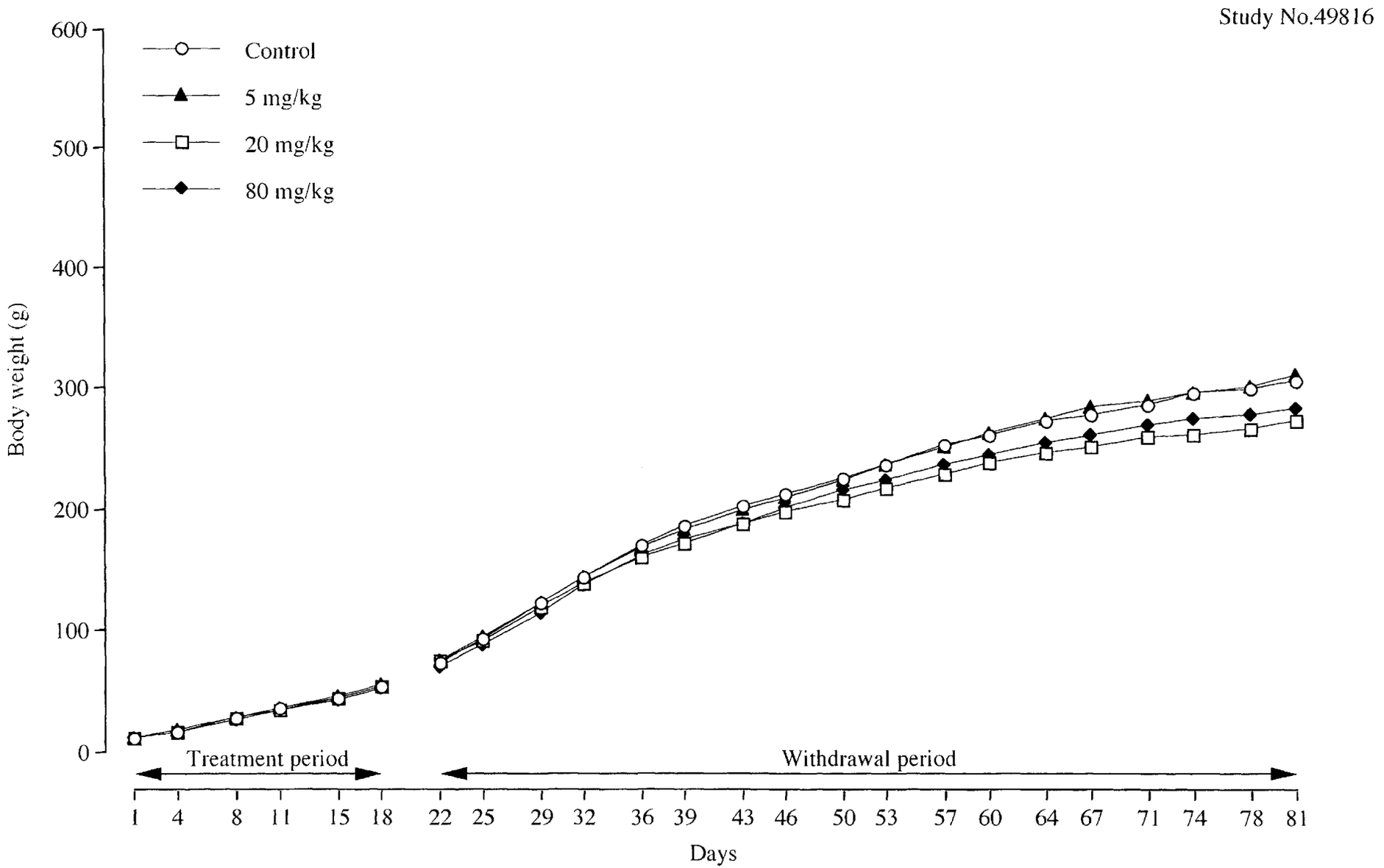


Fig. 2 Body weight changes in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period.

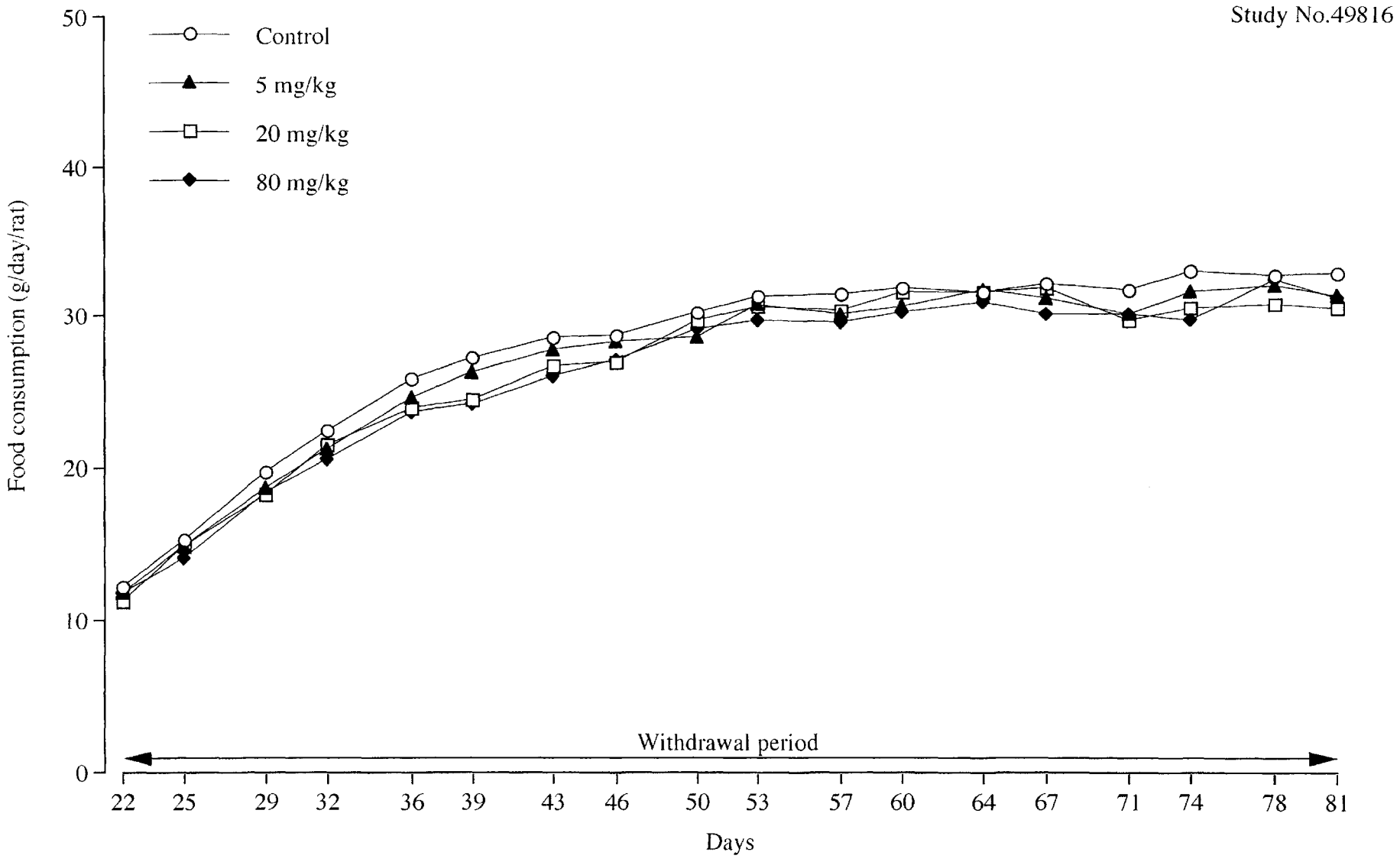


Fig. 3 Food consumption in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period.

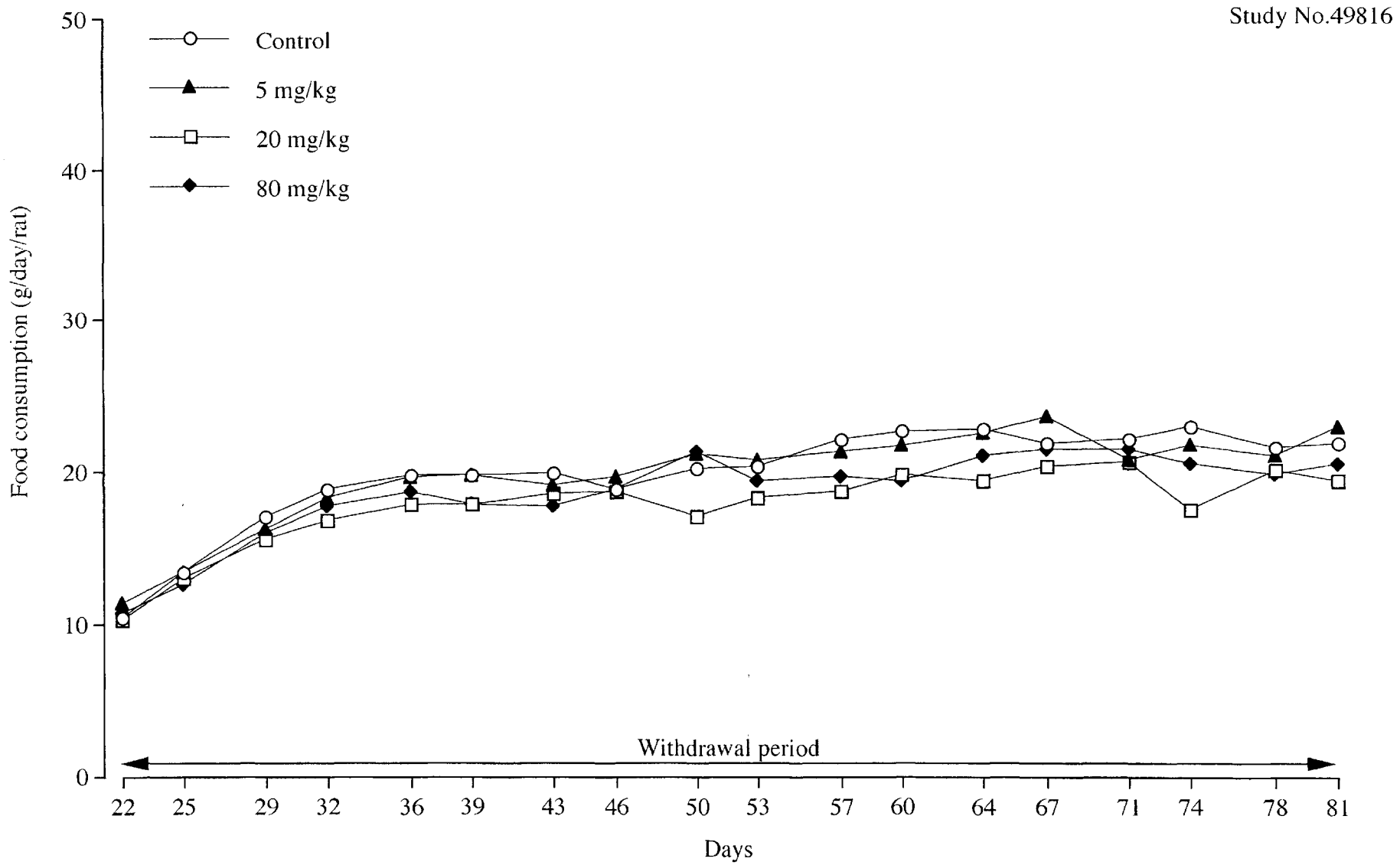


Fig. 4 Food consumption in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period.

Table 1 Clinical signs in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Clinical sign	Days																	
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Male	Control	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	5 mg/kg	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	0	0	0	0	0	0	0	0	0	12	12	12	12	12	12	12	12	12
		Abnormality of tooth	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20 mg/kg	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	0	0	0	0	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	80 mg/kg	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	0	0	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Female	Control	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	5 mg/kg	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	12	12	12	12	12	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	0	0	0	0	0	0	0	0	0	12	12	12	12	12	12	12	12	12
	20 mg/kg	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	12	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	0	0	0	0	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	80 mg/kg	Number of examined	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
		No abnormality	12	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	0	0	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12

Table 1 - continued Clinical signs in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Clinical sign	Days																		
			19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
Male	Control	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		Abnormality of tooth	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Female	Control	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	20 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Table 1 - continued Clinical signs in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Clinical sign	Days																		
			38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56
Male	Control	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		Abnormality of tooth	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	20 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Female	Control	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	20 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Table 1 - continued Clinical signs in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Clinical sign	Days																		
			57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75
Male	Control	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	1	1	1	1	1	1	1	1	3	3	3	3	4	4	4	4	4	4
		Yellow coloration of hair	6	5	5	5	5	5	5	5	5	3	3	3	3	2	2	2	2	2	2
		Abnormality of tooth	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Female	Control	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	2	2	2	2	3	3	3	3	4	4
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	4	4	4	4	3	3	3	3	2	2
	20 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Table 1 - continued Clinical signs in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Clinical sign	Days 76	77	78	79	80	81
Male	Control	Number of examined	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6
		No abnormality	4	4	4	4	4	5
		Yellow coloration of hair	2	2	2	2	2	1
		Abnormality of tooth	0	0	0	0	0	0
	20 mg/kg	Number of examined	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6
Female	Control	Number of examined	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6
	5 mg/kg	Number of examined	6	6	6	6	6	6
		No abnormality	4	6	6	6	6	6
		Yellow coloration of hair	2	0	0	0	0	0
	20 mg/kg	Number of examined	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6
	80 mg/kg	Number of examined	6	6	6	6	6	6
		No abnormality	0	0	0	0	0	0
		Yellow coloration of hair	6	6	6	6	6	6

Table 2 Body weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Body weight(g) on day									
			1	4	8	11	15	18	22	25	29	32
Male	Control	N	12	12	12	12	12	12	6	6	6	6
		Mean	11.2	18.5	29.5	37.3	47.2	57.6	82.2	104.9	142.2	171.2
		S.D.	±0.4	±1.3	±1.9	±3.0	±3.9	±4.7	±6.5	±7.2	±10.7	±12.6
	5 mg/kg	N	12	12	12	12	12	12	6	6	6	6
		Mean	10.9	17.9	28.7	36.5	46.6	56.7	80.3	101.5	136.1	163.8
		S.D.	±0.4	±1.0	±1.7	±2.2	±2.5	±3.1	±4.8	±7.0	±11.4	±13.9
	20 mg/kg	N	12	12	12	12	12	12	6	6	6	6
		Mean	11.1	18.2	29.0	37.1	46.3	57.3	79.9	101.2	135.3	163.7
		S.D.	±0.5	±1.0	±1.9	±2.7	±4.0	±4.6	±6.4	±7.7	±10.2	±11.6
	80 mg/kg	N	12	12	12	12	12	12	6	6	6	6
		Mean	11.0	17.3*	27.4*	35.3	44.9	55.0	78.7	99.0	132.2	159.3
		S.D.	±0.6	±1.2	±1.7	±2.0	±2.7	±2.9	±2.7	±4.8	±6.8	±7.1
Female	Control	N	12	12	12	12	12	12	6	6	6	6
		Mean	10.0	16.2	26.7	34.2	43.3	52.7	72.3	91.8	121.2	143.0
		S.D.	±0.6	±0.9	±1.8	±2.3	±2.7	±3.7	±5.4	±7.4	±8.8	±9.2
	5 mg/kg	N	12	12	12	12	12	12	6	6	6	6
		Mean	10.1	16.4	27.3	34.9	44.2	53.8	74.1	92.9	121.3	141.9
		S.D.	±0.4	±0.9	±1.7	±1.9	±2.3	±2.6	±3.3	±3.8	±6.2	±8.4
	20 mg/kg	N	12	12	12	12	12	12	6	6	6	6
		Mean	9.9	16.1	26.8	34.1	43.4	52.6	73.3	90.9	118.1	136.9
		S.D.	±0.4	±1.1	±1.7	±2.7	±3.1	±3.7	±4.2	±4.2	±5.1	±5.4
	80 mg/kg	N	12	12	12	12	12	12	6	6	6	6
		Mean	10.0	15.7	25.3	32.7	42.0	51.7	69.1	86.7	113.9	135.5
		S.D.	±0.5	±0.9	±1.4	±2.3	±3.1	±4.5	±2.0	±2.1	±4.4	±5.7

*: $P<0.05$ (significantly different from control).

Table 2 - continued Body weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Body weight(g) on day									
			36	39	43	46	50	53	57	60	64	67
Male	Control	N	6	6	6	6	6	6	6	6	6	6
		Mean	211.1	238.7	275.4	303.5	338.0	365.8	395.1	415.8	437.7	452.2
		S.D.	±17.3	±19.4	±23.0	±24.5	±27.2	±30.7	±33.5	±36.1	±39.6	±43.1
	5 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	204.4	231.8	267.8	295.8	324.2	350.3	381.6	402.8	425.8	442.1
		S.D.	±19.9	±21.2	±25.6	±29.2	±27.3	±30.0	±33.1	±36.0	±37.2	±39.7
	20 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	201.0	226.4	262.3	288.9	323.9	350.6	381.0	403.1	424.6	440.1
		S.D.	±13.6	±15.1	±17.0	±16.1	±18.7	±23.3	±22.2	±25.5	±26.3	±28.2
	80 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	194.7	219.7	255.2	283.1	317.3	344.6	377.2	397.3	419.6	434.0
		S.D.	±9.4	±11.7	±15.0	±17.2	±19.8	±22.9	±26.4	±28.6	±34.0	±35.3
Female	Control	N	6	6	6	6	6	6	6	6	6	6
		Mean	169.0	185.3	200.7	210.3	224.3	234.8	251.9	260.2	271.4	276.1
		S.D.	±10.0	±9.9	±10.3	±9.5	±10.8	±11.2	±14.9	±19.6	±19.3	±17.0
	5 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	166.5	181.7	197.5	207.4	223.0	235.2	249.9	261.4	272.4	281.9
		S.D.	±11.4	±13.5	±13.6	±15.2	±15.5	±15.6	±16.5	±17.6	±15.7	±20.1
	20 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	158.9	170.1*	185.7*	197.0	206.0*	216.1*	227.7*	236.1*	244.6*	249.9*
		S.D.	±5.7	±5.0	±5.2	±4.6	±5.2	±5.5	±5.5	±8.7	±11.1	±10.0
	80 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	160.9	173.3	187.0	198.8	213.7	221.5	235.7	244.0	252.6	259.3
		S.D.	±8.4	±8.9	±9.1	±12.0	±12.5	±12.7	±14.5	±14.3	±15.2	±15.4

*: $P<0.05$ (significantly different from control).

Table 2 - continued Body weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Body weight(g) on day 71	74	78	81
Male	Control	N	6	6	6	6
		Mean	474.0	493.5	503.0	518.8
		S.D.	±44.0	±45.8	±45.2	±47.9
	5 mg/kg	N	6	6	6	6
		Mean	463.0	480.9	492.8	506.7
		S.D.	±42.1	±45.5	±46.4	±47.3
	20 mg/kg	N	6	6	6	6
		Mean	458.7	477.2	487.9	499.4
		S.D.	±28.3	±28.8	±27.7	±29.6
	80 mg/kg	N	6	6	6	6
		Mean	454.8	471.1	483.1	498.0
		S.D.	±37.8	±36.3	±35.3	±35.9
Female	Control	N	6	6	6	6
		Mean	283.8	293.7	297.8	304.4
		S.D.	±18.3	±19.9	±20.2	±20.9
	5 mg/kg	N	6	6	6	6
		Mean	287.5	294.1	299.3	308.0
		S.D.	±21.2	±20.8	±23.1	±20.2
	20 mg/kg	N	6	6	6	6
		Mean	257.8*	260.1**	265.3*	271.2*
		S.D.	±11.6	±13.3	±14.6	±11.6
	80 mg/kg	N	6	6	6	6
		Mean	267.3	273.3	275.6	280.8
		S.D.	±15.3	±15.3	±12.8	±18.6

*: $P<0.05$, **: $P<0.01$ (significantly different from control).

Table 3 Food consumption in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Food consumption(g) on day									
			22	25	29	32	36	39	43	46	50	53
Male	Control	N	6	6	6	6	6	6	6	6	6	6
		Mean	12.1	15.3	19.8	22.5	25.9	27.2	28.6	28.7	30.2	31.3
		S.D.	±0.9	±1.0	±1.6	±1.8	±2.0	±2.9	±2.7	±2.6	±3.2	±3.3
	5 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	11.8	14.8	18.7	21.3	24.6	26.2	27.8	28.3	28.6	30.8
		S.D.	±1.6	±1.7	±2.3	±2.5	±2.6	±2.3	±3.0	±2.5	±2.1	±3.6
	20 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	11.2	14.9	18.3	21.5	24.0	24.5	26.6	27.0	29.7	30.6
		S.D.	±0.8	±1.3	±1.6	±1.4	±1.9	±1.6	±2.7	±0.9	±2.1	±2.5
	80 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	11.8	14.0	18.4	20.5	23.7	24.2	26.0	27.1	29.1	29.6
		S.D.	±0.9	±1.0	±0.8	±1.2	±2.0	±2.2	±1.6	±2.8	±2.1	±2.8
Female	Control	N	6	6	6	6	6	6	6	6	6	6
		Mean	10.4	13.4	17.0	18.8	19.8	19.7	19.9	18.8	20.1	20.3
		S.D.	±0.9	±1.7	±1.7	±1.2	±1.1	±1.3	±1.8	±1.1	±1.9	±1.3
	5 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	11.3	13.4	16.2	18.2	19.6	19.7	19.1	19.6	21.1	20.7
		S.D.	±0.6	±0.6	±1.4	±1.3	±1.4	±1.9	±1.2	±2.4	±2.8	±1.2
	20 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	10.2	12.9	15.5	16.7*	17.8	17.9	18.5	18.7	17.0	18.2*
		S.D.	±0.6	±0.4	±1.1	±1.2	±1.4	±1.1	±1.6	±0.7	±2.4	±1.3
	80 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	10.6	12.6	15.9	17.7	18.7	17.9	17.7	18.8	21.2	19.4
		S.D.	±0.9	±0.7	±1.3	±1.6	±2.2	±1.0	±1.5	±2.1	±2.4	±1.2

*: $P<0.05$ (significantly different from control).

Table 3 - continued Food consumption in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Food consumption(g) on day							
			57	60	64	67	71	74	78	81
Male	Control	N	6	6	6	6	6	6	6	6
		Mean	31.4	31.8	31.5	32.1	31.7	32.9	32.6	32.8
		S.D.	±2.8	±2.2	±3.4	±4.7	±3.6	±4.1	±4.7	±4.3
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	30.0	30.6	31.7	31.1	30.1	31.5	32.0	31.3
		S.D.	±4.1	±3.6	±3.4	±3.7	±3.9	±4.7	±3.7	±3.6
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	30.3	31.6	31.6	31.8	29.6	30.4	30.7	30.5
		S.D.	±1.2	±1.8	±1.9	±2.9	±1.3	±3.5	±2.9	±2.2
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	29.5	30.2	30.9	30.1	30.0	29.7	32.3	31.2
		S.D.	±1.6	±3.1	±3.3	±2.2	±2.1	±2.2	±3.4	±2.0
Female	Control	N	6	6	6	6	6	6	6	6
		Mean	22.0	22.6	22.7	21.8	22.0	22.9	21.5	21.8
		S.D.	±3.4	±3.2	±2.5	±1.8	±1.9	±2.1	±2.3	±2.6
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	21.2	21.7	22.5	23.6	20.7	21.6	21.0	22.9
		S.D.	±1.7	±1.4	±0.7	±2.7	±2.9	±2.6	±2.6	±2.6
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	18.6*	19.7	19.4	20.3	20.6	17.4**	20.0	19.4
		S.D.	±1.7	±1.5	±2.8	±2.1	±2.4	±1.7	±2.7	±3.1
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	19.6	19.3	20.9	21.4	21.4	20.4	19.8	20.4
		S.D.	±1.6	±2.8	±2.4	±3.1	±1.7	±1.7	±0.8	±2.4

*: $P<0.05$, **: $P<0.01$ (significantly different from control).

Table 4 Postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		Control	5 mg/kg	20 mg/kg	80 mg/kg
No. of male offspring					
Pinna detachment	(4 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Piliation	(8 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Incisor eruption	(10 days)	8/12 (66.67)	12/12 (100)*	8/12 (66.67)	9/12 (75.00)
	(11 days)	12/12 (100)	-	12/12 (100)	12/12 (100)
Eyelid separation	(15 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Gait	(15 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Descensus testis	(21 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Cleavage of the balanopreputial gland					
	(42 days)	2/6 (33.33)	1/6 (16.67)	2/6 (33.33)	3/6 (50.00)
	(43 days)	3/6 (50.00)	1/6 (16.67)	3/6 (50.00)	3/6 (50.00)
	(44 days)	4/6 (66.67)	2/6 (33.33)	4/6 (66.67)	3/6 (50.00)
	(45 days)	6/6 (100)	6/6 (100)	5/6 (83.33)	5/6 (83.33)
	(46 days)	-	-	6/6 (100)	6/6 (100)
No. of female offspring					
Pinna detachment	(4 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Piliation	(8 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Incisor eruption	(10 days)	9/12 (75.00)	6/12 (50.00)	9/12 (75.00)	8/12 (66.67)
	(11 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Eyelid separation	(15 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Gait	(15 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Vaginal opening	(42 days)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)

*: $P<0.05$ (significantly different from control).
Values in parentheses represent percentages to the number of offspring examined.

Table 5 Function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		Control	5 mg/kg	20 mg/kg	80 mg/kg
No. of male offspring					
Righting reflex	(5 days)	12/12 (100)	12/12 (100)	10/12 (83.33)	12/12 (100)
	(6 days)	-	-	12/12 (100)	-
Ipsilateral flexor reflex	(5 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Visual placing	(16 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Preyer's reflex 500 Hz(60 dB)	(28 days)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)
Preyer's reflex 20000 Hz(60 dB)	(28 days)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)
No. of female offspring					
Righting reflex	(5 days)	12/12 (100)	11/12 (91.67)	10/12 (83.33)	10/12 (83.33)
	(6 days)	-	12/12 (100)	12/12 (100)	12/12 (100)
Ipsilateral flexor reflex	(5 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Visual placing	(16 days)	12/12 (100)	12/12 (100)	12/12 (100)	12/12 (100)
Preyer's reflex 500 Hz(60 dB)	(28 days)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)
Preyer's reflex 20000 Hz(60 dB)	(28 days)	6/6 (100)	6/6 (100)	6/6 (100)	6/6 (100)

Not significantly different from control.
Values in parentheses represent percentages to the number of offspring examined.

Table 6 Urinary findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Urine volume (mL/24hr)	Osmotic pressure (Osm/kg)	Specific gravity
Male	Control	N	6	6	6
		Mean	23.2	1.354	1.041
		S.D.	±6.3	±0.232	±0.008
	5 mg/kg	N	6	6	6
		Mean	20.8	1.338	1.040
		S.D.	±5.6	±0.439	±0.014
	20 mg/kg	N	6	6	6
		Mean	19.2	1.436	1.044
		S.D.	±5.1	±0.344	±0.010
	80 mg/kg	N	6	6	6
		Mean	25.0	0.999	1.031
		S.D.	±4.0	±0.262	±0.008
Female	Control	N	6	6	6
		Mean	9.6	1.371	1.042
		S.D.	±2.2	±0.312	±0.010
	5 mg/kg	N	6	6	6
		Mean	11.6	1.287	1.040
		S.D.	±2.4	±0.148	±0.005
	20 mg/kg	N	6	6	6
		Mean	13.4	1.231	1.038
		S.D.	±9.7	±0.332	±0.010
	80 mg/kg	N	6	6	6
		Mean	10.8	1.188	1.037
		S.D.	±2.2	±0.198	±0.007

Not significantly different from control.

Table 6 - continued Urinary findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Number of animals	Color		pH				Protein					Glucose	Ketone body
			PY	Y	6.5	7.5	8.0	8.5	-	±	+	++	+++	-	-
Male	Control	6	0	6	0	1	5	0	0	0	3	3	0	6	6
	5 mg/kg	6	1	5	0	1	4	1	0	1	1	3	1	6	6
	20 mg/kg	6	1	5	0	0	6	0	0	1	1	4	0	6	6
	80 mg/kg	6	2	4	0	0	5	1	0	0	3	3	0	6	6
Female	Control	6	0	6	0	3	3	0	4	2	0	0	0	6	6
	5 mg/kg	6	0	6	1	2	3	0	2	4	0	0	0	6	6
	20 mg/kg	6	1	5	1	0	4	1	5	0	1	0	0	6	6
	80 mg/kg	6	0	6	0	2	3	1	4	2	0	0	0	6	6

Abbreviation: PY, pale yellow; Y, yellow.
Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked.

Table 6 - continued Urinary findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Number of animals	Bilirubin	Occult blood			Urobilinogen (mg/dL)
			-	-	++	+++	<1
Male	Control	6	6	6	0	0	6
	5 mg/kg	6	6	5	0	1	6
	20 mg/kg	6	6	5	1	0	6
	80 mg/kg	6	6	6	0	0	6
Female	Control	6	6	6	0	0	6
	5 mg/kg	6	6	6	0	0	6
	20 mg/kg	6	6	6	0	0	6
	80 mg/kg	6	6	6	0	0	6

Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked.

Table 6 - continued Urinary findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose	Number of animals	Urinary sediment								
			Epithelial cells	Erythrocytes		Leukocytes	Casts	Crystals			
			-	-	+	-	-	-	+	++	+++
Male	Control	6	6	6	0	6	6	4	1	1	0
	5 mg/kg	6	6	5	1	6	6	3	1	1	1
	20 mg/kg	6	6	5	1	6	6	6	0	0	0
	80 mg/kg	6	6	6	0	6	6	5	0	1	0
Female	Control	6	6	6	0	6	6	5	1	0	0
	5 mg/kg	6	6	6	0	6	6	6	0	0	0
	20 mg/kg	6	6	6	0	6	6	6	0	0	0
	80 mg/kg	6	6	6	0	6	6	6	0	0	0

Grade signs are as follows.
Epithelial cells: -, < 3/field; +, 3/field ≦ and < 10/field; ++, 10/field ≦ and < 20/field; +++, ≧ 20/field.
Erythrocytes : -, < 10/field; +, 10/field ≦ and < 30/field; ++, 30/field ≦ and < 100/field; +++, countless.
Leukocytes : -, < 3/field; +, 3/field ≦ and < 20/field; ++, 20/field ≦ and < 40/field; +++, ≧ 40/field.
Casts : -, none; +, ≧ 1/all field.
Crystals : -, < 10/field; +, 10/field ≦ and < 20/field; ++, 20/field ≦ and < 30/field; +++, countless.

Table 7 Hematological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Leukocytes (10^2 /μL)	Erythrocytes (10^4 /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelets (10^4 /μL)
Male	Control	N	6	6	6	6	6	6	6	6
		Mean	63	488	9.1	33.3	69	18.7	27.3	119.1
		S.D.	±16	±34	±0.6	±2.0	±5	±1.6	±0.7	±9.5
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	66	492	9.1	33.3	68	18.7	27.4	118.4
		S.D.	±8	±39	±0.5	±1.3	±5	±1.8	±0.8	±4.6
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	62	482	8.9	32.6	68	18.5	27.3	111.2
		S.D.	±15	±36	±0.6	±1.9	±2	±0.8	±0.8	±5.8
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	74	499	9.1	33.8	68	18.1	26.8	109.1
		S.D.	±37	±20	±0.7	±2.2	±4	±1.1	±0.5	±11.9
Female	Control	N	6	6	6	6	6	6	6	6
		Mean	66	480	9.1	32.8	68	18.9	27.8	117.8
		S.D.	±29	±13	±1.1	±3.4	±6	±1.9	±0.7	±7.0
	5 mg/kg	N	5	5	5	5	5	5	5	5
		Mean	61	504	9.7	34.6	69	19.2	27.9	113.9
		S.D.	±15	±23	±0.9	±2.3	±3	±1.0	±0.7	±14.8
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	65	496	9.2	33.5	68	18.6	27.5	107.9
		S.D.	±19	±21	±0.7	±2.0	±4	±1.5	±0.7	±11.1
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	85	499	9.3	34.6	70	18.6	26.8	109.2
		S.D.	±31	±30	±0.9	±2.1	±4	±1.5	±1.2	±14.6

Not significantly different from control.

Table 7 - continued Hematological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Differential leukocyte count					
			Eosinophil (%)	Stab neutrophil (%)	Segmented neutrophil (%)	Lymphocyte (%)	Basophil (%)	Monocyte (%)
Male	Control	N	6	6	6	6	6	6
		Mean	0.5	0.3	17.8	79.5	0.0	1.8
		S.D.	±0.8	±0.8	±2.3	±2.6	±0.0	±0.8
	5 mg/kg	N	6	6	6	6	6	6
		Mean	0.5	0.5	18.3	79.0	0.0	1.7
		S.D.	±0.5	±0.5	±2.4	±2.1	±0.0	±1.0
	20 mg/kg	N	6	6	6	6	6	6
		Mean	0.3	0.2	18.3	78.7	0.0	2.5
		S.D.	±0.5	±0.4	±5.0	±6.1	±0.0	±1.5
	80 mg/kg	N	6	6	6	6	6	6
		Mean	0.5	0.3	19.7	76.2	0.0	3.3
		S.D.	±0.5	±0.5	±1.4	±2.3	±0.0	±1.0
Female	Control	N	6	6	6	6	6	6
		Mean	0.5	0.8	16.5	79.7	0.0	2.5
		S.D.	±0.8	±0.8	±4.7	±5.3	±0.0	±1.9
	5 mg/kg	N	6	6	6	6	6	6
		Mean	0.7	0.7	16.7	81.0	0.0	1.0
		S.D.	±0.8	±0.8	±5.2	±5.0	±0.0	±0.9
	20 mg/kg	N	6	6	6	6	6	6
		Mean	0.7	0.7	16.5	80.7	0.0	1.5
		S.D.	±0.8	±0.8	±6.0	±6.7	±0.0	±1.5
	80 mg/kg	N	6	6	6	6	6	6
		Mean	0.7	0.2	20.2	76.7	0.0	2.3
		S.D.	±0.5	±0.4	±9.4	±10.9	±0.0	±1.5

Not significantly different from control.

Table 8 Hematological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Leukocytes (10^2 /μL)	Erythrocytes (10^4 /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelets (10^4 /μL)	PT (sec)	APTT (sec)
Male	Control	N	6	6	6	6	6	6	6	6	6	6
		Mean	69	869	14.8	47.2	54	17.1	31.5	100.0	15.1	22.9
		S.D.	±7	±37	±0.5	±1.8	±2	±0.5	±0.8	±11.6	±1.9	±1.4
	5 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	66	819*	14.7	46.4	57	17.9*	31.6	89.6	14.4	22.1
		S.D.	±4	±24	±0.8	±2.4	±2	±0.6	±0.4	±5.3	±2.1	±2.6
	20 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	76	846	15.2	47.7	57	18.0*	31.8	95.2	15.0	21.4
		S.D.	±8	±38	±0.6	±2.1	±2	±0.5	±0.3	±6.8	±2.9	±4.1
	80 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	79	811*	14.4	45.9	56	17.7	31.4	94.8	13.4	20.1*
		S.D.	±18	±26	±0.6	±1.5	±2	±0.6	±0.8	±13.7	±1.4	±0.9
Female	Control	N	6	6	6	6	6	6	6	6	6	6
		Mean	54	798	14.5	45.6	57	18.2	31.8	103.3	12.2	17.6
		S.D.	±13	±20	±0.4	±0.9	±1	±0.3	±0.5	±9.3	±0.6	±1.2
	5 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	63	768	14.0	44.0	57	18.3	31.9	99.7	12.1	18.5
		S.D.	±20	±34	±0.5	±1.4	±1	±0.4	±0.1	±7.6	±0.5	±1.1
	20 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	53	820	14.5	46.0	56	17.7	31.6	98.9	11.7	17.4
		S.D.	±17	±48	±0.7	±2.2	±2	±0.5	±0.5	±7.8	±1.0	±1.9
	80 mg/kg	N	6	6	6	6	6	6	6	6	6	6
		Mean	51	805	14.5	45.4	56	18.0	31.8	96.9	12.3	17.6
		S.D.	±12	±30	±0.5	±1.4	±2	±0.4	±0.6	±1.8	±0.5	±1.0

*: $P<0.05$ (significantly different from control).

Table 8 - continued Hematological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Differential leukocyte count					
			Eosinophil (%)	Stab neutrophil (%)	Segmented neutrophil (%)	Lymphocyte (%)	Basophil (%)	Monocyte (%)
Male	Control	N	6	6	6	6	6	6
		Mean	1.2	0.2	10.3	86.3	0.0	2.0
		S.D.	±1.0	±0.4	±2.7	±2.7	±0.0	±1.1
	5 mg/kg	N	6	6	6	6	6	6
		Mean	0.8	0.2	8.0	89.3	0.0	1.7
		S.D.	±0.8	±0.4	±1.8	±2.3	±0.0	±0.8
	20 mg/kg	N	6	6	6	6	6	6
		Mean	1.2	0.0	9.0	87.7	0.0	2.2
		S.D.	±0.8	±0.0	±3.5	±4.5	±0.0	±1.6
	80 mg/kg	N	6	6	6	6	6	6
		Mean	0.8	0.0	10.5	87.3	0.0	1.3
		S.D.	±0.8	±0.0	±4.1	±5.1	±0.0	±1.8
Female	Control	N	6	6	6	6	6	6
		Mean	1.0	0.2	9.8	87.5	0.0	1.5
		S.D.	±0.6	±0.4	±3.3	±4.4	±0.0	±1.5
	5 mg/kg	N	6	6	6	6	6	6
		Mean	1.0	0.0	8.0	90.2	0.0	0.8
		S.D.	±0.6	±0.0	±3.9	±3.7	±0.0	±0.8
	20 mg/kg	N	6	6	6	6	6	6
		Mean	0.5	0.0	8.3	90.3	0.0	0.8
		S.D.	±0.8	±0.0	±3.1	±3.8	±0.0	±0.8
	80 mg/kg	N	6	6	6	6	6	6
		Mean	1.5	0.0	10.0	87.3	0.0	1.2
		S.D.	±1.0	±0.0	±4.8	±5.8	±0.0	±1.2

Not significantly different from control.

Table 9 Biochemical findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		T.Protein (g/dL)	Albumin (g/dL)	A/G ratio	T.Bilirubin (mg/dL)	GOT (IU/L)	GPT (IU/L)	γ-GTP (IU/L)	ALP (IU/L)	T.Cholesterol (mg/dL)
Male	Control	N	6	6	6	6	6	6	6	6	6
		Mean	4.7	3.6	3.39	0.0	97	23	0.3	916	107
		S.D.	±0.2	±0.2	±0.37	±0.0	±5	±2	±0.3	±96	±11
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	4.7	3.6	3.32	0.0	96	24	0.3	881	97
		S.D.	±0.3	±0.1	±0.41	±0.0	±8	±4	±0.2	±71	±8
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	4.6	3.5	3.51	0.0	91	24	0.4	931	104
		S.D.	±0.2	±0.1	±0.32	±0.0	±6	±5	±0.4	±73	±8
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	4.6	3.5	3.43	0.0	98	23	0.2	869	97
		S.D.	±0.2	±0.1	±0.29	±0.0	±13	±4	±0.1	±78	±14
Female	Control	N	6	6	6	6	6	6	6	6	6
		Mean	4.6	3.5	3.26	0.0	112	23	0.3	889	109
		S.D.	±0.2	±0.1	±0.48	±0.0	±23	±4	±0.3	±130	±16
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	4.5	3.4	3.29	0.0	107	23	0.3	783	100
		S.D.	±0.3	±0.2	±0.37	±0.0	±27	±2	±0.2	±124	±15
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	4.5	3.5	3.56	0.0	103	21	0.1	795	102
		S.D.	±0.2	±0.1	±0.51	±0.0	±9	±2	±0.1	±139	±9
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	4.6	3.6	3.57	0.0	95	22	0.2	856	100
		S.D.	±0.1	±0.1	±0.43	±0.0	±9	±1	±0.1	±130	±12

Not significantly different from control.

Table 9 - continued Biochemical findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Triglycerides (mg/dL)	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)
Male	Control	N	6	6	6	6	6	6	6	6	6
		Mean	138	211	157	13.4	0.4	10.2	11.3	143.2	4.78
		S.D.	±64	±30	±11	±0.8	±0.0	±0.4	±0.3	±0.9	±0.30
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	116	190	161	14.3	0.4	10.0	11.2	143.6	4.74
		S.D.	±40	±15	±11	±1.0	±0.1	±0.4	±0.3	±0.7	±0.19
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	129	206	151	14.8	0.4	10.1	11.4	143.2	4.78
		S.D.	±54	±20	±5	±2.4	±0.1	±0.7	±0.4	±1.0	±0.24
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	155	201	150	15.6	0.4	9.7	11.3	142.6	4.59
		S.D.	±67	±25	±6	±2.2	±0.0	±0.5	±0.4	±1.4	±0.21
Female	Control	N	6	6	6	6	6	6	6	6	6
		Mean	99	208	155	16.3	0.4	10.1	11.1	144.3	4.85
		S.D.	±53	±17	±8	±2.7	±0.0	±0.3	±0.2	±1.1	±0.42
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	97	192	162	15.5	0.4	10.1	10.7	144.0	4.96
		S.D.	±49	±26	±16	±2.5	±0.1	±0.4	±0.4	±1.3	±0.44
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	82	197	156	14.6	0.4	10.2	11.0	143.5	4.94
		S.D.	±20	±15	±10	±1.9	±0.1	±0.4	±0.2	±1.7	±0.32
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	133	206	153	16.5	0.4	10.1	11.3	143.7	4.79
		S.D.	±31	±24	±7	±1.7	±0.0	±0.4	±0.3	±1.2	±0.52

Not significantly different from control.

Table 9 - continued Biochemical findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Cl (mEq/L)
Male	Control	N	6
		Mean	103.7
		S.D.	±1.3
	5 mg/kg	N	6
		Mean	104.7
		S.D.	±0.9
	20 mg/kg	N	6
		Mean	104.3
		S.D.	±1.1
	80 mg/kg	N	6
		Mean	103.2
		S.D.	±0.8
Female	Control	N	6
		Mean	105.6
		S.D.	±0.9
	5 mg/kg	N	6
		Mean	104.5
		S.D.	±1.1
	20 mg/kg	N	6
		Mean	104.2
		S.D.	±1.5
	80 mg/kg	N	6
		Mean	104.0
		S.D.	±1.7

Not significantly different from control.

Table 10 Biochemical findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		T.Protein (g/dL)	Albumin (g/dL)	A/G ratio	T.Bilirubin (mg/dL)	GOT (IU/L)	GPT (IU/L)	γ-GTP (IU/L)	ALP (IU/L)	T.Cholesterol (mg/dL)
Male	Control	N	6	6	6	6	6	6	6	6	6
		Mean	5.6	3.8	2.19	0.0	82	20	0.7	267	46
		S.D.	±0.1	±0.1	±0.27	±0.0	±10	±2	±0.1	±55	±8
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	5.6	3.9	2.31	0.0	76	19	0.6	253	61
		S.D.	±0.2	±0.2	±0.23	±0.0	±8	±3	±0.3	±49	±12
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	5.5	3.8	2.17	0.0	89	21	0.7	250	58
		S.D.	±0.3	±0.2	±0.31	±0.0	±11	±3	±0.2	±27	±23
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	5.3*	3.7	2.31	0.0	79	19	0.4	260	61
		S.D.	±0.3	±0.2	±0.43	±0.0	±7	±1	±0.3	±28	±15
Female	Control	N	6	6	6	6	6	6	6	6	6
		Mean	5.6	4.0	2.52	0.0	76	17	0.8	164	51
		S.D.	±0.2	±0.2	±0.22	±0.1	±11	±1	±0.4	±30	±7
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	5.6	3.9	2.43	0.1	78	16	0.9	145	62
		S.D.	±0.3	±0.3	±0.37	±0.1	±7	±3	±0.4	±25	±21
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	5.7	4.2	2.85	0.1	76	15	0.8	162	61
		S.D.	±0.3	±0.3	±0.56	±0.1	±12	±1	±0.2	±15	±12
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	5.8	4.2	2.64	0.0	73	18	0.9	158	60
		S.D.	±0.2	±0.2	±0.35	±0.0	±14	±4	±0.3	±19	±10

*: $P<0.05$ (significantly different from control).

Table 10 - continued Biochemical findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Triglycerides (mg/dL)	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)
Male	Control	N	6	6	6	6	6	6	6	6	6
		Mean	53	93	133	14.8	0.4	7.1	10.3	144.5	4.12
		S.D.	±6	±11	±11	±1.8	±0.0	±0.3	±0.1	±1.1	±0.23
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	38	107	133	17.5	0.5	7.1	10.0	145.3	4.06
		S.D.	±17	±15	±13	±3.2	±0.1	±0.7	±0.1	±0.8	±0.24
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	67	107	140	16.2	0.5	7.2	10.1	144.5	4.23
		S.D.	±22	±29	±16	±2.4	±0.1	±0.2	±0.3	±0.9	±0.14
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	46	108	130	17.1	0.4	7.2	10.0*	144.7	4.08
		S.D.	±21	±19	±15	±2.9	±0.0	±0.4	±0.2	±1.4	±0.21
Female	Control	N	6	6	6	6	6	6	6	6	6
		Mean	18	103	112	16.9	0.5	6.5	10.0	144.5	4.10
		S.D.	±7	±12	±10	±1.6	±0.0	±0.6	±0.3	±1.0	±0.40
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	18	124	108	16.8	0.5	7.0	9.9	144.5	3.94
		S.D.	±9	±36	±8	±1.2	±0.1	±0.5	±0.3	±0.5	±0.17
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	21	126	119	15.6	0.5	7.6**	10.0	144.1	4.23
		S.D.	±10	±20	±13	±3.0	±0.1	±0.5	±0.3	±1.0	±0.42
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	22	120	117	18.4	0.5	6.9	10.2	144.7	4.18
		S.D.	±11	±13	±12	±2.4	±0.1	±0.4	±0.2	±1.2	±0.15

*: $P<0.05$, **: $P<0.01$ (significantly different from control).

Table 10 - continued Biochemical findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Cl (mEq/L)
Male	Control	N	6
		Mean	104.6
		S.D.	±2.1
	5 mg/kg	N	6
		Mean	104.9
		S.D.	±1.7
	20 mg/kg	N	6
		Mean	104.3
		S.D.	±1.1
	80 mg/kg	N	6
		Mean	104.7
		S.D.	±1.2
Female	Control	N	6
		Mean	109.0
		S.D.	±1.2
	5 mg/kg	N	6
		Mean	107.5
		S.D.	±1.5
	20 mg/kg	N	6
		Mean	107.5
		S.D.	±1.0
	80 mg/kg	N	6
		Mean	107.8
		S.D.	±2.5

Not significantly different from control.

Table 11 Necropsy findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Male											
Group and dose	Control			5 mg/kg			20 mg/kg			80 mg/kg		
Necropsy timing	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total
Organs and findings / Number of animals	6	0	6	6	0	6	6	0	6	6	0	6
Integumentary system												
Integument												
Coloration, hair, yellow	0	0	0	6	0	6	6	0	6	6	0	6

No appreciable changes in all other organs and tissues.

Table 11 - continued Necropsy findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings	Sex	Female											
	Group and dose	Control			5 mg/kg			20 mg/kg			80 mg/kg		
	Necropsy timing	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total
	Number of animals	6	0	6	6	0	6	6	0	6	6	0	6
Integumentary system													
Integument													
Coloration, hair, yellow		0	0	0	6	0	6	6	0	6	6	0	6

No appreciable changes in all other organs and tissues.

Table 12 Necropsy findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Male											
Group and dose	Control			5 mg/kg			20 mg/kg			80 mg/kg		
Necropsy timing	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total
Organs and findings / Number of animals	6	0	6	6	0	6	6	0	6	6	0	6
Urinary system												
Kidney												
Dilatation, pelvic cavity	0	0	0	0	0	0	0	0	0	0	0	0
Genital system												
Testis												
Small	0	0	0	0	0	0	2	0	2	0	0	0
Enlargement	1	0	1	0	0	0	0	0	0	0	0	0
Epididymis												
Macule, light yellow	0	0	0	0	0	0	0	0	0	1	0	1
Small	0	0	0	0	0	0	1	0	1	0	0	0
Integumentary system												
Integument												
Coloration, hair, yellow	0	0	0	1	0	1	6	0	6	6	0	6

No appreciable changes in all other organs and tissues.

Table 12 - continued Necropsy findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Female											
Group and dose	Control			5 mg/kg			20 mg/kg			80 mg/kg		
Necropsy timing	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total	Scheduled	Dead	Total
Organs and findings / Number of animals	6	0	6	6	0	6	6	0	6	6	0	6
Urinary system												
Kidney												
Dilatation, pelvic cavity	0	0	0	1	0	1	0	0	0	0	0	0
Genital system												
Testis	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Small												
Enlargement												
Epididymis	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Macule, light yellow												
Small												
Integumentary system												
Integument												
Coloration, hair, yellow	0	0	0	0	0	0	6	0	6	6	0	6

NA, not applicable.
No appreciable changes in all other organs and tissues.

Table 13 Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Final body weight	Brain		Pituitary		Thyroids		Heart	
			(g)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Male	Control	N	6	6	6	6	6	6	6	6	6
		Mean	63.4	1.66	2.63	2.4	3.9	7.7	12.2	349.3	551.9
		S.D.	±4.9	±0.05	±0.14	±0.5	±0.9	±1.4	±2.2	±29.9	±42.2
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	63.0	1.63	2.60	2.6	4.1	6.7	10.7	343.9	544.6
		S.D.	±2.8	±0.05	±0.12	±0.4	±0.6	±2.1	±3.2	±41.3	±42.3
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	63.7	1.64	2.60	2.6	4.0	8.0	12.4	329.9	517.2
		S.D.	±5.7	±0.06	±0.32	±0.6	±0.8	±2.2	±2.4	±37.0	±22.5
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	61.8	1.61	2.62	2.6	4.3	7.5	12.2	340.3	550.6
		S.D.	±4.8	±0.07	±0.20	±0.2	±0.5	±1.0	±2.1	±33.6	±24.2
Female	Control	N	6	6	6	6	6	6	6	6	6
		Mean	59.0	1.57	2.67	3.0	5.1	6.8	11.6	332.9	564.5
		S.D.	±3.3	±0.06	±0.14	±0.4	±0.8	±0.7	±1.6	±33.9	±44.5
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	59.6	1.57	2.64	2.7	4.5	7.1	11.9	315.0	528.5
		S.D.	±2.3	±0.05	±0.11	±0.3	±0.5	±1.1	±1.8	±18.1	±14.1
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	57.0	1.56	2.76	2.7	4.8	6.7	11.8	308.1	539.7
		S.D.	±4.6	±0.01	±0.21	±0.6	±0.9	±1.2	±1.8	±50.4	±61.9
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	58.8	1.53	2.61	2.8	4.8	8.0	13.7	354.2	601.9
		S.D.	±5.3	±0.04	±0.18	±0.4	±1.1	±1.7	±3.1	±38.8	±34.3

Not significantly different from control.

Table 13 - continued Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Lungs		Thymus		Liver		Spleen	
			(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)
Male	Control	N	6	6	6	6	6	6	6	6
		Mean	525.6	829.0	289.3	457.6	2.69	4.25	341.9	536.0
		S.D.	±59.6	±70.8	±22.7	±37.5	±0.22	±0.16	±67.7	±69.7
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	500.3	793.1	278.7	442.0	2.74	4.35	354.1	561.1
		S.D.	±54.1	±59.7	±52.8	±74.8	±0.14	±0.12	±58.6	±79.3
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	503.3	790.9	272.8	428.2	2.79	4.38	380.9	598.4
		S.D.	±51.4	±53.2	±27.0	±18.4	±0.24	±0.08	±41.5	±50.8
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	546.7	884.6	288.7	470.6	2.97	4.79**	372.6	600.9
		S.D.	±62.7	±59.8	±46.2	±90.6	±0.38	±0.28	±56.8	±53.1
Female	Control	N	6	6	6	6	6	6	6	6
		Mean	453.0	767.3	267.0	453.0	2.46	4.18	319.4	540.5
		S.D.	±45.0	±46.4	±16.4	±18.5	±0.22	±0.35	±40.5	±48.2
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	466.7	783.2	256.7	431.6	2.44	4.09	329.1	553.5
		S.D.	±37.4	±54.8	±21.6	±42.2	±0.24	±0.29	±39.2	±73.5
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	443.5	777.6	281.4	493.2	2.33	4.09	291.5	511.6
		S.D.	±53.5	±46.2	±34.7	±34.9	±0.25	±0.19	±54.3	±78.2
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	472.4	803.1	268.8	457.4	2.75	4.67*	367.5	623.5
		S.D.	±49.4	±44.9	±37.1	±57.8	±0.28	±0.19	±46.7	±32.7

*: $P<0.05$, **: $P<0.01$ (significantly different from control).

Table 13 - continued Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Kidneys		Adrenals		Epididymides		Testes	
			(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Male	Control	N	6	6	6	6	6	6	6	6
		Mean	0.74	1.16	18.0	28.4	57.6	91.1	325.9	513.0
		S.D.	±0.12	±0.12	±1.4	±1.2	±4.6	±6.9	±47.1	±54.0
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	0.73	1.16	17.1	27.2	55.4	87.9	302.1	479.0
		S.D.	±0.08	±0.09	±0.9	±1.8	±6.0	±7.2	±27.0	±26.2
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	0.77	1.21	17.4	27.3	57.6	91.3	319.4	503.7
		S.D.	±0.03	±0.10	±1.9	±1.5	±7.3	±16.4	±21.7	±44.0
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	0.73	1.18	17.1	27.7	50.3	81.9	294.7	478.2
		S.D.	±0.12	±0.12	±1.6	±2.2	±3.7	±7.9	±19.5	±26.7
Female	Control	N	6	6	6	6				
		Mean	0.69	1.17	16.4	27.7				
		S.D.	±0.05	±0.09	±1.6	±2.0				
	5 mg/kg	N	6	6	6	6				
		Mean	0.69	1.16	16.6	27.8				
		S.D.	±0.06	±0.08	±2.0	±2.4				
	20 mg/kg	N	6	6	6	6				
		Mean	0.66	1.16	16.4	28.8				
		S.D.	±0.06	±0.10	±2.4	±2.6				
	80 mg/kg	N	6	6	6	6				
		Mean	0.70	1.20	16.1	27.4				
		S.D.	±0.05	±0.06	±2.2	±2.5				

Not significantly different from control.

Table 13 - continued Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Sex	Group and dose		Ovaries (mg)	Ovaries (mg/100gB.W.)
Male	Control	N		
		Mean		
		S.D.		
	5 mg/kg	N		
		Mean		
		S.D.		
	20 mg/kg	N		
		Mean		
		S.D.		
	80 mg/kg	N		
		Mean		
		S.D.		
Female	Control	N	6	6
		Mean	19.7	33.3
		S.D.	±2.2	±2.2
	5 mg/kg	N	6	6
		Mean	17.3	29.1
		S.D.	±3.0	±5.3
	20 mg/kg	N	6	6
		Mean	15.6*	27.2*
		S.D.	±2.9	±3.5
	80 mg/kg	N	6	6
		Mean	19.0	32.5
		S.D.	±1.8	±3.6

*: $P<0.05$ (significantly different from control).

Table 14 Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Final body weight	Brain		Pituitary		Thyroids		Heart	
			(g)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Male	Control	N	6	6	6	6	6	6	6	6	6
		Mean	479.4	2.27	0.48	14.5	3.0	22.1	4.6	1605.1	336.1
		S.D.	±45.5	±0.18	±0.02	±1.5	±0.1	±3.7	±0.7	±152.5	±31.9
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	465.0	2.24	0.48	13.9	3.0	22.2	4.8	1631.4	351.6
		S.D.	±43.8	±0.10	±0.03	±2.2	±0.3	±4.0	±0.8	±149.6	±23.8
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	460.8	2.23	0.49	14.2	3.1	20.6	4.5	1529.5	332.6
		S.D.	±28.5	±0.14	±0.04	±2.2	±0.4	±4.8	±1.0	±60.4	±15.7
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	460.1	2.21	0.48	12.7	2.8	22.0	4.8	1541.6	335.6
		S.D.	±37.4	±0.04	±0.03	±0.5	±0.2	±2.9	±0.5	±94.8	±13.3
Female	Control	N	6	6	6	6	6	6	6	6	6
		Mean	278.5	2.02	0.73	14.9	5.4	18.3	6.6	966.4	347.2
		S.D.	±21.1	±0.08	±0.05	±1.1	±0.4	±3.9	±1.2	±82.1	±15.0
	5 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	283.2	2.09	0.74	16.5	5.8	17.3	6.2	1006.9	356.1
		S.D.	±22.6	±0.07	±0.06	±1.3	±0.5	±2.4	±0.9	±85.0	±26.0
	20 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	249.6*	2.01	0.81*	15.2	6.1	14.9	6.0	972.7	389.9*
		S.D.	±12.1	±0.07	±0.03	±1.0	±0.6	±2.0	±0.8	±82.7	±30.1
	80 mg/kg	N	6	6	6	6	6	6	6	6	6
		Mean	256.9	1.93	0.75	14.0	5.5	16.9	6.5	965.3	376.6
		S.D.	±15.3	±0.04	±0.05	±1.8	±0.6	±3.3	±0.9	±76.0	±33.4

*: $P<0.05$ (significantly different from control).

Table 14 - continued Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Lungs		Thymus		Liver		Spleen	
			(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)
Male	Control	N	6	6	6	6	6	6	6	6
		Mean	1580.1	329.1	507.8	107.1	14.71	3.07	888.2	186.2
		S.D.	±195.4	±16.0	±101.8	±24.4	±1.59	±0.13	±94.6	±22.6
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	1504.1	324.4	541.9	116.0	13.29	2.86	873.9	187.5
		S.D.	±99.7	±16.1	±131.6	±21.6	±1.65	±0.29	±128.8	±14.8
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	1454.5	315.6	573.8	124.9	14.43	3.13	833.0	181.0
		S.D.	±142.4	±22.7	±150.3	±33.0	±1.71	±0.31	±78.3	±16.3
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	1483.3	322.5	550.2	119.5	14.21	3.08	924.4	199.1
		S.D.	±122.1	±11.7	±112.6	±22.0	±2.15	±0.29	±236.0	±35.2
Female	Control	N	6	6	6	6	6	6	6	6
		Mean	1127.3	404.1	501.0	179.2	7.45	2.68	591.0	211.7
		S.D.	±118.6	±15.5	±72.0	±14.6	±0.54	±0.07	±111.0	±31.6
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	1171.0	412.8	537.8	189.9	7.75	2.73	618.9	217.6
		S.D.	±139.7	±25.7	±89.9	±28.2	±1.05	±0.17	±113.1	±27.4
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	1040.7	417.9	430.2	171.8	6.89	2.77	540.2	216.6
		S.D.	±21.1	±23.9	±92.4	±31.4	±0.44	±0.24	±36.3	±12.9
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	991.9	386.1	458.4	179.1	6.99	2.72	540.3	211.1
		S.D.	±67.7	±13.6	±106.7	±43.3	±0.60	±0.12	±85.0	±36.6

Not significantly different from control.

Table 14 - continued Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Kidneys		Adrenals		Epididymides		Testes	
			(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Male	Control	N	6	6	6	6	6	6	6	6
		Mean	3.41	0.71	61.8	12.9	1249.8	262.0	3952.4	826.0
		S.D.	±0.41	±0.04	±10.1	±1.3	±139.7	±32.0	±575.7	±99.1
	5 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	2.99	0.65	71.2	15.2*	1212.5	262.7	3514.9	761.2
		S.D.	±0.28	±0.06	±13.1	±1.6	±135.5	±36.8	±259.4	±87.7
	20 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	3.18	0.69	66.9	14.5	1034.6	223.2	2872.3	619.6
		S.D.	±0.36	±0.07	±9.1	±1.5	±351.8	±70.4	±1231.0	±258.1
	80 mg/kg	N	6	6	6	6	6	6	6	6
		Mean	2.98	0.65	60.2	13.0	1133.5	246.9	3352.9	728.5
		S.D.	±0.15	±0.03	±10.9	±1.9	±96.7	±19.8	±323.2	±33.7
Female	Control	N	6	6	6	6				
		Mean	1.88	0.68	74.1	26.6				
		S.D.	±0.13	±0.03	±12.1	±3.4				
	5 mg/kg	N	6	6	6	6				
		Mean	1.95	0.69	77.3	27.3				
		S.D.	±0.16	±0.06	±9.5	±2.9				
	20 mg/kg	N	6	6	6	6				
		Mean	1.73	0.70	73.2	29.5				
		S.D.	±0.08	±0.05	±8.8	±4.6				
	80 mg/kg	N	6	6	6	6				
		Mean	1.76	0.69	66.4	25.9				
		S.D.	±0.10	±0.04	±5.3	±2.5				

*: $P<0.05$ (significantly different from control).

Table 14 - continued Organ weights in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Sex	Group and dose		Ovaries (mg)	Ovaries (mg/100gB.W.)
Male	Control	N		
		Mean		
		S.D.		
	5 mg/kg	N		
		Mean		
		S.D.		
	20 mg/kg	N		
		Mean		
		S.D.		
	80 mg/kg	N		
		Mean		
		S.D.		
Female	Control	N	6	6
		Mean	87.9	31.5
		S.D.	±13.2	±3.4
	5 mg/kg	N	6	6
		Mean	84.3	29.8
		S.D.	±10.9	±4.0
	20 mg/kg	N	6	6
		Mean	75.1	30.2
		S.D.	±15.0	±6.1
	80 mg/kg	N	6	6
		Mean	71.8	27.9
		S.D.	±10.7	±3.4

Not significantly different from control.

Table 15 Histopathological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings \ Sex	Male																			
Group and dose	Control					5 mg/kg					20 mg/kg					80 mg/kg				
Number of animals	6					6					6					6				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Urinary system																				
Kidney			(6)					(0)					(0)					(6)		
Dilatation, tubule, focal	5	1	0	0	1											4	2	0	0	2

Not significantly different from control.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
Figures in parentheses are number of animals with tissues examined histopathologically.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, testis, epididymis, pituitary, thyroid, adrenal and brain in control and 80 mg/kg groups, and in the integument in 80 mg/kg group.

Table 15 - continued Histopathological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings \ Sex	Female																			
Group and dose	Control					5 mg/kg					20 mg/kg					80 mg/kg				
Number of animals	6					6					6					6				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Urinary system																				
Kidney			(6)					(0)					(0)					(6)		
Dilatation, tubule, focal	4	2	0	0	2											5	1	0	0	1

Not significantly different from control.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
Figures in parentheses are number of animals with tissues examined histopathologically.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, ovary, pituitary, thyroid, adrenal and brain in control and 80 mg/kg groups, and in the integument in 80 mg/kg group.

Study No.49816

Table 16 Histopathological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrwal period

Organs and findings \ Sex	Male																			
Group and dose	Control					5 mg/kg					20 mg/kg					80 mg/kg				
Number of animals	6					6					6					6				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Urinary system																				
Kidney			(6)					(0)					(0)					(6)		
Dilatation, pelvic cavity	6	0	0	0	0											6	0	0	0	0
Mineralization	6	0	0	0	0											6	0	0	0	0
Genital system																				
Testis			(6)					(0)					(2)					(6)		
Atrophy, seminiferous tubule	6	0	0	0	0						0	0	0	2	2*	6	0	0	0	0
Dilatation, seminiferous tubule	5	1	0	0	1						2	0	0	0	0	6	0	0	0	0
Epididymis			(6)					(0)					(1)					(6)		
Decrease, sperm, lumen	6	0	0	0	0						0	0	0	1	1*	6	0	0	0	0
Debris, germ cell, lumen	6	0	0	0	0						0	1	0	0	1*	6	0	0	0	0
Granuloma, spermatic	6	0	0	0	0						1	0	0	0	0	5	1	0	0	1
Nervous system																				
Cerebrum			(6)					(0)					(0)					(6)		
Dilatation, ventricle	5	1	0	0	1											6	0	0	0	0

*: P<0.05 (significantly different from control).
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
Figures in parentheses are number of animals with tissues examined histopathologically.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, pituitary, thyroid, adrenal and cerebellum in control and 80 mg/kg groups, and in the integument in 80 mg/kg group.

Table 16 - continued Histopathological findings in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrwal period

Organs and findings \ Sex	Female																			
Group and dose	Control					5 mg/kg					20 mg/kg					80 mg/kg				
Number of animals	6					6					6					6				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Urinary system																				
Kidney			(6)					(1)					(0)					(6)		
Dilatation, pelvic cavity	6	0	0	0	0	0	1	0	0	1*						6	0	0	0	0
Mineralization	3	3	0	0	3	1	0	0	0	0						6	0	0	0	0
Genital system																				
Testis			NA					NA					NA					NA		
Atrophy, seminiferous tubule																				
Dilatation, seminiferous tubule																				
Epididymis			NA					NA					NA					NA		
Decrease, sperm, lumen																				
Debris, germ cell, lumen																				
Granuloma, spermatic																				
Nervous system																				
Cerebrum			(6)					(0)					(0)					(6)		
Dilatation, ventricle	6	0	0	0	0											6	0	0	0	0

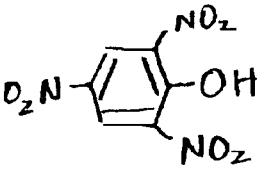
*: P<0.05 (significantly different from control).
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
NA, not applicable.
Figures in parentheses are number of animals with tissues examined histopathologically.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, ovary, pituitary, thyroid, adrenal and cerebellum in control and 80 mg/kg groups, and in the integument in 80 mg/kg group.

2,4,6-トリニトロフェノールのラット新生児における哺育期投与試験

添 付 資 料

1. 被験物質原体の分析成績書
2. 被験液の安定性試験報告書
3. 被験液の濃度確認成績書

（別紙２）

化学物質の名称	2,4,6－トリニトロフェノール		
別　　名	ピクリン酸		
構造式又は示性式			
化学物質の純度（サンプル）	81.4 wt%	化学物質のLot.No（サンプル）	8802403
不純物の名称及び純度	不明分 0.1 % 水 18.5 %		
ＣＡＳ番号	88－89－1	蒸気圧（摂氏25度）	知見なし
分　子　量	229.05	分配係数	2.03
融　　点	122 ℃	常温における性状	黄色結晶
沸　　点	>300 ℃		
安定性（水、熱、光等）	MSDS参照		

溶媒に対する溶解性	溶　媒	溶　解　度	溶　媒	溶　解　度
	水	1/冷水100 7/沸騰水100	DMSO	
	アセトン		その他（　）	

その他	有害性情報（急性毒性等） その他の物理化学的性質（ｐＨ、ｐＫａ等） 溶媒中の安定性 取扱い上の留意点（危険性、有害性等） 廃棄方法　等 MSDS参照

注）様式については、特に、本様式にこだわるものではありませんが、上記の事項は試験を実施するに必要最小限の情報ですので、記載方よろしくお願いします。

平成12年1月15日

試　験　成　績　表

株式会社パナファーム・ラボラトリーズ御中

三井化学株式会社
精密化学品事業部
[redacted]

物質名	2,4,6-トリニトロフェノール
別名	ピクリン酸
製品名	
製造番号	8802403
製造年月	

試験項目	単位	毒性試験前 (平成11年1月19日分析)	毒性試験後 (平成12年1月7日分析)
純度	wt%	81.4	81.2
水分	〃	18.5	18.7
硫酸分	〃	0.08	0.09

品質上問題なし。

以上

証明番号 ： 8L655-001
受付番号 ： 404

分析証明書

1999 年 2 月 23 日
㈱三菱化学安全科学研究所　鹿島研究所

分析責任者 [redacted]

分析担当者

試験物質　：2,4,6-トリニトロフェノール
ロット番号　：8802403
分析内容　：調製物の均一性・安定性確認［媒体：0.1%Tween80添加0.5%CMC-Na水溶液］
（表示濃度：0.1，200 mg/mL）
分析方法　：分析フローに準ずる
保存条件　：室温
分析実施日：1999年 2 月 15, 17, 19, 23 日
分析結果　：以下に示すように，2,4,6-トリニトロフェノールの調製物は均一であり，0.1mg/mLは調製後８日間まで，200mg/mLは調製後４日間まで安定であった．

［分析結果］

濃度 ＼ 分析日		'99.02.15 (0日)*	'99.02.17 (2日)	'99.02.19 (4日)	'99.02.23 (8日)
0.1	測定濃度	0.0968 √ 0.0973 √ 0.1044 √	0.0963 √ 0.1000 √	0.0970 √ 0.0960 √	0.0928 √ 0.0944 √
	平均値	0.0995 √	0.0982 √	0.0965 √	0.0936 √
	S.D	0.00425 √	–	–	–
	C.V(%)	4.3 √	–	–	–
対初期値 濃度(%)		100.0 √	98.7 √	97.0 √	94.1 √
200	測定濃度	183 √ 191 √ 200 √	204 √ 207 √	212 √ 221 √ 200 √ 196 √	249 √ 259 √
	平均値	191 √	206 √	207	254 √
	S.D	8.5 √	–	–	–
	C.V(%)	4.5 √	–	–	–
対初期値 濃度(%)		100.0 √	107.9 √	108.4 √	133.0 √

単位：mg/mL

*均一性（安定性初日に実施）

データ確認：[redacted]

証明番号 ： 8L660-001
受付番号 ： 4/1

分析証明書

1999 年 3 月 3 日
㈱三菱化学安全科学研究所　鹿島研究所
分析責任者 [redacted]
分析担当者

試験物質　：2,4,6-トリニトロフェノール
ロット番号　：8802403
分析内容　：調製物の均一性・安定性確認［媒体：0.1%Tween80添加0.5%CMC-Na水溶液］
（表示濃度：10 mg/mL）
分析方法　：分析フローに準ずる
保存条件　：室温
分析実施日：1999年 2 月 23日，3 月 3日
分析結果　：以下に示すように，2,4,6-トリニトロフェノールの調製物は均一であり
調製後8日間まで安定であった.

［分析結果］

濃度 ＼ 分析日		'99.02.23 (0日)*	'99.03.03 (8日)
10	測定濃度	9.70	9.64
		9.82	
		9.56	9.62
	平均値	9.69	9.63
	S.D	0.130	−
	C.V(%)	1.3	−
対初期値 濃度(%)		100.0	99.4

単位：mg/mL

*均一性（安定性初日に実施）

データ確認：[redacted]

試験番号49816

分析成績書

１．試験番号：49816

２．分析番号：AN99117

３．分析項目：濃度測定

４．被験物質名：2,4,6-ﾄﾘﾆﾄﾛﾌｪﾉｰﾙ(TS9804)

５．調　製　日：1999年 8月 27日

６．濃度確認日：1999年 8月 27日

７．試験結果　：

表示濃度 (mg/mL)	試料	濃度 (mg/mL)	含有率 (%)	平均濃度 (mg/mL)	平均含有率 (%)	均一性* (%)
0.1	上	0.995	99.5	1.001	100.1	99.4
	中	0.997	99.7			99.6
	下	1.011	101.1			101.0
0.4	上	4.035	100.9	4.047	101.2	99.7
	中	4.087	102.2			101.0
	下	4.020	100.5			99.3
1.6	上	16.53	103.3	16.27	101.7	101.6
	中	16.10	100.6			99.0
	下	16.19	101.2			99.5

*：各層の濃度が平均濃度に対して±10%以内であること

８．判　　定：投与液として適合

分析責任者

1999 年 9 月 2 日 [redacted]

株式会社パナファーム・ラボラトリーズ　研究本部　研究第３部

試験責任者

1999 年 9 月 2 日 [redacted]

株式会社パナファーム・ラボラトリーズ　研究本部　研究第１部

2,4,6-トリニトロフェノールのラット新生児における哺育期投与試験

APPENDIX
(個別データ)

目 次

目 次 (続 き)

目 次 (続 き)

Appendix 1 Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 1	2	3	4	5	6	7	8	9	10	11
Control	901	-	-	-	-	-	-	-	-	-	-	-
	902	-	-	-	-	-	-	-	-	-	-	-
	903	-	-	-	-	-	-	-	-	-	-	-
	904	-	-	-	-	-	-	-	-	-	-	-
	905	-	-	-	-	-	-	-	-	-	-	-
	906	-	-	-	-	-	-	-	-	-	-	-
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913	-	-	-	-	-	-	-	-	-	a	a
	914	-	-	-	-	-	-	-	-	-	a	a
	915	-	-	-	-	-	-	-	-	-	a	a
	916	-	-	-	-	-	-	-	-	-	a	a
	917	-	-	-	-	-	-	-	-	-	a	a
	918	-	-	-	-	-	-	-	-	-	a	a
	919	-	-	-	-	-	-	-	-	-	a	a
	920	-	-	-	-	-	-	-	-	-	a	a
	921	-	-	-	-	-	-	-	-	-	a	a
	922	-	-	-	-	-	-	-	-	-	a	a
	923	-	-	-	-	-	-	-	-	-	a	a
	924	-	-	-	-	-	-	-	-	-	a	a
20 mg/kg	925	-	-	-	-	a	a	a	a	a	a	a
	926	-	-	-	-	a	a	a	a	a	a	a
	927	-	-	-	-	a	a	a	a	a	a	a
	928	-	-	-	-	a	a	a	a	a	a	a
	929	-	-	-	-	a	a	a	a	a	a	a
	930	-	-	-	-	a	a	a	a	a	a	a
	931	-	-	-	-	a	a	a	a	a	a	a
	932	-	-	-	-	a	a	a	a	a	a	a
	933	-	-	-	-	a	a	a	a	a	a	a
	934	-	-	-	-	a	a	a	a	a	a	a
	935	-	-	-	-	a	a	a	a	a	a	a
	936	-	-	-	-	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		1	2	3	4	5	6	7	8	9	10	11
80 mg/kg	937	-	-	a	a	a	a	a	a	a	a	a
	938	-	-	a	a	a	a	a	a	a	a	a
	939	-	-	a	a	a	a	a	a	a	a	a
	940	-	-	a	a	a	a	a	a	a	a	a
	941	-	-	a	a	a	a	a	a	a	a	a
	942	-	-	a	a	a	a	a	a	a	a	a
	943	-	-	a	a	a	a	a	a	a	a	a
	944	-	-	a	a	a	a	a	a	a	a	a
	945	-	-	a	a	a	a	a	a	a	a	a
	946	-	-	a	a	a	a	a	a	a	a	a
	947	-	-	a	a	a	a	a	a	a	a	a
	948	-	-	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 12	13	14	15	16	17	18	19	20	21	22
Control	901	-	-	-	-	-	-	-				
	902	-	-	-	-	-	-	-				
	903	-	-	-	-	-	-	-				
	904	-	-	-	-	-	-	-				
	905	-	-	-	-	-	-	-				
	906	-	-	-	-	-	-	-				
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913	a	a	a	a	a	a	a				
	914	a	a	a	a	a	a	a				
	915	a	a	a	a	a	a	a				
	916	a	a	a	a	a	a	a				
	917	a	a	a	a	a	a	a				
	918	a	a	a	a	a	a	a				
	919	a	a	a	a	a	a	a	a	a	a	a
	920	a	a	a	a	a	a	a	a	a	a	a
	921	a	a	a	a	a	a	a	a	a	a	a
	922	a	a	a	a	a	a	a	a	a	a	a
	923	a	a	a	a	a	a	a	a	a	a	a
	924	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	925	a	a	a	a	a	a	a				
	926	a	a	a	a	a	a	a				
	927	a	a	a	a	a	a	a				
	928	a	a	a	a	a	a	a				
	929	a	a	a	a	a	a	a				
	930	a	a	a	a	a	a	a				
	931	a	a	a	a	a	a	a	a	a	a	a
	932	a	a	a	a	a	a	a	a	a	a	a
	933	a	a	a	a	a	a	a	a	a	a	a
	934	a	a	a	a	a	a	a	a	a	a	a
	935	a	a	a	a	a	a	a	a	a	a	a
	936	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		12	13	14	15	16	17	18	19	20	21	22
80 mg/kg	937	a	a	a	a	a	a	a				
	938	a	a	a	a	a	a	a				
	939	a	a	a	a	a	a	a				
	940	a	a	a	a	a	a	a				
	941	a	a	a	a	a	a	a				
	942	a	a	a	a	a	a	a				
	943	a	a	a	a	a	a	a	a	a	a	a
	944	a	a	a	a	a	a	a	a	a	a	a
	945	a	a	a	a	a	a	a	a	a	a	a
	946	a	a	a	a	a	a	a	a	a	a	a
	947	a	a	a	a	a	a	a	a	a	a	a
	948	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		23	24	25	26	27	28	29	30	31	32	33
Control	901											
	902											
	903											
	904											
	905											
	906											
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913											
	914											
	915											
	916											
	917											
	918											
	919	a	a	a	a	a	a	a	a	a	a	a
	920	a	a	a	a	a	a	a	a	a	a	a
	921	a	a	a	a	a	a	a	a	a	a	a
	922	a	a	a	a	a	a	a	a	a	a	a
	923	a	a	a	a	a	a	a	a	a	a	a
	924	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	925											
	926											
	927											
	928											
	929											
	930											
	931	a	a	a	a	a	a	a	a	a	a	a
	932	a	a	a	a	a	a	a	a	a	a	a
	933	a	a	a	a	a	a	a	a	a	a	a
	934	a	a	a	a	a	a	a	a	a	a	a
	935	a	a	a	a	a	a	a	a	a	a	a
	936	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		23	24	25	26	27	28	29	30	31	32	33
80 mg/kg	937											
	938											
	939											
	940											
	941											
	942											
	943	a	a	a	a	a	a	a	a	a	a	a
	944	a	a	a	a	a	a	a	a	a	a	a
	945	a	a	a	a	a	a	a	a	a	a	a
	946	a	a	a	a	a	a	a	a	a	a	a
	947	a	a	a	a	a	a	a	a	a	a	a
	948	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		34	35	36	37	38	39	40	41	42	43	44
Control	901											
	902											
	903											
	904											
	905											
	906											
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913											
	914											
	915											
	916											
	917											
	918											
	919	a	a	a	a	a	a	a	a	a	a	a
	920	a	a	a	a	a	a	a	a	a	a	a
	921	a	a	a	a	a	a	a	a	a	a	a
	922	a	a	a	a	a	a	a	a	a	a	a
	923	a	a	a	a	a	a	a	a	a	a	a
	924	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	925											
	926											
	927											
	928											
	929											
	930											
	931	a	a	a	a	a	a	a	a	a	a	a
	932	a	a	a	a	a	a	a	a	a	a	a
	933	a	a	a	a	a	a	a	a	a	a	a
	934	a	a	a	a	a	a	a	a	a	a	a
	935	a	a	a	a	a	a	a	a	a	a	a
	936	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		34	35	36	37	38	39	40	41	42	43	44
80 mg/kg	937											
	938											
	939											
	940											
	941											
	942											
	943	a	a	a	a	a	a	a	a	a	a	a
	944	a	a	a	a	a	a	a	a	a	a	a
	945	a	a	a	a	a	a	a	a	a	a	a
	946	a	a	a	a	a	a	a	a	a	a	a
	947	a	a	a	a	a	a	a	a	a	a	a
	948	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 45	46	47	48	49	50	51	52	53	54	55
Control	901											
	902											
	903											
	904											
	905											
	906											
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913											
	914											
	915											
	916											
	917											
	918											
	919	a	a	a	a	a	a	a	a	a	a	a
	920	a	a	a	a	a	a	a	a	a	a	a
	921	a	a	a	a	a	a	a	a	a	a	a
	922	a	a	a	a	a	a	a	a	a	a	a
	923	a	a	a	a	a	a	a	a	a	a	a
	924	a	a	a	a	a, b	a, b	a, b	a, b	a, b	a, b	a, b
20 mg/kg	925											
	926											
	927											
	928											
	929											
	930											
	931	a	a	a	a	a	a	a	a	a	a	a
	932	a	a	a	a	a	a	a	a	a	a	a
	933	a	a	a	a	a	a	a	a	a	a	a
	934	a	a	a	a	a	a	a	a	a	a	a
	935	a	a	a	a	a	a	a	a	a	a	a
	936	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		45	46	47	48	49	50	51	52	53	54	55
80 mg/kg	937											
	938											
	939											
	940											
	941											
	942											
	943	a	a	a	a	a	a	a	a	a	a	a
	944	a	a	a	a	a	a	a	a	a	a	a
	945	a	a	a	a	a	a	a	a	a	a	a
	946	a	a	a	a	a	a	a	a	a	a	a
	947	a	a	a	a	a	a	a	a	a	a	a
	948	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 56	57	58	59	60	61	62	63	64	65	66
Control	901											
	902											
	903											
	904											
	905											
	906											
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913											
	914											
	915											
	916											
	917											
	918											
	919	a	a	a	a	a	a	a	a	a	a	a
	920	a	a	a	a	a	a	a	a	a	a	a
	921	a	a	a	a	a	a	a	a	a	a	-
	922	a	a	a	a	a	a	a	a	a	a	-
	923	a	a	a	a	a	a	a	a	a	a	a
	924	a, b	a	-	-	-	-	-	-	-	-	-
20 mg/kg	925											
	926											
	927											
	928											
	929											
	930											
	931	a	a	a	a	a	a	a	a	a	a	a
	932	a	a	a	a	a	a	a	a	a	a	a
	933	a	a	a	a	a	a	a	a	a	a	a
	934	a	a	a	a	a	a	a	a	a	a	a
	935	a	a	a	a	a	a	a	a	a	a	a
	936	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		56	57	58	59	60	61	62	63	64	65	66
80 mg/kg	937											
	938											
	939											
	940											
	941											
	942											
	943	a	a	a	a	a	a	a	a	a	a	a
	944	a	a	a	a	a	a	a	a	a	a	a
	945	a	a	a	a	a	a	a	a	a	a	a
	946	a	a	a	a	a	a	a	a	a	a	a
	947	a	a	a	a	a	a	a	a	a	a	a
	948	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		67	68	69	70	71	72	73	74	75	76	77
Control	901											
	902											
	903											
	904											
	905											
	906											
	907	-	-	-	-	-	-	-	-	-	-	-
	908	-	-	-	-	-	-	-	-	-	-	-
	909	-	-	-	-	-	-	-	-	-	-	-
	910	-	-	-	-	-	-	-	-	-	-	-
	911	-	-	-	-	-	-	-	-	-	-	-
	912	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	913											
	914											
	915											
	916											
	917											
	918											
	919	a	a	a	a	a	a	a	a	a	a	a
	920	a	a	a	-	-	-	-	-	-	-	-
	921	-	-	-	-	-	-	-	-	-	-	-
	922	-	-	-	-	-	-	-	-	-	-	-
	923	a	a	a	a	a	a	a	a	a	a	a
	924	-	-	-	-	-	-	-	-	-	-	-
20 mg/kg	925											
	926											
	927											
	928											
	929											
	930											
	931	a	a	a	a	a	a	a	a	a	a	a
	932	a	a	a	a	a	a	a	a	a	a	a
	933	a	a	a	a	a	a	a	a	a	a	a
	934	a	a	a	a	a	a	a	a	a	a	a
	935	a	a	a	a	a	a	a	a	a	a	a
	936	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		67	68	69	70	71	72	73	74	75	76	77
80 mg/kg	937											
	938											
	939											
	940											
	941											
	942											
	943	a	a	a	a	a	a	a	a	a	a	a
	944	a	a	a	a	a	a	a	a	a	a	a
	945	a	a	a	a	a	a	a	a	a	a	a
	946	a	a	a	a	a	a	a	a	a	a	a
	947	a	a	a	a	a	a	a	a	a	a	a
	948	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 78	79	80	81
Control	901				
	902				
	903				
	904				
	905				
	906				
	907	-	-	-	-
	908	-	-	-	-
	909	-	-	-	-
	910	-	-	-	-
	911	-	-	-	-
	912	-	-	-	-
5 mg/kg	913				
	914				
	915				
	916				
	917				
	918				
	919	a	a	a	a
	920	-	-	-	-
	921	-	-	-	-
	922	-	-	-	-
	923	a	a	a	-
	924	-	-	-	-
20 mg/kg	925				
	926				
	927				
	928				
	929				
	930				
	931	a	a	a	a
	932	a	a	a	a
	933	a	a	a	a
	934	a	a	a	a
	935	a	a	a	a
	936	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 1 - continued Individual clinical signs in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 78	79	80	81
80 mg/kg	937				
	938				
	939				
	940				
	941				
	942				
	943	a	a	a	a
	944	a	a	a	a
	945	a	a	a	a
	946	a	a	a	a
	947	a	a	a	a
	948	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair; b, Abnormality of tooth.

Appendix 2 Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 1	2	3	4	5	6	7	8	9	10	11
Control	951	-	-	-	-	-	-	-	-	-	-	-
	952	-	-	-	-	-	-	-	-	-	-	-
	953	-	-	-	-	-	-	-	-	-	-	-
	954	-	-	-	-	-	-	-	-	-	-	-
	955	-	-	-	-	-	-	-	-	-	-	-
	956	-	-	-	-	-	-	-	-	-	-	-
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963	-	-	-	-	-	-	-	-	-	a	a
	964	-	-	-	-	-	-	-	-	-	a	a
	965	-	-	-	-	-	-	-	-	-	a	a
	966	-	-	-	-	-	-	-	-	-	a	a
	967	-	-	-	-	-	-	-	-	-	a	a
	968	-	-	-	-	-	-	-	-	-	a	a
	969	-	-	-	-	-	-	-	-	-	a	a
	970	-	-	-	-	-	-	-	-	-	a	a
	971	-	-	-	-	-	-	-	-	-	a	a
	972	-	-	-	-	-	-	-	-	-	a	a
	973	-	-	-	-	-	-	-	-	-	a	a
	974	-	-	-	-	-	-	-	-	-	a	a
20 mg/kg	975	-	-	-	-	a	a	a	a	a	a	a
	976	-	-	-	-	a	a	a	a	a	a	a
	977	-	-	-	-	a	a	a	a	a	a	a
	978	-	-	-	-	a	a	a	a	a	a	a
	979	-	-	-	-	a	a	a	a	a	a	a
	980	-	-	-	-	a	a	a	a	a	a	a
	981	-	-	-	-	a	a	a	a	a	a	a
	982	-	-	-	-	a	a	a	a	a	a	a
	983	-	-	-	-	a	a	a	a	a	a	a
	984	-	-	-	-	a	a	a	a	a	a	a
	985	-	-	-	-	a	a	a	a	a	a	a
	986	-	-	-	-	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		1	2	3	4	5	6	7	8	9	10	11
80 mg/kg	987	-	-	a	a	a	a	a	a	a	a	a
	988	-	-	a	a	a	a	a	a	a	a	a
	989	-	-	a	a	a	a	a	a	a	a	a
	990	-	-	a	a	a	a	a	a	a	a	a
	991	-	-	a	a	a	a	a	a	a	a	a
	992	-	-	a	a	a	a	a	a	a	a	a
	993	-	-	a	a	a	a	a	a	a	a	a
	994	-	-	a	a	a	a	a	a	a	a	a
	995	-	-	a	a	a	a	a	a	a	a	a
	996	-	-	a	a	a	a	a	a	a	a	a
	997	-	-	a	a	a	a	a	a	a	a	a
	998	-	-	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		12	13	14	15	16	17	18	19	20	21	22
Control	951	-	-	-	-	-	-	-				
	952	-	-	-	-	-	-	-				
	953	-	-	-	-	-	-	-				
	954	-	-	-	-	-	-	-				
	955	-	-	-	-	-	-	-				
	956	-	-	-	-	-	-	-				
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963	a	a	a	a	a	a	a				
	964	a	a	a	a	a	a	a				
	965	a	a	a	a	a	a	a				
	966	a	a	a	a	a	a	a				
	967	a	a	a	a	a	a	a				
	968	a	a	a	a	a	a	a				
	969	a	a	a	a	a	a	a	a	a	a	a
	970	a	a	a	a	a	a	a	a	a	a	a
	971	a	a	a	a	a	a	a	a	a	a	a
	972	a	a	a	a	a	a	a	a	a	a	a
	973	a	a	a	a	a	a	a	a	a	a	a
	974	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	975	a	a	a	a	a	a	a				
	976	a	a	a	a	a	a	a				
	977	a	a	a	a	a	a	a				
	978	a	a	a	a	a	a	a				
	979	a	a	a	a	a	a	a				
	980	a	a	a	a	a	a	a				
	981	a	a	a	a	a	a	a	a	a	a	a
	982	a	a	a	a	a	a	a	a	a	a	a
	983	a	a	a	a	a	a	a	a	a	a	a
	984	a	a	a	a	a	a	a	a	a	a	a
	985	a	a	a	a	a	a	a	a	a	a	a
	986	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		12	13	14	15	16	17	18	19	20	21	22
80 mg/kg	987	a	a	a	a	a	a	a				
	988	a	a	a	a	a	a	a				
	989	a	a	a	a	a	a	a				
	990	a	a	a	a	a	a	a				
	991	a	a	a	a	a	a	a				
	992	a	a	a	a	a	a	a				
	993	a	a	a	a	a	a	a	a	a	a	a
	994	a	a	a	a	a	a	a	a	a	a	a
	995	a	a	a	a	a	a	a	a	a	a	a
	996	a	a	a	a	a	a	a	a	a	a	a
	997	a	a	a	a	a	a	a	a	a	a	a
	998	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 23	24	25	26	27	28	29	30	31	32	33
Control	951											
	952											
	953											
	954											
	955											
	956											
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963											
	964											
	965											
	966											
	967											
	968											
	969	a	a	a	a	a	a	a	a	a	a	a
	970	a	a	a	a	a	a	a	a	a	a	a
	971	a	a	a	a	a	a	a	a	a	a	a
	972	a	a	a	a	a	a	a	a	a	a	a
	973	a	a	a	a	a	a	a	a	a	a	a
	974	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	975											
	976											
	977											
	978											
	979											
	980											
	981	a	a	a	a	a	a	a	a	a	a	a
	982	a	a	a	a	a	a	a	a	a	a	a
	983	a	a	a	a	a	a	a	a	a	a	a
	984	a	a	a	a	a	a	a	a	a	a	a
	985	a	a	a	a	a	a	a	a	a	a	a
	986	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		23	24	25	26	27	28	29	30	31	32	33
80 mg/kg	987											
	988											
	989											
	990											
	991											
	992											
	993	a	a	a	a	a	a	a	a	a	a	a
	994	a	a	a	a	a	a	a	a	a	a	a
	995	a	a	a	a	a	a	a	a	a	a	a
	996	a	a	a	a	a	a	a	a	a	a	a
	997	a	a	a	a	a	a	a	a	a	a	a
	998	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 34	35	36	37	38	39	40	41	42	43	44
Control	951											
	952											
	953											
	954											
	955											
	956											
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963											
	964											
	965											
	966											
	967											
	968											
	969	a	a	a	a	a	a	a	a	a	a	a
	970	a	a	a	a	a	a	a	a	a	a	a
	971	a	a	a	a	a	a	a	a	a	a	a
	972	a	a	a	a	a	a	a	a	a	a	a
	973	a	a	a	a	a	a	a	a	a	a	a
	974	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	975											
	976											
	977											
	978											
	979											
	980											
	981	a	a	a	a	a	a	a	a	a	a	a
	982	a	a	a	a	a	a	a	a	a	a	a
	983	a	a	a	a	a	a	a	a	a	a	a
	984	a	a	a	a	a	a	a	a	a	a	a
	985	a	a	a	a	a	a	a	a	a	a	a
	986	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		34	35	36	37	38	39	40	41	42	43	44
80 mg/kg	987											
	988											
	989											
	990											
	991											
	992											
	993	a	a	a	a	a	a	a	a	a	a	a
	994	a	a	a	a	a	a	a	a	a	a	a
	995	a	a	a	a	a	a	a	a	a	a	a
	996	a	a	a	a	a	a	a	a	a	a	a
	997	a	a	a	a	a	a	a	a	a	a	a
	998	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 45	46	47	48	49	50	51	52	53	54	55
Control	951											
	952											
	953											
	954											
	955											
	956											
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963											
	964											
	965											
	966											
	967											
	968											
	969	a	a	a	a	a	a	a	a	a	a	a
	970	a	a	a	a	a	a	a	a	a	a	a
	971	a	a	a	a	a	a	a	a	a	a	a
	972	a	a	a	a	a	a	a	a	a	a	a
	973	a	a	a	a	a	a	a	a	a	a	a
	974	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	975											
	976											
	977											
	978											
	979											
	980											
	981	a	a	a	a	a	a	a	a	a	a	a
	982	a	a	a	a	a	a	a	a	a	a	a
	983	a	a	a	a	a	a	a	a	a	a	a
	984	a	a	a	a	a	a	a	a	a	a	a
	985	a	a	a	a	a	a	a	a	a	a	a
	986	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		45	46	47	48	49	50	51	52	53	54	55
80 mg/kg	987											
	988											
	989											
	990											
	991											
	992											
	993	a	a	a	a	a	a	a	a	a	a	a
	994	a	a	a	a	a	a	a	a	a	a	a
	995	a	a	a	a	a	a	a	a	a	a	a
	996	a	a	a	a	a	a	a	a	a	a	a
	997	a	a	a	a	a	a	a	a	a	a	a
	998	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 56	57	58	59	60	61	62	63	64	65	66
Control	951											
	952											
	953											
	954											
	955											
	956											
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963											
	964											
	965											
	966											
	967											
	968											
	969	a	a	a	a	a	a	a	a	a	a	a
	970	a	a	a	a	a	a	a	a	a	a	-
	971	a	a	a	a	a	a	a	a	a	a	-
	972	a	a	a	a	a	a	a	a	a	a	a
	973	a	a	a	a	a	a	a	a	a	a	a
	974	a	a	a	a	a	a	a	a	a	a	a
20 mg/kg	975											
	976											
	977											
	978											
	979											
	980											
	981	a	a	a	a	a	a	a	a	a	a	a
	982	a	a	a	a	a	a	a	a	a	a	a
	983	a	a	a	a	a	a	a	a	a	a	a
	984	a	a	a	a	a	a	a	a	a	a	a
	985	a	a	a	a	a	a	a	a	a	a	a
	986	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		56	57	58	59	60	61	62	63	64	65	66
80 mg/kg	987											
	988											
	989											
	990											
	991											
	992											
	993	a	a	a	a	a	a	a	a	a	a	a
	994	a	a	a	a	a	a	a	a	a	a	a
	995	a	a	a	a	a	a	a	a	a	a	a
	996	a	a	a	a	a	a	a	a	a	a	a
	997	a	a	a	a	a	a	a	a	a	a	a
	998	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		67	68	69	70	71	72	73	74	75	76	77
Control	951											
	952											
	953											
	954											
	955											
	956											
	957	-	-	-	-	-	-	-	-	-	-	-
	958	-	-	-	-	-	-	-	-	-	-	-
	959	-	-	-	-	-	-	-	-	-	-	-
	960	-	-	-	-	-	-	-	-	-	-	-
	961	-	-	-	-	-	-	-	-	-	-	-
	962	-	-	-	-	-	-	-	-	-	-	-
5 mg/kg	963											
	964											
	965											
	966											
	967											
	968											
	969	a	a	a	-	-	-	-	-	-	-	-
	970	-	-	-	-	-	-	-	-	-	-	-
	971	-	-	-	-	-	-	-	-	-	-	-
	972	a	a	a	a	a	a	a	a	a	a	-
	973	a	a	a	a	a	a	a	-	-	-	-
	974	a	a	a	a	a	a	a	a	a	a	-
20 mg/kg	975											
	976											
	977											
	978											
	979											
	980											
	981	a	a	a	a	a	a	a	a	a	a	a
	982	a	a	a	a	a	a	a	a	a	a	a
	983	a	a	a	a	a	a	a	a	a	a	a
	984	a	a	a	a	a	a	a	a	a	a	a
	985	a	a	a	a	a	a	a	a	a	a	a
	986	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days										
		67	68	69	70	71	72	73	74	75	76	77
80 mg/kg	987											
	988											
	989											
	990											
	991											
	992											
	993	a	a	a	a	a	a	a	a	a	a	a
	994	a	a	a	a	a	a	a	a	a	a	a
	995	a	a	a	a	a	a	a	a	a	a	a
	996	a	a	a	a	a	a	a	a	a	a	a
	997	a	a	a	a	a	a	a	a	a	a	a
	998	a	a	a	a	a	a	a	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 78	79	80	81
Control	951				
	952				
	953				
	954				
	955				
	956				
	957	-	-	-	-
	958	-	-	-	-
	959	-	-	-	-
	960	-	-	-	-
	961	-	-	-	-
	962	-	-	-	-
5 mg/kg	963				
	964				
	965				
	966				
	967				
	968				
	969	-	-	-	-
	970	-	-	-	-
	971	-	-	-	-
	972	-	-	-	-
	973	-	-	-	-
	974	-	-	-	-
20 mg/kg	975				
	976				
	977				
	978				
	979				
	980				
	981	a	a	a	a
	982	a	a	a	a
	983	a	a	a	a
	984	a	a	a	a
	985	a	a	a	a
	986	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 2 - continued Individual clinical signs in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Days 78	79	80	81
80 mg/kg	987				
	988				
	989				
	990				
	991				
	992				
	993	a	a	a	a
	994	a	a	a	a
	995	a	a	a	a
	996	a	a	a	a
	997	a	a	a	a
	998	a	a	a	a

Clinical sign: -, No abnormality; a, Yellow coloration of hair.

Appendix 3 Individual body weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		1	4	8	11	15	18	22	25	29	32	36
Control	901	11.4	19.6	29.3	36.6	46.7	55.2					
	902	11.0	18.8	32.0	42.0	52.8	64.9					
	903	11.3	19.6	32.4	40.5	53.1	63.4					
	904	11.3	18.2	27.8	35.5	45.9	56.1					
	905	11.4	17.1	27.4	34.5	44.1	55.2					
	906	10.6	16.8	27.9	34.4	44.0	54.8					
	907	11.1	19.9	31.6	39.8	50.3	63.6	89.6	114.1	154.8	186.4	230.3
	908	10.9	17.5	27.1	33.3	41.3	49.5	74.2	96.5	129.6	155.1	185.8
	909	11.0	17.9	28.3	34.2	42.4	53.5	77.6	102.2	140.5	173.6	217.5
	910	10.5	16.7	28.9	36.4	46.6	56.2	78.5	99.0	132.5	159.4	195.7
	911	11.7	19.8	31.6	40.5	49.5	58.4	83.4	104.6	140.8	169.3	211.4
	912	11.9	20.3	29.7	39.3	49.3	60.9	89.9	112.9	154.9	183.6	225.8
5 mg/kg	913	10.7	17.4	28.6	35.9	46.3	55.2					
	914	11.2	18.7	30.8	39.3	50.1	58.7					
	915	10.9	18.3	29.0	36.0	48.7	60.7					
	916	11.2	18.3	27.8	36.3	46.7	55.6					
	917	10.6	16.8	27.5	35.5	46.1	55.9					
	918	11.0	17.8	29.9	36.9	47.2	57.0					
	919	11.0	18.1	30.0	38.4	47.5	58.4	78.0	95.0	121.3	144.8	177.5
	920	10.9	17.7	27.8	33.5	42.9	53.3	77.9	100.1	137.8	166.9	208.6
	921	10.6	18.7	30.1	37.7	45.9	55.3	78.7	97.7	130.0	154.6	187.4
	922	10.0	15.5	25.0	32.0	41.9	50.5	74.9	95.7	129.5	158.4	201.8
	923	11.6	19.4	31.0	39.8	50.1	61.9	87.4	110.7	146.1	175.7	220.9
	924	11.2	18.3	27.3	36.4	45.9	57.6	84.8	109.9	151.9	182.4	230.3
20 mg/kg	925	10.9	17.7	28.8	38.4	48.8	61.4					
	926	11.4	19.1	32.1	41.6	54.5	65.2					
	927	11.0	17.6	30.2	38.9	47.4	58.9					
	928	11.1	18.5	27.7	34.4	43.1	52.7					
	929	10.4	16.8	27.5	35.6	45.0	57.0					
	930	10.8	17.8	28.0	34.9	43.5	53.8					
	931	11.4	18.7	29.9	38.2	48.6	57.5	81.9	106.2	143.8	172.1	212.0
	932	11.1	18.8	28.6	36.6	42.2	53.6	74.9	95.4	125.3	153.0	184.2
	933	11.0	17.7	27.8	33.6	41.5	50.1	70.7	89.7	121.5	148.7	186.3
	934	10.7	16.9	26.0	33.6	42.3	54.1	78.9	99.1	133.0	159.1	197.3
	935	12.3	20.5	32.3	40.4	49.8	59.9	86.3	109.2	144.7	174.6	214.0
	936	11.1	18.5	29.5	38.5	48.8	63.0	86.7	107.5	143.5	174.9	212.3

Appendix 3 - continued Individual body weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		1	4	8	11	15	18	22	25	29	32	36
80 mg/kg	937	11.0	15.8	24.1	32.8	42.6	53.5					
	938	11.2	18.3	30.5	39.5	50.1	60.8					
	939	11.2	17.8	27.9	38.2	49.4	57.3					
	940	11.4	19.0	28.3	35.7	44.5	53.6					
	941	10.5	17.1	26.9	34.0	43.1	51.0					
	942	10.8	16.9	27.7	34.7	44.7	57.1					
	943	11.4	17.7	28.6	35.4	45.1	56.0	78.2	96.7	129.0	157.8	195.7
	944	10.5	16.4	26.9	34.4	41.1	52.5	79.0	101.0	135.9	165.5	204.7
	945	10.3	16.5	28.0	35.5	44.3	53.1	77.7	98.1	131.0	156.7	187.0
	946	10.4	15.0	25.1	32.1	42.9	51.7	75.6	95.3	126.8	152.9	184.3
	947	12.0	18.9	28.2	35.7	46.7	56.7	83.8	107.7	144.2	170.3	206.9
	948	11.8	17.8	27.1	35.1	44.6	56.4	78.1	95.2	126.3	152.7	189.6

Appendix 3 - continued Individual body weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		39	43	46	50	53	57	60	64	67	71	74
Control	901											
	902											
	903											
	904											
	905											
	906											
	907	258.2	298.3	324.2	364.4	399.7	430.4	455.5	478.8	496.2	523.0	546.5
	908	211.6	241.8	267.6	299.8	326.5	348.1	366.0	382.6	392.0	413.0	432.3
	909	247.8	284.5	311.2	346.9	372.8	404.7	421.0	444.1	461.0	481.4	500.7
	910	218.8	253.2	280.7	310.2	333.5	361.7	382.4	400.6	410.6	431.4	447.6
	911	240.1	278.9	307.7	342.4	366.0	400.2	417.7	441.2	457.6	480.5	498.7
	912	255.7	295.5	329.6	364.0	396.2	425.7	452.2	478.7	495.6	514.4	535.2
5 mg/kg	913											
	914											
	915											
	916											
	917											
	918											
	919	204.5	235.1	259.1	288.3	313.4	341.1	361.8	383.4	397.3	419.0	431.8
	920	237.6	274.5	304.2	337.9	363.9	396.1	415.1	434.9	455.2	478.4	500.9
	921	213.8	246.9	269.0	298.5	320.6	347.3	364.6	384.3	396.8	412.8	426.6
	922	225.2	258.1	287.0	318.2	343.7	374.4	392.2	420.8	434.9	451.8	469.9
	923	249.9	291.5	325.3	358.2	391.3	423.1	448.8	473.7	489.1	509.2	524.3
	924	259.5	300.7	330.1	343.9	368.6	407.7	434.0	457.5	479.3	506.5	531.9
20 mg/kg	925											
	926											
	927											
	928											
	929											
	930											
	931	238.7	277.0	301.4	335.0	363.8	396.2	417.4	439.7	451.4	472.4	492.3
	932	209.3	241.5	270.3	302.9	322.4	352.1	371.0	389.9	406.2	428.0	440.5
	933	210.3	245.5	272.7	303.6	331.3	362.7	381.1	403.9	413.7	428.3	447.7
	934	219.2	255.9	281.3	317.5	338.8	370.9	395.3	416.5	433.5	452.8	475.7
	935	241.8	272.7	299.1	336.7	364.0	395.1	414.1	435.0	453.4	469.9	491.3
	936	238.8	281.3	308.3	347.9	383.2	408.8	439.7	462.5	482.4	500.9	515.8

Appendix 3 - continued Individual body weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day 78	81
Control	901		
	902		
	903		
	904		
	905		
	906		
	907	548.3	566.9
	908	445.8	454.7
	909	511.4	530.7
	910	454.4	470.7
	911	505.6	520.3
	912	552.5	569.6
5 mg/kg	913		
	914		
	915		
	916		
	917		
	918		
	919	448.5	464.6
	920	511.7	526.7
	921	432.0	444.9
	922	482.3	491.2
	923	539.3	551.7
	924	542.7	560.9
20 mg/kg	925		
	926		
	927		
	928		
	929		
	930		
	931	495.3	507.6
	932	453.2	464.2
	933	462.3	470.6
	934	485.6	497.0
	935	501.3	512.2
	936	529.5	544.8

Appendix 3 - continued Individual body weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight (g) on day 78	81
80 mg/kg	937		
	938		
	939		
	940		
	941		
	942		
	943	467.7	479.6
	944	501.8	518.9
	945	457.5	471.3
	946	459.2	474.2
	947	547.2	562.2
	948	465.4	481.9

Appendix 4 Individual body weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		1	4	8	11	15	18	22	25	29	32	36
Control	951	9.4	15.1	25.9	33.4	44.1	50.8					
	952	10.3	17.1	29.1	37.8	47.3	58.0					
	953	10.7	17.3	27.3	35.8	45.0	56.4					
	954	9.1	15.7	24.9	31.5	40.6	50.5					
	955	9.3	15.1	25.4	33.8	43.4	54.8					
	956	9.8	15.8	25.9	32.5	42.1	50.8					
	957	10.1	16.4	29.6	37.7	48.1	59.4	82.5	106.4	138.9	161.6	186.4
	958	9.9	16.3	26.5	32.6	39.5	48.4	70.7	89.5	118.3	138.2	159.9
	959	11.2	17.6	29.7	36.6	44.1	51.9	71.2	90.3	116.8	138.9	164.1
	960	9.7	15.1	25.6	32.8	41.2	50.5	71.4	90.6	118.5	141.9	175.1
	961	10.1	16.7	26.4	33.8	43.6	52.2	72.1	88.6	119.4	139.1	163.5
	962	10.2	15.9	24.3	31.6	40.5	48.2	66.0	85.4	115.5	138.5	164.7
5 mg/kg	963	9.6	15.4	27.9	36.3	44.5	53.4					
	964	10.4	17.4	29.7	38.5	49.4	58.8					
	965	10.5	16.9	28.3	36.1	45.4	53.8					
	966	9.5	16.3	25.9	32.5	42.3	51.5					
	967	9.7	14.9	25.4	33.1	43.9	54.0					
	968	10.3	17.0	28.5	35.1	43.4	55.1					
	969	10.0	16.2	25.7	34.1	44.9	56.4	74.5	90.4	114.8	133.9	156.4
	970	10.0	16.1	26.3	33.3	40.4	50.5	70.9	91.6	120.5	140.5	166.6
	971	10.9	17.5	29.3	35.3	43.7	52.3	73.7	92.2	120.3	139.7	161.5
	972	9.7	15.0	24.5	32.1	41.9	49.3	70.2	89.4	116.7	134.6	156.4
	973	10.1	16.9	27.6	36.1	45.8	55.4	78.9	100.0	132.6	156.4	186.1
	974	10.4	17.4	28.0	36.0	44.3	55.1	76.3	94.0	122.7	146.0	172.2
20 mg/kg	975	9.0	14.4	23.9	29.0	37.9	47.0					
	976	10.0	16.3	29.2	38.2	47.5	57.4					
	977	10.1	16.0	27.6	35.7	45.1	54.0					
	978	9.5	16.0	25.0	32.0	39.8	49.4					
	979	9.6	14.7	25.2	31.8	41.8	50.0					
	980	10.0	16.6	28.0	34.0	43.3	53.8					
	981	9.9	17.2	29.1	38.0	48.9	59.4	78.2	95.6	120.9	138.7	158.7
	982	10.3	17.0	27.4	34.0	42.1	53.5	72.6	91.6	117.7	136.3	153.7
	983	10.5	16.7	27.4	34.3	41.8	51.1	71.6	89.8	118.3	138.1	163.5
	984	9.6	14.3	24.6	31.6	41.8	47.9	66.9	84.3	111.9	130.7	156.2
	985	10.3	17.2	27.4	35.7	45.1	54.4	77.5	95.2	126.0	145.8	167.7
	986	10.1	16.7	27.3	35.4	45.3	52.7	72.8	88.9	113.5	132.0	153.5

Appendix 4 - continued Individual body weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		1	4	8	11	15	18	22	25	29	32	36
80 mg/kg	987	9.5	15.2	25.3	34.5	43.4	52.4					
	988	10.5	17.0	28.3	37.2	48.0	59.9					
	989	10.5	16.9	26.8	35.9	46.8	58.6					
	990	9.5	14.7	23.6	29.8	38.7	47.1					
	991	9.0	14.1	24.2	31.5	40.8	51.4					
	992	10.4	15.8	24.7	33.0	42.4	54.1					
	993	10.3	16.1	26.5	33.7	43.6	54.7	71.9	87.5	115.0	136.3	156.5
	994	10.0	16.2	25.5	32.1	39.1	46.5	66.9	85.2	115.1	136.1	159.9
	995	10.8	16.7	26.3	32.4	39.9	48.6	70.7	90.3	121.2	143.9	173.3
	996	9.5	14.5	24.3	31.7	42.5	51.2	69.7	86.5	112.0	135.5	165.2
	997	10.1	15.6	23.6	30.0	37.8	46.7	67.3	84.3	108.3	126.0	148.3
	998	10.2	15.6	24.4	30.7	40.6	48.7	67.8	86.6	111.7	135.3	162.3

Appendix 4 - continued Individual body weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		39	43	46	50	53	57	60	64	67	71	74
Control	951											
	952											
	953											
	954											
	955											
	956											
	957	202.7	215.9	222.7	237.3	249.2	267.2	270.5	279.4	287.4	298.7	304.0
	958	176.8	193.5	207.5	219.9	231.6	248.0	256.2	265.9	270.9	281.3	293.2
	959	184.4	202.9	212.8	225.4	235.6	251.7	262.5	274.1	280.8	286.6	304.7
	960	190.4	206.3	215.5	228.9	236.3	264.0	278.9	289.7	284.7	286.8	295.5
	961	178.2	186.2	194.3	205.5	215.5	225.3	223.4	235.6	244.0	249.5	255.2
	962	179.2	199.6	209.1	228.6	240.3	255.1	269.7	283.5	288.8	299.8	309.8
5 mg/kg	963											
	964											
	965											
	966											
	967											
	968											
	969	168.7	188.2	193.8	211.5	223.9	240.4	249.0	259.2	263.0	269.3	281.5
	970	179.6	192.9	205.1	216.9	228.9	237.7	253.6	263.5	270.8	277.6	281.8
	971	174.3	191.0	198.6	211.4	225.9	243.1	250.0	263.2	266.1	271.2	276.0
	972	171.5	185.1	197.4	214.6	225.0	240.9	251.5	267.1	282.9	281.5	286.0
	973	202.9	220.5	234.2	249.8	263.1	280.5	293.3	300.6	316.1	323.7	328.8
	974	193.0	207.2	215.3	233.5	244.4	257.0	271.2	280.6	292.4	301.5	310.4
20 mg/kg	975											
	976											
	977											
	978											
	979											
	980											
	981	168.6	183.1	194.4	200.7	213.0	221.3	225.2	234.0	236.7	245.1	257.5
	982	165.1	182.2	191.5	205.4	212.1	225.5	238.2	250.2	254.1	263.2	264.2
	983	171.9	188.8	199.8	211.5	224.8	236.4	250.8	263.0	266.5	278.0	281.4
	984	167.4	179.1	195.0	199.4	210.1	223.1	231.1	237.9	244.8	251.4	242.1
	985	179.3	193.4	204.6	211.7	219.4	230.5	232.6	235.4	246.9	252.0	251.7
	986	168.2	187.7	196.5	207.0	217.0	229.2	238.5	247.1	250.1	257.3	263.5

Appendix 4 - continued Individual body weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day										
		39	43	46	50	53	57	60	64	67	71	74
80 mg/kg	987											
	988											
	989											
	990											
	991											
	992											
	993	172.1	185.4	198.5	209.1	216.4	226.3	232.4	238.6	247.4	253.2	262.4
	994	169.3	185.6	194.3	208.4	219.5	234.6	245.7	256.8	259.7	271.2	278.8
	995	182.6	196.4	215.2	232.5	239.3	258.6	266.3	276.8	283.3	293.7	298.2
	996	178.6	193.1	207.6	222.5	233.6	247.0	252.2	259.6	263.2	266.8	278.8
	997	158.0	170.6	180.0	196.4	205.1	219.5	226.5	235.6	238.6	251.3	255.5
	998	178.9	190.6	197.0	213.1	214.8	228.4	241.0	247.9	263.4	267.7	266.3

Appendix 4 - continued Individual body weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day 78	81
Control	951		
	952		
	953		
	954		
	955		
	956		
	957	309.8	324.2
	958	294.1	301.9
	959	307.1	311.6
	960	303.7	306.8
	961	258.8	264.7
	962	313.0	317.0
5 mg/kg	963		
	964		
	965		
	966		
	967		
	968		
	969	280.0	294.6
	970	291.1	299.3
	971	281.1	293.7
	972	288.8	296.6
	973	337.7	344.4
	974	317.0	319.1
20 mg/kg	975		
	976		
	977		
	978		
	979		
	980		
	981	252.9	262.9
	982	266.6	268.6
	983	286.4	287.3
	984	245.2	255.1
	985	271.6	273.4
	986	269.2	279.7

Appendix 4 - continued Individual body weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Body weight(g) on day 78	81
80 mg/kg	987		
	988		
	989		
	990		
	991		
	992		
	993	264.4	265.8
	994	280.3	285.0
	995	296.5	315.1
	996	279.7	282.5
	997	261.7	267.6
	998	271.0	269.0

Appendix 5 Individual food consumption in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Food consumption(g) on day										
		22	25	29	32	36	39	43	46	50	53	57
Control	907	12.1	16.0	21.0	22.8	28.4	28.6	28.6	27.2	34.8	34.4	33.6
	908	11.8	15.2	19.1	21.1	24.2	25.3	27.1	26.9	27.0	29.7	30.0
	909	12.3	15.7	20.6	24.9	26.5	29.1	29.8	30.2	31.8	32.3	31.3
	910	11.2	13.6	17.4	19.9	22.9	22.2	24.3	25.8	26.2	25.5	26.5
	911	11.5	14.7	18.8	22.5	27.3	28.5	32.1	28.9	30.3	32.2	34.0
	912	13.8	16.4	21.7	23.8	25.9	29.5	29.5	33.0	30.8	33.6	32.7
5 mg/kg	919	9.6	12.8	16.6	17.0	21.1	23.5	25.1	25.3	25.2	27.3	26.5
	920	11.1	15.2	18.7	21.9	25.7	27.4	27.8	30.9	31.0	34.1	31.4
	921	12.0	13.3	17.6	20.1	21.4	24.0	25.3	25.2	27.5	27.0	24.0
	922	11.9	14.3	17.8	21.9	26.5	25.0	26.2	28.3	29.0	29.1	31.0
	923	11.9	16.0	18.6	22.5	26.6	27.7	29.5	29.8	30.3	31.9	31.6
	924	14.4	17.3	23.1	24.4	26.1	29.3	32.9	30.2	28.6	35.5	35.5
20 mg/kg	931	11.9	16.9	20.6	22.6	26.0	25.7	28.0	28.4	31.1	31.5	31.7
	932	10.3	13.6	16.1	19.5	21.0	21.7	22.8	25.8	28.5	27.4	28.8
	933	10.6	13.5	17.3	20.3	22.7	24.3	24.8	27.3	25.9	29.1	29.1
	934	11.7	15.0	19.1	21.3	24.1	24.3	25.3	27.0	30.7	29.9	30.6
	935	12.1	15.4	17.6	22.5	25.6	26.2	29.8	26.8	30.7	31.2	31.5
	936	10.7	14.7	19.2	22.8	24.5	25.0	28.6	26.6	31.0	34.6	29.8
80 mg/kg	943	11.3	13.0	17.4	20.3	25.7	26.7	26.7	26.3	27.9	28.2	27.3
	944	12.7	14.8	19.1	20.6	23.4	25.3	27.9	31.8	30.0	32.2	28.9
	945	11.6	14.2	17.5	20.3	23.4	23.7	26.3	28.1	30.2	28.9	30.3
	946	11.4	13.3	18.9	19.6	20.7	23.3	23.2	24.5	26.7	27.3	28.7
	947	13.0	15.5	19.3	22.7	26.1	25.6	26.4	27.8	32.3	33.9	32.1
	948	10.8	13.0	18.3	19.4	22.8	20.6	25.4	24.3	27.3	27.2	29.6

Appendix 5 - continued Individual food consumption in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Food consumption(g) on day 60	64	67	71	74	78	81
Control	907	33.3	33.9	38.3	33.7	37.9	32.8	33.1
	908	30.0	27.7	27.5	29.1	28.9	30.7	29.9
	909	30.9	29.4	31.3	32.3	34.5	36.3	34.2
	910	29.2	28.3	26.9	25.8	27.1	24.5	28.7
	911	32.4	34.1	31.9	35.1	35.0	33.3	30.3
	912	35.1	35.6	36.7	34.4	34.1	37.7	40.5
5 mg/kg	919	27.4	28.5	27.6	30.3	29.1	30.0	29.1
	920	32.9	32.8	31.9	31.7	36.1	34.3	32.3
	921	25.9	26.7	26.4	23.9	25.1	25.7	27.2
	922	30.3	32.9	33.6	30.4	29.6	34.1	30.7
	923	31.8	33.1	30.4	28.7	31.5	31.6	30.5
	924	35.5	36.0	36.4	35.7	37.6	36.0	37.8
20 mg/kg	931	31.4	31.6	32.5	30.8	33.0	32.1	29.5
	932	30.9	28.3	32.4	28.6	26.7	27.6	28.1
	933	29.6	31.2	27.7	28.0	27.2	27.2	28.6
	934	33.8	31.8	29.4	31.2	29.1	31.1	32.1
	935	30.0	32.6	32.5	30.4	35.8	31.2	31.2
	936	33.7	34.0	36.1	28.7	30.7	34.8	33.7
80 mg/kg	943	28.5	30.3	30.1	31.2	29.0	29.7	29.4
	944	30.3	32.8	30.7	29.8	28.3	35.3	32.1
	945	29.6	30.3	31.6	29.4	29.2	28.3	28.5
	946	26.2	26.1	27.2	26.5	30.6	32.3	30.8
	947	35.5	35.9	32.8	32.9	33.7	37.4	33.3
	948	31.2	30.0	27.9	29.9	27.5	31.0	33.3

Appendix 6 Individual food consumption in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Food consumption(g) on day										
		22	25	29	32	36	39	43	46	50	53	57
Control	957	11.5	16.0	20.3	20.9	20.6	21.5	21.5	18.3	20.5	22.2	25.5
	958	11.3	14.5	16.4	18.2	18.4	17.8	19.9	19.7	17.8	18.8	19.1
	959	10.2	13.4	15.7	18.4	18.9	19.2	19.8	19.4	19.2	20.9	21.5
	960	10.7	12.6	16.2	18.5	21.4	20.6	20.5	20.0	21.5	20.8	25.6
	961	9.7	11.8	16.6	17.6	19.5	20.3	16.5	16.9	18.6	19.1	17.2
	962	9.2	11.8	16.8	19.2	20.2	19.0	21.0	18.6	22.9	20.2	23.0
5 mg/kg	969	10.5	12.8	14.2	16.0	17.8	17.1	19.0	17.0	18.6	20.2	22.8
	970	11.4	14.1	16.0	18.2	21.7	19.7	17.4	20.0	20.7	22.8	19.3
	971	11.6	13.9	17.5	18.6	19.1	18.1	19.2	17.9	18.0	20.8	21.2
	972	11.0	13.1	16.1	17.8	18.5	19.7	19.0	18.5	21.2	19.6	22.5
	973	10.8	13.6	17.9	19.8	20.6	21.3	21.1	23.7	25.8	20.9	22.5
	974	12.2	12.7	15.4	18.9	19.6	22.3	18.9	20.2	22.3	19.7	18.8
20 mg/kg	981	9.8	12.8	14.5	16.5	16.5	16.3	17.1	18.3	15.9	18.0	16.8
	982	10.2	13.4	15.7	16.4	16.2	17.4	19.6	18.2	19.0	16.7	16.8
	983	10.8	13.3	15.6	18.2	19.0	18.3	18.6	18.5	18.3	20.0	18.0
	984	9.3	12.5	15.5	14.9	17.8	17.5	16.2	18.4	12.6	16.8	19.4
	985	10.5	13.0	17.4	17.8	19.9	19.5	19.1	20.1	18.1	18.9	21.1
	986	10.8	12.6	14.2	16.5	17.6	18.5	20.3	18.8	17.8	18.7	19.5
80 mg/kg	993	9.3	11.7	15.6	17.2	15.7	17.2	17.0	18.6	19.8	19.7	18.9
	994	11.8	12.8	17.8	18.0	19.3	18.4	20.1	18.8	20.2	20.3	19.7
	995	11.4	13.8	16.5	19.6	21.6	18.7	16.4	22.4	25.6	20.9	21.8
	996	10.4	12.3	14.2	16.6	18.7	17.4	17.3	18.9	21.1	19.5	21.1
	997	9.8	12.5	14.9	15.6	16.7	16.6	16.2	15.9	18.5	17.5	17.6
	998	10.6	12.2	16.4	19.4	20.2	19.3	18.9	17.9	21.7	18.4	18.6

Appendix 6 - continued Individual food consumption in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Food consumption(g) on day 60	64	67	71	74	78	81
Control	957	21.8	22.5	21.5	23.7	23.6	22.0	25.2
	958	23.5	21.4	20.2	22.7	22.7	21.3	20.5
	959	23.5	22.2	23.5	21.1	26.2	22.2	24.3
	960	25.3	24.2	21.8	19.9	20.7	24.1	21.3
	961	16.6	19.2	19.6	20.0	20.5	17.2	17.9
	962	25.1	26.6	24.1	24.5	23.6	22.4	21.7
5 mg/kg	969	19.9	22.6	20.8	17.6	20.2	17.7	22.5
	970	22.1	21.5	25.0	21.0	19.3	22.1	26.5
	971	20.2	22.1	20.2	19.0	19.8	19.3	21.2
	972	21.9	23.5	22.9	18.3	20.3	20.0	22.2
	973	23.6	23.0	26.2	24.4	25.0	25.0	25.5
	974	22.3	22.3	26.2	23.9	24.9	21.9	19.5
20 mg/kg	981	18.2	16.5	17.1	16.1	17.7	18.0	18.9
	982	19.6	20.7	22.2	21.5	17.9	20.1	14.9
	983	21.9	23.3	21.8	23.0	19.7	21.4	18.5
	984	20.8	20.6	19.6	21.2	14.4	17.5	18.5
	985	18.2	15.8	22.1	21.7	17.1	24.7	24.0
	986	19.6	19.6	19.0	19.9	17.5	18.3	21.8
80 mg/kg	993	14.9	17.7	18.0	20.1	21.6	20.6	17.4
	994	20.5	23.7	24.3	22.6	20.3	18.9	21.4
	995	22.2	22.1	23.9	24.0	23.2	18.6	24.4
	996	18.2	19.2	18.9	19.5	19.8	20.1	20.3
	997	17.8	19.3	18.7	20.3	19.0	19.8	19.2
	998	22.0	23.1	24.3	21.7	18.7	20.5	19.7

Appendix 7 Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		Control					
Male							
Animal No.		901	902	903	904	905	906
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	0/1	1/1	1/1	1/1	1/1
	(11 days)	-	1/1	-	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	-	-	-	-	-	-
	(43 days)	-	-	-	-	-	-
	(44 days)	-	-	-	-	-	-
	(45 days)	-	-	-	-	-	-
	(46 days)	-	-	-	-	-	-
Female							
Animal No.		951	952	953	954	955	956
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	0/1	0/1	1/1	1/1	1/1
	(11 days)	-	1/1	1/1	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	-	-	-	-	-	-

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		Control					
Male							
Animal No.		907	908	909	910	911	912
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	0/1	1/1	1/1	1/1	0/1	0/1
	(11 days)	1/1	-	-	-	1/1	1/1
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	0/1	1/1	1/1	0/1	0/1	0/1
	(43 days)	0/1	-	-	0/1	0/1	1/1
	(44 days)	0/1	-	-	1/1	0/1	-
	(45 days)	1/1	-	-	-	1/1	-
	(46 days)	-	-	-	-	-	-
Female							
Animal No.		957	958	959	960	961	962
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	1/1	1/1	1/1	0/1
	(11 days)	-	-	-	-	-	1/1
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		5 mg/kg					
Male							
Animal No.		913	914	915	916	917	918
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(11 days)	-	-	-	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	-	-	-	-	-	-
	(43 days)	-	-	-	-	-	-
	(44 days)	-	-	-	-	-	-
	(45 days)	-	-	-	-	-	-
	(46 days)	-	-	-	-	-	-
Female							
Animal No.		963	964	965	966	967	968
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	1/1	1/1	0/1	1/1
	(11 days)	-	-	-	-	1/1	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	-	-	-	-	-	-

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		5 mg/kg					
Male							
Animal No.		919	920	921	922	923	924
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(11 days)	-	-	-	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	0/1	0/1	0/1	1/1	0/1	0/1
	(43 days)	0/1	0/1	0/1	-	0/1	0/1
	(44 days)	0/1	1/1	0/1	-	0/1	0/1
	(45 days)	1/1	-	1/1	-	1/1	1/1
	(46 days)	-	-	-	-	-	-
Female							
Animal No.		969	970	971	972	973	974
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	0/1	0/1	0/1	0/1	1/1	0/1
	(11 days)	1/1	1/1	1/1	1/1	-	1/1
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		20 mg/kg					
Male							
Animal No.		925	926	927	928	929	930
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	0/1	1/1	1/1	1/1	1/1
	(11 days)	-	1/1	-	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	-	-	-	-	-	-
	(43 days)	-	-	-	-	-	-
	(44 days)	-	-	-	-	-	-
	(45 days)	-	-	-	-	-	-
	(46 days)	-	-	-	-	-	-
Female							
Animal No.		975	976	977	978	979	980
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	0/1	1/1	0/1	1/1	1/1	1/1
	(11 days)	1/1	-	1/1	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	-	-	-	-	-	-

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		20 mg/kg					
Male							
Animal No.		931	932	933	934	935	936
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	0/1	0/1	0/1	1/1	1/1	1/1
	(11 days)	1/1	1/1	1/1	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	0/1	1/1	1/1	0/1	0/1	0/1
	(43 days)	0/1	-	-	1/1	0/1	0/1
	(44 days)	1/1	-	-	-	0/1	0/1
	(45 days)	-	-	-	-	1/1	0/1
	(46 days)	-	-	-	-	-	1/1
Female							
Animal No.		981	982	983	984	985	986
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	1/1	0/1	1/1	1/1
	(11 days)	-	-	-	1/1	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		80 mg/kg					
Male							
Animal No.		937	938	939	940	941	942
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(11 days)	-	-	-	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	-	-	-	-	-	-
	(43 days)	-	-	-	-	-	-
	(44 days)	-	-	-	-	-	-
	(45 days)	-	-	-	-	-	-
	(46 days)	-	-	-	-	-	-
Female							
Animal No.		987	988	989	990	991	992
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	0/1	1/1	1/1	0/1	0/1
	(11 days)	-	1/1	-	-	1/1	1/1
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	-	-	-	-	-	-

Appendix 7 - continued Individual postnatal differentiation in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		80 mg/kg					
Male							
Animal No.		943	944	945	946	947	948
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	0/1	0/1	0/1	1/1	1/1	1/1
	(11 days)	1/1	1/1	1/1	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Descensus testis	(21 days)	1/1	1/1	1/1	1/1	1/1	1/1
Cleavage of the balanopreputial gland							
	(42 days)	1/1	0/1	0/1	1/1	1/1	0/1
	(43 days)	-	0/1	0/1	-	-	0/1
	(44 days)	-	0/1	0/1	-	-	0/1
	(45 days)	-	0/1	1/1	-	-	1/1
	(46 days)	-	1/1	-	-	-	-
Female							
Animal No.		993	994	995	996	997	998
Pinna detachment	(4 days)	1/1	1/1	1/1	1/1	1/1	1/1
Piliation	(8 days)	1/1	1/1	1/1	1/1	1/1	1/1
Incisor eruption	(10 days)	1/1	1/1	0/1	1/1	1/1	1/1
	(11 days)	-	-	1/1	-	-	-
Eyelid separation	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Gait	(15 days)	1/1	1/1	1/1	1/1	1/1	1/1
Vaginal opening	(42 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 8 Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No. 49816

Group and dose		Control					
Male							
Animal No.		901	902	903	904	905	906
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz (60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz (60 dB)	(28 days)	-	-	-	-	-	-
Female							
Animal No.		951	952	953	954	955	956
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz (60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz (60 dB)	(28 days)	-	-	-	-	-	-

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		Control					
Male							
Animal No.		907	908	909	910	911	912
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Female							
Animal No.		957	958	959	960	961	962
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		5 mg/kg					
Male							
Animal No.		913	914	915	916	917	918
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Female							
Animal No.		963	964	965	966	967	968
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz(60 dB)	(28 days)	-	-	-	-	-	-

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		5 mg/kg					
Male							
Animal No.		919	920	921	922	923	924
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Female							
Animal No.		969	970	971	972	973	974
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	0/1
	(6 days)	-	-	-	-	-	1/1
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		20 mg/kg					
Male							
Animal No.		925	926	927	928	929	930
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Female							
Animal No.		975	976	977	978	979	980
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	0/1
	(6 days)	-	-	-	-	-	1/1
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz(60 dB)	(28 days)	-	-	-	-	-	-

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Study No.49816

Group and dose		20 mg/kg					
Male							
Animal No.		931	932	933	934	935	936
Righting reflex	(5 days)	0/1	1/1	1/1	1/1	1/1	0/1
	(6 days)	1/1	-	-	-	-	1/1
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Female							
Animal No.		981	982	983	984	985	986
Righting reflex	(5 days)	1/1	1/1	0/1	1/1	1/1	1/1
	(6 days)	-	-	1/1	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		80 mg/kg					
Male							
Animal No.		937	938	939	940	941	942
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Female							
Animal No.		987	988	989	990	991	992
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	-	-	-	-	-	-
Preyer's reflex 20000 Hz(60 dB)	(28 days)	-	-	-	-	-	-

Appendix 8 - continued Individual function test in juvenile rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period Study No.49816

Group and dose		80 mg/kg					
Male							
Animal No.		943	944	945	946	947	948
Righting reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
	(6 days)	-	-	-	-	-	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Female							
Animal No.		993	994	995	996	997	998
Righting reflex	(5 days)	0/1	1/1	1/1	1/1	0/1	1/1
	(6 days)	1/1	-	-	-	1/1	-
Ipsilateral flexor reflex	(5 days)	1/1	1/1	1/1	1/1	1/1	1/1
Visual placing	(16 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 500 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1
Preyer's reflex 20000 Hz(60 dB)	(28 days)	1/1	1/1	1/1	1/1	1/1	1/1

Appendix 9 Individual urinary findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Urine volume (mL/24hr)	Osmotic pressure (Osm/kg)	Specific gravity
Control	907	27.0	1.322	1.039
	908	23.6	1.303	1.038
	909	15.8	1.671	1.050
	910	22.0	1.147	1.036
	911	17.6	1.589	1.050
	912	33.0	1.094	1.031
5 mg/kg	919	21.8	0.997	1.029
	920	19.2	1.423	1.041
	921	23.4	0.967	1.028
	922	12.2	2.042	1.064
	923	29.2	0.981	1.030
	924	19.2	1.616	1.048
20 mg/kg	931	17.4	1.520	1.045
	932	27.0	0.975	1.030
	933	16.0	1.418	1.045
	934	24.2	1.109	1.036
	935	15.0	1.744	1.054
	936	15.4	1.847	1.056
80 mg/kg	943	24.8	0.896	1.028
	944	31.8	0.537	1.017
	945	22.6	1.037	1.033
	946	20.0	1.146	1.037
	947	26.8	1.300	1.038
	948	24.0	1.077	1.033

Appendix 9 - continued Individual urinary findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Color	pH	Protein	Glucose	Ketone body	Bilirubin	Occult blood	Urobilinogen (mg/dL)
Control	907	Y	7.5	++	-	-	-	-	<1
	908	Y	8.0	+	-	-	-	-	<1
	909	Y	8.0	++	-	-	-	-	<1
	910	Y	8.0	+	-	-	-	-	<1
	911	Y	8.0	++	-	-	-	-	<1
	912	Y	8.0	+	-	-	-	-	<1
5 mg/kg	919	Y	8.0	++	-	-	-	-	<1
	920	Y	8.5	++	-	-	-	-	<1
	921	Y	8.0	+	-	-	-	-	<1
	922	Y	7.5	++	-	-	-	-	<1
	923	PY	8.0	±	-	-	-	-	<1
	924	Y	8.0	+++	-	-	-	+++	<1
20 mg/kg	931	Y	8.0	++	-	-	-	++	<1
	932	PY	8.0	±	-	-	-	-	<1
	933	Y	8.0	++	-	-	-	-	<1
	934	Y	8.0	+	-	-	-	-	<1
	935	Y	8.0	++	-	-	-	-	<1
	936	Y	8.0	++	-	-	-	-	<1
80 mg/kg	943	PY	8.0	++	-	-	-	-	<1
	944	PY	8.0	++	-	-	-	-	<1
	945	Y	8.5	++	-	-	-	-	<1
	946	Y	8.0	+	-	-	-	-	<1
	947	Y	8.0	+	-	-	-	-	<1
	948	Y	8.0	+	-	-	-	-	<1

Abbreviation: PY, pale yellow; Y, yellow.
Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked; ++++, very marked.

Appendix 9 - continued Individual urinary findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Urinary sediment				
		Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
Control	907	-	-	-	-	++
	908	-	-	-	-	-
	909	-	-	-	-	-
	910	-	-	-	-	-
	911	-	-	-	-	+
	912	-	-	-	-	-
5 mg/kg	919	-	-	-	-	+++
	920	-	-	-	-	-
	921	-	-	-	-	-
	922	-	-	-	-	++
	923	-	-	-	-	-
	924	-	+	-	-	+
20 mg/kg	931	-	+	-	-	-
	932	-	-	-	-	-
	933	-	-	-	-	-
	934	-	-	-	-	-
	935	-	-	-	-	-
	936	-	-	-	-	-
80 mg/kg	943	-	-	-	-	++
	944	-	-	-	-	-
	945	-	-	-	-	-
	946	-	-	-	-	-
	947	-	-	-	-	-
	948	-	-	-	-	-

Grade signs are as follows.
Epithelial cells: -, < 3/field; +, 3/field ≦ and < 10/field; ++, 10/field ≦ and < 20/field; +++, ≧ 20/field.
Erythrocytes : -, < 10/field; +, 10/field ≦ and < 30/field; ++, 30/field ≦ and < 100/field; +++, countless.
Leukocytes : -, < 3/field; +, 3/field ≦ and < 20/field; ++, 20/field ≦ and < 40/field; +++, ≧ 40/field.
Casts : -, none; +, ≧ 1/all field.
Crystals : -, < 10/field; +, 10/field ≦ and < 20/field; ++, 20/field ≦ and < 30/field; +++, countless.

Appendix 10 Individual urinary findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Urine volume (mL/24hr)	Osmotic pressure (Osm/kg)	Specific gravity
Control	957	11.6	1.326	1.042
	958	11.0	1.175	1.036
	959	5.8	1.990	1.062
	960	11.4	1.147	1.034
	961	9.0	1.330	1.040
	962	9.0	1.258	1.039
5 mg/kg	969	11.0	1.294	1.040
	970	10.2	1.141	1.035
	971	9.2	1.445	1.045
	972	9.8	1.313	1.039
	973	15.0	1.438	1.045
	974	14.2	1.089	1.033
20 mg/kg	981	7.0	1.213	1.037
	982	7.6	1.465	1.044
	983	32.6	0.581	1.018
	984	8.8	1.456	1.045
	985	10.6	1.360	1.042
	986	14.0	1.309	1.041
80 mg/kg	993	11.4	0.844	1.025
	994	14.8	1.145	1.035
	995	9.4	1.353	1.042
	996	10.0	1.400	1.045
	997	8.4	1.152	1.036
	998	10.6	1.233	1.038

Appendix 10 - continued Individual urinary findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Color	pH	Protein	Glucose	Ketone body	Bilirubin	Occult blood	Urobilinogen (mg/dL)
Control	957	Y	7.5	±	-	-	-	-	<1
	958	Y	8.0	-	-	-	-	-	<1
	959	Y	7.5	±	-	-	-	-	<1
	960	Y	8.0	-	-	-	-	-	<1
	961	Y	8.0	-	-	-	-	-	<1
	962	Y	7.5	-	-	-	-	-	<1
5 mg/kg	969	Y	6.5	-	-	-	-	-	<1
	970	Y	7.5	±	-	-	-	-	<1
	971	Y	8.0	-	-	-	-	-	<1
	972	Y	8.0	±	-	-	-	-	<1
	973	Y	7.5	±	-	-	-	-	<1
	974	Y	8.0	±	-	-	-	-	<1
20 mg/kg	981	Y	6.5	-	-	-	-	-	<1
	982	Y	8.0	-	-	-	-	-	<1
	983	PY	8.5	-	-	-	-	-	<1
	984	Y	8.0	+	-	-	-	-	<1
	985	Y	8.0	-	-	-	-	-	<1
	986	Y	8.0	-	-	-	-	-	<1
80 mg/kg	993	Y	8.0	-	-	-	-	-	<1
	994	Y	7.5	-	-	-	-	-	<1
	995	Y	8.0	±	-	-	-	-	<1
	996	Y	7.5	±	-	-	-	-	<1
	997	Y	8.5	-	-	-	-	-	<1
	998	Y	8.0	-	-	-	-	-	<1

Abbreviation: PY, pale yellow; Y, yellow.
Grade sign: -, none; ±, trace; +, mild; ++, moderate; +++, marked; ++++, very marked.

Appendix 10 - continued Individual urinary findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Urinary sediment				
		Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals
Control	957	-	-	-	-	+
	958	-	-	-	-	-
	959	-	-	-	-	-
	960	-	-	-	-	-
	961	-	-	-	-	-
	962	-	-	-	-	-
5 mg/kg	969	-	-	-	-	-
	970	-	-	-	-	-
	971	-	-	-	-	-
	972	-	-	-	-	-
	973	-	-	-	-	-
	974	-	-	-	-	-
20 mg/kg	981	-	-	-	-	-
	982	-	-	-	-	-
	983	-	-	-	-	-
	984	-	-	-	-	-
	985	-	-	-	-	-
	986	-	-	-	-	-
80 mg/kg	993	-	-	-	-	-
	994	-	-	-	-	-
	995	-	-	-	-	-
	996	-	-	-	-	-
	997	-	-	-	-	-
	998	-	-	-	-	-

Grade signs are as follows.

Epithelial cells: -, < 3/field; +, 3/field ≦ and < 10/field; ++, 10/field ≦ and < 20/field; +++, ≧ 20/field.
Erythrocytes : -, < 10/field; +, 10/field ≦ and < 30/field; ++, 30/field ≦ and < 100/field; +++, countless.
Leukocytes : -, < 3/field; +, 3/field ≦ and < 20/field; ++, 20/field ≦ and < 40/field; +++, ≧ 40/field.
Casts : -, none; +, ≧ 1/all field.
Crystals : -, < 10/field; +, 10/field ≦ and < 20/field; ++, 20/field ≦ and < 30/field; +++, countless.

Appendix 11 Individual hematological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Leukocytes (10^2 /μL)	Erythrocytes (10^4 /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelets (10^4 /μL)
Control	901	39	486	8.0	29.6	61	16.5	27.0	107.2
	902	53	554	9.6	35.4	64	17.3	27.1	116.7
	903	63	476	9.6	33.8	71	20.2	28.4	120.3
	904	81	474	8.7	32.9	69	18.4	26.4	130.3
	905	63	455	9.2	33.2	73	20.2	27.7	129.4
	906	81	480	9.4	34.8	73	19.6	27.0	110.5
5 mg/kg	913	71	526	8.6	32.0	61	16.3	26.9	114.2
	914	57	547	9.2	33.9	62	16.8	27.1	121.5
	915	59	456	9.5	32.9	72	20.8	28.9	112.3
	916	73	454	8.6	32.5	72	18.9	26.5	122.3
	917	74	498	9.9	35.7	72	19.9	27.7	123.4
	918	59	469	9.0	32.8	70	19.2	27.4	116.7
20 mg/kg	925	71	431	8.2	30.8	71	19.0	26.6	104.9
	926	55	456	8.1	30.2	66	17.8	26.8	117.3
	927	49	471	9.3	32.3	69	19.7	28.8	103.5
	928	60	524	9.4	34.8	66	17.9	27.0	115.1
	929	50	495	8.9	32.9	66	18.0	27.1	115.3
	930	89	514	9.6	34.8	68	18.7	27.6	110.9
80 mg/kg	937	70	476	8.5	32.6	68	17.9	26.1	97.7
	938	55	487	8.3	31.2	64	17.0	26.6	114.9
	939	59	523	10.2	37.2	71	19.5	27.4	94.7
	940	53	505	8.9	32.9	65	17.6	27.1	104.8
	941	55	521	9.0	33.0	63	17.3	27.3	118.5
	942	149	484	9.4	35.6	74	19.4	26.4	124.2

Appendix 11 - continued Individual hematological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Differential leukocyte count					
		Eosinophil (%)	Stab neutrophil (%)	Segmented neutrophil (%)	Lymphocyte (%)	Basophil (%)	Monocyte (%)
Control	901	0.0	0.0	21.0	77.0	0.0	2.0
	902	0.0	0.0	16.0	81.0	0.0	3.0
	903	0.0	2.0	17.0	80.0	0.0	1.0
	904	1.0	0.0	18.0	80.0	0.0	1.0
	905	0.0	0.0	15.0	83.0	0.0	2.0
	906	2.0	0.0	20.0	76.0	0.0	2.0
5 mg/kg	913	1.0	0.0	17.0	79.0	0.0	3.0
	914	0.0	0.0	21.0	77.0	0.0	2.0
	915	1.0	0.0	19.0	78.0	0.0	2.0
	916	0.0	1.0	15.0	82.0	0.0	2.0
	917	1.0	1.0	17.0	81.0	0.0	0.0
	918	0.0	1.0	21.0	77.0	0.0	1.0
20 mg/kg	925	0.0	0.0	20.0	77.0	0.0	3.0
	926	0.0	1.0	11.0	87.0	0.0	1.0
	927	1.0	0.0	20.0	76.0	0.0	3.0
	928	1.0	0.0	20.0	78.0	0.0	1.0
	929	0.0	0.0	14.0	84.0	0.0	2.0
	930	0.0	0.0	25.0	70.0	0.0	5.0
80 mg/kg	937	1.0	1.0	18.0	77.0	0.0	3.0
	938	0.0	1.0	20.0	76.0	0.0	3.0
	939	1.0	0.0	21.0	74.0	0.0	4.0
	940	1.0	0.0	21.0	73.0	0.0	5.0
	941	0.0	0.0	20.0	78.0	0.0	2.0
	942	0.0	0.0	18.0	79.0	0.0	3.0

Appendix 12 Individual hematological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Leukocytes (10^2 /μL)	Erythrocytes (10^4 /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelets (10^4 /μL)
Control	951	56	480	7.6	28.3	59	15.8	26.9	123.7
	952	50	467	8.3	29.5	63	17.8	28.1	123.3
	953	64	502	10.5	36.4	73	20.9	28.8	117.2
	954	41	470	8.8	32.0	68	18.7	27.5	107.8
	955	122	490	9.8	36.3	74	20.0	27.0	111.0
	956	64	473	9.6	34.0	72	20.3	28.2	123.7
5 mg/kg	964	42	509	9.3	33.6	66	18.3	27.7	118.4
	965	54	536	11.0	38.2	71	20.5	28.8	97.8
	966	81	477	9.2	33.8	71	19.3	27.2	101.3
	967	57	487	8.8	32.2	66	18.1	27.3	134.4
	968	69	511	10.0	35.1	69	19.6	28.5	117.4
20 mg/kg	975	91	522	8.6	32.6	62	16.5	26.4	118.8
	976	56	495	8.9	32.5	66	18.0	27.4	99.3
	977	43	482	10.2	35.9	74	21.2	28.4	110.4
	978	84	518	9.8	35.6	69	18.9	27.5	107.7
	979	54	466	8.5	30.6	66	18.2	27.8	119.9
	980	62	493	9.2	33.5	68	18.7	27.5	91.3
80 mg/kg	987	70	506	8.5	32.7	65	16.8	26.0	118.3
	988	70	464	9.0	32.9	71	19.4	27.4	103.8
	989	52	540	10.9	38.5	71	20.2	28.3	91.6
	990	143	520	8.7	34.8	67	16.7	25.0	117.3
	991	82	501	9.3	34.0	68	18.6	27.4	128.9
	992	91	464	9.3	34.7	75	20.0	26.8	95.3

Excluding data of one animal(No. 963) in the 5 mg/kg group, since blood sample coagulated.

Appendix 12 - continued Individual hematological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Differential leukocyte count					
		Eosinophil (%)	Stab neutrophil (%)	Segmented neutrophil (%)	Lymphocyte (%)	Basophil (%)	Monocyte (%)
Control	951	0.0	1.0	25.0	70.0	0.0	4.0
	952	1.0	2.0	14.0	78.0	0.0	5.0
	953	2.0	1.0	14.0	83.0	0.0	0.0
	954	0.0	0.0	13.0	85.0	0.0	2.0
	955	0.0	0.0	19.0	80.0	0.0	1.0
	956	0.0	1.0	14.0	82.0	0.0	3.0
5 mg/kg	963	0.0	1.0	20.0	77.0	0.0	2.0
	964	1.0	0.0	13.0	85.0	0.0	1.0
	965	0.0	2.0	15.0	83.0	0.0	0.0
	966	0.0	1.0	21.0	76.0	0.0	2.0
	967	2.0	0.0	9.0	88.0	0.0	1.0
	968	1.0	0.0	22.0	77.0	0.0	0.0
20 mg/kg	975	2.0	2.0	21.0	75.0	0.0	0.0
	976	0.0	0.0	15.0	84.0	0.0	1.0
	977	0.0	1.0	16.0	81.0	0.0	2.0
	978	1.0	0.0	6.0	91.0	0.0	2.0
	979	0.0	1.0	18.0	81.0	0.0	0.0
	980	1.0	0.0	23.0	72.0	0.0	4.0
80 mg/kg	987	1.0	0.0	17.0	80.0	0.0	2.0
	988	1.0	0.0	38.0	56.0	0.0	5.0
	989	1.0	0.0	14.0	82.0	0.0	3.0
	990	1.0	0.0	23.0	74.0	0.0	2.0
	991	0.0	0.0	13.0	86.0	0.0	1.0
	992	0.0	1.0	16.0	82.0	0.0	1.0

Appendix 13 Individual hematological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Leukocytes (10^2 /μL)	Erythrocytes (10^4 /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelets (10^4 /μL)	PT (sec)	APTT (sec)
Control	907	72	828	14.1	43.7	53	17.0	32.3	102.1	13.6	23.4
	908	69	848	14.4	47.6	56	17.0	30.3	82.5	17.0	24.4
	909	60	913	15.2	47.3	52	16.6	32.1	110.2	13.5	21.3
	910	78	833	15.1	48.3	58	18.1	31.3	95.8	13.7	20.9
	911	72	889	15.1	47.5	53	17.0	31.8	94.7	15.0	23.5
	912	61	900	15.0	48.5	54	16.7	30.9	114.5	18.0	23.8
5 mg/kg	919	60	779	13.5	43.4	56	17.3	31.1	82.7	13.5	21.7
	920	70	821	14.4	44.9	55	17.5	32.1	90.4	12.4	17.7
	921	63	852	15.7	50.0	59	18.4	31.4	91.8	18.4	25.5
	922	64	818	14.8	46.4	57	18.1	31.9	83.3	15.0	23.4
	923	71	829	15.4	48.5	59	18.6	31.8	94.8	13.6	22.2
	924	69	815	14.1	45.4	56	17.3	31.1	94.3	13.6	21.9
20 mg/kg	931	77	839	14.6	46.2	55	17.4	31.6	91.9	15.3	21.9
	932	87	833	14.9	46.4	56	17.9	32.1	104.4	12.9	20.4
	933	66	890	16.3	51.5	58	18.3	31.7	101.3	20.7	26.5
	934	68	809	15.0	46.6	58	18.5	32.2	96.3	13.2	19.8
	935	80	894	15.6	48.7	54	17.4	32.0	90.7	14.4	24.9
	936	78	808	14.7	47.0	58	18.2	31.3	86.6	13.7	15.0
80 mg/kg	943	82	833	15.4	47.4	57	18.5	32.5	106.9	14.7	21.1
	944	92	792	14.4	47.0	59	18.2	30.6	83.7	13.3	20.3
	945	60	769	13.6	43.4	56	17.7	31.3	83.7	14.8	18.3
	946	78	831	14.6	45.7	55	17.6	31.9	109.8	11.2	20.3
	947	104	817	14.3	46.9	57	17.5	30.5	79.9	12.6	20.1
	948	58	826	14.0	44.8	54	16.9	31.3	104.8	13.6	20.4

Appendix 13 - continued Individual hematological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Differential leukocyte count					
		Eosinophil (%)	Stab neutrophil (%)	Segmented neutrophil (%)	Lymphocyte (%)	Basophil (%)	Monocyte (%)
Control	907	0.0	1.0	12.0	85.0	0.0	2.0
	908	1.0	0.0	6.0	91.0	0.0	2.0
	909	1.0	0.0	14.0	83.0	0.0	2.0
	910	3.0	0.0	10.0	86.0	0.0	1.0
	911	1.0	0.0	9.0	86.0	0.0	4.0
	912	1.0	0.0	11.0	87.0	0.0	1.0
5 mg/kg	919	1.0	0.0	10.0	87.0	0.0	2.0
	920	0.0	0.0	6.0	93.0	0.0	1.0
	921	1.0	0.0	6.0	91.0	0.0	2.0
	922	1.0	0.0	8.0	88.0	0.0	3.0
	923	2.0	1.0	8.0	88.0	0.0	1.0
	924	0.0	0.0	10.0	89.0	0.0	1.0
20 mg/kg	931	1.0	0.0	4.0	93.0	0.0	2.0
	932	1.0	0.0	13.0	85.0	0.0	1.0
	933	0.0	0.0	9.0	87.0	0.0	4.0
	934	2.0	0.0	13.0	81.0	0.0	4.0
	935	1.0	0.0	7.0	92.0	0.0	0.0
	936	2.0	0.0	8.0	88.0	0.0	2.0
80 mg/kg	943	1.0	0.0	6.0	92.0	0.0	1.0
	944	0.0	0.0	12.0	84.0	0.0	4.0
	945	2.0	0.0	11.0	87.0	0.0	0.0
	946	0.0	0.0	5.0	95.0	0.0	0.0
	947	1.0	0.0	15.0	84.0	0.0	0.0
	948	1.0	0.0	14.0	82.0	0.0	3.0

Appendix 14 Individual hematological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Leukocytes (10^2 /μL)	Erythrocytes (10^4 /μL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (%)	Platelets (10^4 /μL)	PT (sec)	APTT (sec)
Control	957	71	760	14.0	44.7	59	18.4	31.3	88.8	12.1	18.2
	958	52	817	14.9	46.4	57	18.2	32.1	114.6	12.9	19.3
	959	43	796	14.0	44.8	56	17.6	31.3	98.1	12.7	17.8
	960	39	804	14.5	45.3	56	18.0	32.0	107.3	12.2	15.7
	961	51	811	14.7	45.2	56	18.1	32.5	110.2	12.1	17.3
	962	68	802	14.9	47.0	59	18.6	31.7	101.0	11.3	17.1
5 mg/kg	969	47	740	13.8	43.0	58	18.6	32.1	95.9	12.2	17.6
	970	75	779	13.8	43.6	56	17.7	31.7	96.7	12.7	20.4
	971	54	816	14.8	46.2	57	18.1	32.0	104.0	11.6	18.5
	972	50	763	13.8	43.1	56	18.1	32.0	106.9	12.8	18.3
	973	97	723	13.6	42.7	59	18.8	31.9	87.7	11.9	17.5
	974	53	789	14.4	45.2	57	18.3	31.9	107.0	11.5	18.8
20 mg/kg	981	39	827	15.0	48.0	58	18.1	31.3	89.9	11.5	17.1
	982	47	833	15.2	46.8	56	18.2	32.5	95.6	10.9	14.2
	983	52	849	14.6	46.2	54	17.2	31.6	110.9	13.2	17.8
	984	40	724	13.1	41.7	58	18.1	31.4	98.3	12.5	16.6
	985	55	847	14.6	46.3	55	17.2	31.5	105.3	10.8	18.9
	986	84	838	14.7	46.9	56	17.5	31.3	93.5	11.1	19.7
80 mg/kg	993	35	817	14.3	44.4	54	17.5	32.2	97.6	12.0	17.5
	994	53	837	15.3	47.2	56	18.3	32.4	98.4	12.5	18.5
	995	46	756	13.8	43.5	58	18.3	31.7	99.1	11.9	16.6
	996	45	805	14.1	45.1	56	17.5	31.3	94.5	13.2	18.2
	997	69	785	14.5	46.7	59	18.5	31.0	96.4	12.0	16.4
	998	58	828	14.7	45.5	55	17.8	32.3	95.1	12.3	18.6

Appendix 14 - continued Individual hematological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Differential leukocyte count					
		Eosinophil (%)	Stab neutrophil (%)	Segmented neutrophil (%)	Lymphocyte (%)	Basophil (%)	Monocyte (%)
Control	957	0.0	0.0	15.0	81.0	0.0	4.0
	958	1.0	1.0	10.0	88.0	0.0	0.0
	959	1.0	0.0	9.0	88.0	0.0	2.0
	960	2.0	0.0	12.0	84.0	0.0	2.0
	961	1.0	0.0	6.0	93.0	0.0	0.0
	962	1.0	0.0	7.0	91.0	0.0	1.0
5 mg/kg	969	1.0	0.0	9.0	90.0	0.0	0.0
	970	0.0	0.0	8.0	92.0	0.0	0.0
	971	1.0	0.0	15.0	83.0	0.0	1.0
	972	2.0	0.0	4.0	93.0	0.0	1.0
	973	1.0	0.0	5.0	92.0	0.0	2.0
	974	1.0	0.0	7.0	91.0	0.0	1.0
20 mg/kg	981	2.0	0.0	14.0	83.0	0.0	1.0
	982	0.0	0.0	8.0	92.0	0.0	0.0
	983	0.0	0.0	9.0	91.0	0.0	0.0
	984	1.0	0.0	8.0	90.0	0.0	1.0
	985	0.0	0.0	5.0	94.0	0.0	1.0
	986	0.0	0.0	6.0	92.0	0.0	2.0
80 mg/kg	993	2.0	0.0	17.0	81.0	0.0	0.0
	994	3.0	0.0	14.0	81.0	0.0	2.0
	995	1.0	0.0	11.0	85.0	0.0	3.0
	996	0.0	0.0	6.0	94.0	0.0	0.0
	997	1.0	0.0	6.0	92.0	0.0	1.0
	998	2.0	0.0	6.0	91.0	0.0	1.0

Appendix 15 Individual biochemical findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	T.Protein (g/dL)	Albumin (g/dL)	A/G ratio	T.Bilirubin (mg/dL)	GOT (IU/L)	GPT (IU/L)	γ-GTP (IU/L)	ALP (IU/L)	T.Cholesterol (mg/dL)	Triglycerides (mg/dL)
Control	901	4.7	3.6	3.27	0.0	90	20	0.1	767	124	184
	902	5.0	3.8	3.17	0.0	95	21	0.7	974	104	239
	903	4.6	3.6	3.60	0.0	100	20	0.3	967	112	76
	904	4.7	3.7	3.70	0.0	95	25	0.1	908	107	133
	905	4.6	3.4	2.83	0.0	105	24	0.7	848	102	77
	906	4.3	3.4	3.78	0.0	98	25	0.0	1029	90	120
5 mg/kg	913	5.0	3.7	2.85	0.0	90	22	0.3	913	101	172
	914	5.0	3.8	3.17	0.0	91	21	0.3	826	111	111
	915	4.5	3.5	3.50	0.0	92	31	0.0	777	98	102
	916	4.4	3.4	3.40	0.0	111	21	0.2	945	90	88
	917	4.8	3.6	3.00	0.0	94	24	0.3	957	91	156
	918	4.5	3.6	4.00	0.0	96	24	0.5	870	91	69
20 mg/kg	925	4.6	3.5	3.18	0.0	85	32	0.1	865	112	109
	926	4.9	3.7	3.08	0.0	83	19	0.4	817	102	108
	927	4.3	3.4	3.78	0.0	96	27	0.0	990	95	75
	928	4.6	3.6	3.60	0.0	97	21	0.6	995	116	225
	929	4.5	3.5	3.50	0.0	89	23	0.0	966	103	101
	930	4.4	3.5	3.89	0.0	96	24	1.1	955	97	158
80 mg/kg	937	4.6	3.5	3.18	0.0	100	25	0.2	868	92	133
	938	4.8	3.6	3.00	0.0	104	24	0.3	845	103	186
	939	4.6	3.6	3.60	0.0	95	26	0.0	822	118	98
	940	4.3	3.4	3.78	0.0	88	22	0.3	861	96	146
	941	4.5	3.5	3.50	0.0	81	16	0.2	797	96	274
	942	4.5	3.5	3.50	0.0	119	22	0.0	1019	76	93

Appendix 15 - continued Individual biochemical findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
Control	901	254	154	14.5	0.4	9.9	11.2	142.3	5.04	104.9
	902	233	155	12.8	0.3	9.9	11.1	144.3	4.53	103.5
	903	215	163	13.1	0.4	10.2	11.1	142.2	4.56	101.2
	904	203	171	14.2	0.4	10.9	11.8	143.9	5.11	104.2
	905	190	158	12.5	0.4	10.2	11.3	142.5	4.97	104.0
	906	172	138	13.1	0.4	9.9	11.5	143.8	4.44	104.1
5 mg/kg	913	200	162	13.1	0.3	10.2	11.4	143.4	4.75	104.8
	914	210	182	12.9	0.3	10.2	11.7	143.3	4.99	105.2
	915	194	156	14.3	0.4	9.8	11.2	143.7	4.54	105.4
	916	172	154	15.2	0.3	10.3	10.9	145.0	4.50	105.4
	917	186	153	15.1	0.4	10.3	11.1	143.0	4.88	104.1
	918	176	160	15.0	0.4	9.2	10.9	143.4	4.77	103.0
20 mg/kg	925	201	156	13.1	0.4	10.1	11.6	142.3	4.49	103.6
	926	207	148	17.0	0.4	9.6	11.6	144.1	4.96	106.3
	927	181	157	12.0	0.3	9.2	10.6	142.1	4.66	103.5
	928	240	144	17.9	0.4	11.2	11.8	143.3	5.15	105.0
	929	213	150	12.9	0.3	10.4	11.4	143.0	4.76	103.9
	930	196	149	15.6	0.3	9.9	11.3	144.5	4.66	103.5
80 mg/kg	937	197	154	13.8	0.4	9.5	11.9	143.0	4.58	103.5
	938	214	146	14.9	0.4	9.1	10.9	142.3	4.55	103.3
	939	226	143	18.1	0.4	9.1	11.4	143.7	4.46	102.8
	940	207	148	18.7	0.4	9.9	10.9	144.0	4.89	104.5
	941	209	149	13.6	0.4	10.0	11.2	140.2	4.78	102.8
	942	155	159	14.5	0.4	10.4	11.7	142.6	4.30	102.3

Appendix 16 Individual biochemical findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	T.Protein (g/dL)	Albumin (g/dL)	A/G ratio	T.Bilirubin (mg/dL)	GOT (IU/L)	GPT (IU/L)	γ-GTP (IU/L)	ALP (IU/L)	T.Cholesterol (mg/dL)	Triglycerides (mg/dL)
Control	951	4.4	3.4	3.40	0.0	106	19	0.5	830	108	84
	952	4.8	3.7	3.36	0.0	93	19	0.1	701	135	55
	953	4.6	3.4	2.83	0.0	94	22	0.3	986	117	88
	954	4.4	3.5	3.89	0.0	140	28	0.0	866	92	80
	955	4.5	3.5	3.50	0.0	142	28	0.8	1077	108	82
	956	5.0	3.6	2.57	0.0	99	23	0.3	874	92	204
5 mg/kg	963	4.4	3.3	3.00	0.0	115	22	0.4	597	99	43
	964	4.6	3.5	3.18	0.0	98	20	0.2	721	104	66
	965	4.7	3.6	3.27	0.0	158	27	0.5	734	113	123
	966	4.0	3.2	4.00	0.0	86	25	0.0	946	90	82
	967	4.4	3.3	3.00	0.0	95	23	0.0	837	116	88
	968	4.7	3.6	3.27	0.0	89	23	0.5	862	75	181
20 mg/kg	975	4.6	3.6	3.60	0.0	105	21	0.1	745	114	71
	976	4.8	3.6	3.00	0.0	102	20	0.0	690	108	106
	977	4.4	3.3	3.00	0.0	114	22	0.0	664	88	88
	978	4.5	3.6	4.00	0.0	101	19	0.1	733	100	96
	979	4.5	3.5	3.50	0.0	89	21	0.3	933	106	84
	980	4.2	3.4	4.25	0.1	109	24	0.3	1003	97	49
80 mg/kg	987	4.6	3.7	4.11	0.0	86	21	0.3	674	107	121
	988	4.5	3.4	3.09	0.0	99	22	0.2	970	100	163
	989	4.7	3.7	3.70	0.0	88	20	0.3	759	118	144
	990	4.6	3.5	3.18	0.0	111	22	0.0	810	89	133
	991	4.8	3.7	3.36	0.0	90	24	0.3	1008	99	157
	992	4.5	3.6	4.00	0.0	97	22	0.0	912	84	78

Appendix 16 - continued Individual biochemical findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
Control	951	208	142	12.5	0.4	10.1	10.9	143.2	5.06	106.8
	952	235	152	13.8	0.3	9.7	10.9	143.9	4.14	106.0
	953	214	155	16.1	0.4	10.3	11.0	144.9	4.63	105.2
	954	183	167	19.6	0.4	10.3	11.3	143.8	4.99	104.7
	955	210	158	17.6	0.4	9.6	11.1	146.3	5.36	106.3
	956	200	153	18.0	0.4	10.3	11.4	143.8	4.94	104.6
5 mg/kg	963	185	153	12.3	0.3	10.5	10.4	143.7	5.59	105.8
	964	184	162	13.4	0.4	10.7	11.1	142.1	5.10	103.7
	965	220	190	18.9	0.3	9.8	11.0	144.4	5.28	103.2
	966	164	144	15.6	0.4	10.0	10.2	146.1	4.40	104.6
	967	229	156	15.4	0.4	9.9	10.7	143.3	4.69	104.1
	968	171	167	17.6	0.4	9.6	10.9	144.3	4.72	105.7
20 mg/kg	975	213	149	12.7	0.4	10.1	11.4	141.7	5.17	102.9
	976	206	146	14.2	0.4	10.0	11.0	142.6	4.58	103.3
	977	184	163	14.0	0.3	10.3	10.9	142.9	5.05	104.1
	978	191	147	16.8	0.4	9.7	10.7	146.3	4.53	106.4
	979	209	159	12.7	0.3	11.0	11.0	143.0	5.32	105.6
	980	176	170	16.9	0.4	10.0	10.9	144.7	4.97	102.8
80 mg/kg	987	227	149	17.1	0.4	10.0	11.3	142.2	4.74	103.7
	988	207	153	13.4	0.3	9.6	11.2	144.5	4.07	101.7
	989	234	161	17.7	0.4	9.8	11.1	142.7	4.97	103.4
	990	182	141	17.4	0.4	10.1	11.3	144.5	4.67	104.9
	991	209	159	15.7	0.4	10.8	11.8	143.0	5.65	103.6
	992	174	155	17.9	0.4	10.0	11.1	145.1	4.61	106.8

Appendix 17 Individual biochemical findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	T.Protein (g/dL)	Albumin (g/dL)	A/G ratio	T.Bilirubin (mg/dL)	GOT (IU/L)	GPT (IU/L)	γ-GTP (IU/L)	ALP (IU/L)	T.Cholesterol (mg/dL)	Triglycerides (mg/dL)
Control	907	5.7	3.7	1.85	0.0	91	20	0.8	217	41	45
	908	5.6	3.8	2.11	0.0	70	21	0.6	195	46	58
	909	5.6	3.7	1.95	0.0	73	16	0.5	278	41	53
	910	5.5	3.8	2.24	0.0	80	20	0.7	309	60	55
	911	5.6	4.0	2.50	0.0	97	23	0.7	342	46	60
	912	5.6	4.0	2.50	0.1	81	20	0.8	259	39	49
5 mg/kg	919	5.6	3.9	2.29	0.0	74	22	0.7	266	53	23
	920	5.6	4.0	2.50	0.0	85	21	0.4	204	62	36
	921	5.4	3.9	2.60	0.0	62	19	0.9	338	55	25
	922	5.9	4.1	2.28	0.0	74	22	0.4	254	78	68
	923	5.2	3.6	2.25	0.0	84	14	0.1	205	47	26
	924	5.6	3.7	1.95	0.0	76	18	0.9	248	72	47
20 mg/kg	931	5.4	3.8	2.37	0.0	82	20	0.8	234	40	83
	932	5.4	3.9	2.60	0.0	105	18	0.8	251	68	35
	933	5.4	3.6	2.00	0.0	76	21	0.4	301	28	70
	934	5.9	4.0	2.11	0.0	97	22	0.9	240	86	83
	935	5.2	3.6	2.25	0.0	85	18	0.7	245	50	44
	936	5.7	3.6	1.71	0.0	89	25	0.6	226	77	86
80 mg/kg	943	5.4	3.9	2.60	0.0	84	20	0.2	283	57	48
	944	5.2	3.4	1.89	0.0	72	17	0.7	225	58	81
	945	4.8	3.6	3.00	0.0	81	21	0.3	243	40	24
	946	5.5	3.7	2.06	0.0	82	18	0.8	290	74	26
	947	5.6	3.7	1.95	0.0	68	19	0.0	282	83	53
	948	5.4	3.8	2.37	0.0	87	19	0.6	236	53	45

Appendix 17 - continued

Individual biochemical findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
Control	907	85	132	12.4	0.4	7.2	10.3	144.7	3.86	102.7
	908	90	134	12.8	0.4	7.2	10.2	144.6	3.85	102.7
	909	90	153	16.0	0.5	7.3	10.2	143.3	4.13	102.8
	910	114	131	16.7	0.4	7.5	10.1	143.9	4.37	106.8
	911	94	121	15.3	0.4	6.9	10.4	144.1	4.39	107.0
	912	85	125	15.6	0.4	6.7	10.5	146.4	4.11	105.4
5 mg/kg	919	97	139	21.5	0.5	8.0	10.0	144.8	4.18	104.4
	920	111	141	19.2	0.5	7.9	10.2	144.6	4.47	103.3
	921	104	137	14.7	0.4	6.3	9.8	144.6	4.05	108.2
	922	127	143	13.7	0.4	6.5	10.1	144.9	3.82	104.1
	923	85	108	20.0	0.5	7.2	9.9	146.2	4.00	105.1
	924	120	127	15.7	0.4	6.9	10.1	146.4	3.84	104.3
20 mg/kg	931	92	162	17.5	0.5	7.2	10.1	143.5	4.15	104.1
	932	112	152	17.9	0.5	7.2	9.9	144.5	4.31	102.4
	933	70	136	15.1	0.4	7.3	10.0	144.8	4.07	104.4
	934	140	138	12.1	0.4	6.9	10.4	143.7	4.34	104.0
	935	89	116	18.7	0.4	7.5	9.8	144.6	4.39	105.5
	936	140	135	16.1	0.5	6.9	10.4	146.1	4.10	105.2
80 mg/kg	943	105	142	16.6	0.4	7.4	10.0	144.9	3.95	105.5
	944	113	132	18.0	0.5	7.3	9.8	145.0	4.02	104.2
	945	80	122	15.2	0.4	6.9	9.6	142.4	3.93	104.0
	946	119	141	22.0	0.4	7.6	10.3	144.0	4.39	103.1
	947	133	138	17.4	0.4	6.6	10.0	145.6	3.89	105.0
	948	95	103	13.4	0.4	7.3	10.1	146.4	4.29	106.4

Appendix 18 Individual biochemical findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	T.Protein (g/dL)	Albumin (g/dL)	A/G ratio	T.Bilirubin (mg/dL)	GOT (IU/L)	GPT (IU/L)	γ-GTP (IU/L)	ALP (IU/L)	T.Cholesterol (mg/dL)	Triglycerides (mg/dL)
Control	957	5.2	3.7	2.47	0.1	91	16	0.6	204	44	16
	958	5.5	3.8	2.24	0.0	77	17	0.8	187	64	28
	959	5.8	4.3	2.87	0.1	70	18	1.6	171	50	23
	960	5.8	4.2	2.63	0.0	68	18	0.4	162	52	12
	961	5.7	4.1	2.56	0.0	64	17	0.9	135	45	10
	962	5.7	4.0	2.35	0.0	88	17	0.6	127	49	16
5 mg/kg	969	5.2	3.6	2.25	0.1	80	17	0.8	142	43	11
	970	5.8	4.1	2.41	0.0	67	13	1.4	186	59	18
	971	5.7	4.3	3.07	0.1	71	12	1.1	154	55	13
	972	5.2	3.5	2.06	0.0	86	19	0.3	113	42	11
	973	5.8	4.2	2.63	0.1	83	20	0.6	128	90	34
	974	5.7	3.9	2.17	0.0	81	17	1.0	146	85	19
20 mg/kg	981	5.9	4.5	3.21	0.1	66	14	0.4	165	66	25
	982	6.1	4.2	2.21	0.0	72	14	0.8	166	82	38
	983	5.4	4.0	2.86	0.0	70	17	0.7	174	49	23
	984	5.3	3.6	2.12	0.0	67	15	0.9	133	50	14
	985	5.6	4.3	3.31	0.1	96	15	1.0	165	56	9
	986	5.7	4.4	3.38	0.1	82	17	0.7	169	65	17
80 mg/kg	993	5.8	4.0	2.22	0.0	68	13	0.8	135	53	12
	994	5.9	4.2	2.47	0.0	85	18	1.0	155	66	44
	995	6.0	4.4	2.75	0.0	51	15	0.5	143	43	17
	996	6.0	4.4	2.75	0.1	72	21	0.8	188	65	22
	997	5.5	3.9	2.44	0.0	73	21	0.8	167	63	17
	998	5.5	4.2	3.23	0.0	91	22	1.3	159	68	21

Appendix 18 - continued Individual biochemical findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
Control	957	96	108	17.0	0.5	6.7	9.7	144.0	3.65	108.7
	958	125	103	15.2	0.5	6.3	10.1	144.4	4.10	107.1
	959	106	118	15.3	0.5	5.6	10.4	145.4	3.76	110.1
	960	101	111	17.0	0.5	6.0	9.9	143.1	4.54	110.1
	961	91	102	19.7	0.5	7.2	9.8	144.1	4.61	108.0
	962	100	128	17.2	0.4	7.1	10.3	145.8	3.94	109.7
5 mg/kg	969	90	95	16.9	0.5	6.6	9.3	145.2	3.96	109.9
	970	119	117	17.2	0.5	7.0	9.8	143.6	3.71	106.0
	971	119	108	17.0	0.5	7.8	10.1	144.3	3.99	106.4
	972	89	107	17.7	0.5	7.1	9.8	144.8	4.03	107.7
	973	184	114	17.3	0.4	6.3	10.3	144.7	3.75	106.4
	974	142	108	14.4	0.4	7.1	10.0	144.5	4.17	108.5
20 mg/kg	981	139	123	16.7	0.5	7.8	10.3	144.7	4.26	109.1
	982	153	138	15.2	0.4	7.6	10.3	144.7	4.80	107.6
	983	105	119	19.8	0.5	7.8	9.9	142.4	4.50	106.8
	984	101	116	13.8	0.4	7.6	9.5	144.2	3.58	108.2
	985	127	97	11.1	0.4	6.6	9.8	143.8	3.98	106.4
	986	131	120	16.9	0.5	8.2	10.3	145.0	4.25	106.8
80 mg/kg	993	104	103	22.7	0.6	6.7	9.8	143.2	4.41	108.5
	994	133	127	19.5	0.5	6.6	10.3	143.2	3.95	103.5
	995	103	131	16.2	0.5	6.9	10.3	145.2	4.20	111.2
	996	130	118	17.6	0.4	6.7	10.0	145.6	4.14	107.8
	997	119	104	17.0	0.5	6.9	10.3	145.0	4.26	107.7
	998	129	116	17.5	0.4	7.6	10.2	145.7	4.11	107.9

Appendix 19 Individual necropsy findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings	Group and dose	Control						5 mg/kg					
	Animal No.	901	902	903	904	905	906	913	914	915	916	917	918
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Integumentary system													
Integument													
Coloration, hair, yellow		-	-	-	-	-	-	+	+	+	+	+	+

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 20 Individual necropsy findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings	Group and dose	Control						5 mg/kg					
	Animal No.	951	952	953	954	955	956	963	964	965	966	967	968
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Integumentary system													
Integument													
Coloration, hair, yellow		-	-	-	-	-	-	+	+	+	+	+	+

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 20 - continued Individual necropsy findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings	Group and dose	20 mg/kg						80 mg/kg					
	Animal No.	975	976	977	978	979	980	987	988	989	990	991	992
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Integumentary system													
Integument													
Coloration, hair, yellow		+	+	+	+	+	+	+	+	+	+	+	+

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 21 Individual necropsy findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings \ Group and dose	Control						5 mg/kg					
Animal No.	907	908	909	910	911	912	919	920	921	922	923	924
Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Genital system												
Testis												
Small	-	-	-	-	-	-	-	-	-	-	-	-
Enlargement	-	-	-	-	-	+	-	-	-	-	-	-
Epididymis												
Macule, light yellow	-	-	-	-	-	-	-	-	-	-	-	-
Small	-	-	-	-	-	-	-	-	-	-	-	-
Integumentary system												
Integument												
Coloration, hair, yellow	-	-	-	-	-	-	+	-	-	-	-	-

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 21 - continued Individual necropsy findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings	Group and dose	20 mg/kg						80 mg/kg					
	Animal No.	931	932	933	934	935	936	943	944	945	946	947	948
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Genital system													
Testis													
Small		-	+	-	+	-	-	-	-	-	-	-	-
Enlargement		-	-	-	-	-	-	-	-	-	-	-	-
Epididymis													
Macule, light yellow		-	-	-	-	-	-	-	+	-	-	-	-
Small		-	-	-	+	-	-	-	-	-	-	-	-
Integumentary system													
Integument													
Coloration, hair, yellow		+	+	+	+	+	+	+	+	+	+	+	+

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 22 Individual necropsy findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings	Group and dose	Control						5 mg/kg					
	Animal No.	957	958	959	960	961	962	969	970	971	972	973	974
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system													
Kidney													
Dilatation, pelvic cavity		-	-	-	-	-	-	+	-	-	-	-	-
Integumentary system													
Integument													
Coloration, hair, yellow		-	-	-	-	-	-	-	-	-	-	-	-

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 22 - continued

Individual necropsy findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings	Group and dose	20 mg/kg						80 mg/kg					
	Animal No.	981	982	983	984	985	986	993	994	995	996	997	998
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system													
Kidney													
Dilatation, pelvic cavity		-	-	-	-	-	-	-	-	-	-	-	-
Integumentary system													
Integument													
Coloration, hair, yellow		+	+	+	+	+	+	+	+	+	+	+	+

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
No appreciable changes in all other organs and tissues.

Appendix 23 Individual organ weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Final body weight	Brain		Pituitary		Thyroids		Heart	
		(g)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	901	60.8	1.63	2.68	2.9	4.8	5.4	8.9	349.8	575.3
	902	70.6	1.74	2.46	1.6	2.3	8.5	12.0	388.5	550.3
	903	68.7	1.69	2.46	2.6	3.8	8.4	12.2	350.7	510.5
	904	60.1	1.59	2.65	2.6	4.3	8.6	14.3	373.1	620.8
	905	60.0	1.64	2.73	2.2	3.7	6.4	10.7	305.3	508.8
	906	60.2	1.68	2.79	2.5	4.2	8.9	14.8	328.5	545.7
5 mg/kg	913	60.5	1.69	2.79	2.0	3.3	6.0	9.9	313.2	517.7
	914	64.4	1.69	2.62	2.7	4.2	3.1	4.8	377.3	585.9
	915	67.6	1.63	2.41	2.9	4.3	8.1	12.0	411.6	608.9
	916	60.4	1.56	2.58	3.0	5.0	6.4	10.6	308.1	510.1
	917	61.5	1.58	2.57	2.7	4.4	7.8	12.7	327.7	532.8
	918	63.5	1.65	2.60	2.3	3.6	8.8	13.9	325.4	512.4
20 mg/kg	925	69.0	1.59	2.30	3.1	4.5	8.3	12.0	359.9	521.6
	926	71.2	1.56	2.19	2.8	3.9	11.4	16.0	386.0	542.1
	927	64.3	1.65	2.57	2.2	3.4	9.4	14.6	310.9	483.5
	928	56.6	1.71	3.02	1.6	2.8	6.4	11.3	301.3	532.3
	929	62.9	1.70	2.70	2.8	4.5	7.0	11.1	331.6	527.2
	930	58.3	1.65	2.83	3.0	5.1	5.5	9.4	289.6	496.7
80 mg/kg	937	59.5	1.50	2.52	2.2	3.7	6.8	11.4	332.6	559.0
	938	68.2	1.66	2.43	2.5	3.7	6.4	9.4	370.5	543.3
	939	64.8	1.66	2.56	2.8	4.3	8.0	12.3	349.3	539.0
	940	59.1	1.55	2.62	2.7	4.6	9.3	15.7	315.1	533.2
	941	54.9	1.65	3.01	2.8	5.1	7.1	12.9	292.6	533.0
	942	64.0	1.66	2.59	2.6	4.1	7.4	11.6	381.4	595.9

Appendix 23 - continued Individual organ weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Lungs		Thymus		Liver		Spleen		Kidneys	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)
Control	901	521.1	857.1	273.2	449.3	2.44	4.01	302.4	497.4	0.60	0.99
	902	598.1	847.2	275.4	390.1	3.00	4.25	391.2	554.1	0.89	1.26
	903	553.7	806.0	330.9	481.7	2.91	4.24	455.7	663.3	0.86	1.25
	904	480.0	798.7	298.3	496.3	2.66	4.43	291.2	484.5	0.72	1.20
	905	435.9	726.5	272.0	453.3	2.49	4.15	285.8	476.3	0.62	1.03
	906	565.0	938.5	286.0	475.1	2.66	4.42	325.2	540.2	0.74	1.23
5 mg/kg	913	464.3	767.4	258.0	426.4	2.65	4.38	392.3	648.4	0.69	1.14
	914	569.4	884.2	226.7	352.0	2.82	4.38	353.2	548.4	0.86	1.34
	915	570.4	843.8	370.7	548.4	2.95	4.36	448.7	663.8	0.77	1.14
	916	472.7	782.6	310.6	514.2	2.59	4.29	290.5	481.0	0.64	1.06
	917	465.8	757.4	257.8	419.2	2.79	4.54	334.5	543.9	0.70	1.14
	918	459.1	723.0	248.6	391.5	2.65	4.17	305.6	481.3	0.72	1.13
20 mg/kg	925	594.1	861.0	314.7	456.1	3.09	4.48	422.8	612.8	0.76	1.10
	926	530.5	745.1	291.0	408.7	3.04	4.27	389.3	546.8	0.81	1.14
	927	460.2	715.7	276.0	429.2	2.82	4.39	382.6	595.0	0.72	1.12
	928	464.7	821.0	250.8	443.1	2.52	4.45	301.8	533.2	0.75	1.33
	929	495.4	787.6	262.2	416.9	2.76	4.39	403.2	641.0	0.79	1.26
	930	475.1	814.9	241.9	414.9	2.52	4.32	385.6	661.4	0.76	1.30
80 mg/kg	937	517.2	869.2	230.4	387.2	2.70	4.54	372.8	626.6	0.61	1.03
	938	658.9	966.1	328.8	482.1	3.40	4.99	453.4	664.8	0.95	1.39
	939	558.4	861.7	274.8	424.1	3.22	4.97	416.8	643.2	0.71	1.10
	940	555.9	940.6	333.2	563.8	2.67	4.52	347.7	588.3	0.71	1.20
	941	477.6	869.9	323.9	590.0	2.51	4.57	290.8	529.7	0.65	1.18
	942	512.1	800.2	241.0	376.6	3.31	5.17	353.8	552.8	0.75	1.17

Appendix 23 - continued Individual organ weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Adrenals		Epididymides		Testes	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	901	17.1	28.1	61.4	101.0	316.4	520.4
	902	18.8	26.6	58.9	83.4	387.0	548.2
	903	20.4	29.7	62.7	91.3	350.5	510.2
	904	17.3	28.8	50.0	83.2	281.6	468.6
	905	16.6	27.7	57.0	95.0	264.2	440.3
	906	17.9	29.7	55.6	92.4	355.5	590.5
5 mg/kg	913	17.0	28.1	53.3	88.1	267.7	442.5
	914	16.2	25.2	62.5	97.0	319.7	496.4
	915	18.2	26.9	62.6	92.6	330.4	488.8
	916	18.2	30.1	49.9	82.6	278.5	461.1
	917	16.9	27.5	55.5	90.2	289.1	470.1
	918	16.2	25.5	48.8	76.9	327.1	515.1
20 mg/kg	925	17.9	25.9	61.0	88.4	338.0	489.9
	926	19.8	27.8	52.6	73.9	305.9	429.6
	927	19.3	30.0	50.6	78.7	323.3	502.8
	928	15.1	26.7	53.4	94.3	284.9	503.4
	929	16.7	26.6	57.8	91.9	344.1	547.1
	930	15.5	26.6	70.3	120.6	320.4	549.6
80 mg/kg	937	18.6	31.3	51.9	87.2	272.9	458.7
	938	18.5	27.1	45.0	66.0	298.5	437.7
	939	18.6	28.7	53.7	82.9	325.3	502.0
	940	16.2	27.4	50.5	85.4	284.9	482.1
	941	14.9	27.1	46.8	85.2	279.6	509.3
	942	15.9	24.8	54.0	84.4	306.8	479.4

Appendix 24 Individual organ weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Final body weight	Brain		Pituitary		Thyroids		Heart	
		(g)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	951	56.2	1.55	2.76	3.4	6.0	7.9	14.1	329.9	587.0
	952	62.7	1.64	2.62	3.1	4.9	6.2	9.9	386.6	616.6
	953	62.4	1.52	2.44	3.0	4.8	6.1	9.8	307.1	492.1
	954	55.5	1.59	2.86	3.4	6.1	6.2	11.2	305.1	549.7
	955	60.7	1.63	2.69	2.9	4.8	7.4	12.2	361.0	594.7
	956	56.3	1.50	2.66	2.3	4.1	6.9	12.3	307.9	546.9
5 mg/kg	963	57.7	1.51	2.62	2.7	4.7	8.0	13.9	295.2	511.6
	964	63.0	1.56	2.48	3.1	4.9	6.8	10.8	347.4	551.4
	965	60.7	1.63	2.69	3.0	4.9	6.9	11.4	313.3	516.1
	966	56.5	1.56	2.76	2.6	4.6	5.2	9.2	301.3	533.3
	967	59.5	1.63	2.74	2.4	4.0	8.2	13.8	315.6	530.4
	968	60.1	1.54	2.56	2.2	3.7	7.4	12.3	317.3	528.0
20 mg/kg	975	52.2	1.55	2.97	3.3	6.3	5.4	10.3	310.5	594.8
	976	62.6	1.56	2.49	3.3	5.3	8.2	13.1	398.9	637.2
	977	59.9	1.57	2.62	3.0	5.0	7.2	12.0	313.0	522.5
	978	51.8	1.56	3.01	1.9	3.7	6.2	12.0	256.7	495.6
	979	54.9	1.55	2.82	2.3	4.2	7.7	14.0	265.8	484.2
	980	60.3	1.58	2.62	2.6	4.3	5.5	9.1	303.9	504.0
80 mg/kg	987	58.3	1.53	2.62	2.4	4.1	4.9	8.4	364.9	625.9
	988	66.2	1.57	2.37	2.8	4.2	8.1	12.2	384.1	580.2
	989	62.5	1.53	2.45	2.6	4.2	8.9	14.2	409.1	654.6
	990	50.8	1.47	2.89	3.6	7.1	7.6	15.0	304.8	600.0
	991	55.9	1.50	2.68	2.6	4.7	9.8	17.5	331.8	593.6
	992	59.3	1.56	2.63	2.7	4.6	8.8	14.8	330.5	557.3

Appendix 24 - continued Individual organ weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Lungs		Thymus		Liver		Spleen		Kidneys	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)
Control	951	409.6	728.8	250.1	445.0	2.05	3.65	304.5	541.8	0.71	1.26
	952	522.0	832.5	271.3	432.7	2.51	4.00	356.4	568.4	0.76	1.21
	953	473.8	759.3	275.1	440.9	2.59	4.15	323.3	518.1	0.69	1.11
	954	448.2	807.6	257.7	464.3	2.41	4.34	289.1	520.9	0.71	1.28
	955	465.0	766.1	293.8	484.0	2.58	4.25	374.6	617.1	0.67	1.10
	956	399.4	709.4	253.8	450.8	2.64	4.69	268.3	476.6	0.61	1.08
5 mg/kg	963	416.2	721.3	265.4	460.0	2.18	3.78	286.1	495.8	0.68	1.18
	964	483.4	767.3	273.6	434.3	2.57	4.08	298.6	474.0	0.72	1.14
	965	511.4	842.5	217.7	358.6	2.58	4.25	297.8	490.6	0.78	1.29
	966	457.2	809.2	265.7	470.3	2.10	3.72	351.0	621.2	0.60	1.06
	967	498.3	837.5	272.5	458.0	2.60	4.37	371.4	624.2	0.67	1.13
	968	433.7	721.6	245.3	408.2	2.62	4.36	369.7	615.1	0.68	1.13
20 mg/kg	975	391.0	749.0	237.4	454.8	2.18	4.18	271.1	519.3	0.69	1.32
	976	541.1	864.4	310.2	495.5	2.64	4.22	385.1	615.2	0.67	1.07
	977	450.9	752.8	313.0	522.5	2.60	4.34	233.2	389.3	0.74	1.24
	978	400.2	772.6	238.3	460.0	2.07	4.00	288.3	556.6	0.55	1.06
	979	433.0	788.7	298.5	543.7	2.10	3.83	253.3	461.4	0.63	1.15
	980	445.0	738.0	291.1	482.8	2.38	3.95	318.2	527.7	0.66	1.09
80 mg/kg	987	500.4	858.3	296.3	508.2	2.92	5.01	338.5	580.6	0.68	1.17
	988	553.2	835.6	285.4	431.1	3.07	4.64	450.5	680.5	0.73	1.10
	989	455.1	728.2	271.3	434.1	2.94	4.70	382.2	611.5	0.78	1.25
	990	408.1	803.3	207.0	407.5	2.36	4.65	314.9	619.9	0.65	1.28
	991	452.2	808.9	307.2	549.6	2.50	4.47	353.1	631.7	0.67	1.20
	992	465.2	784.5	245.5	414.0	2.68	4.52	365.8	616.9	0.71	1.20

Appendix 24 - continued Individual organ weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Group and dose	Animal No.	Adrenals		Ovaries	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	951	15.4	27.4	19.1	34.0
	952	18.2	29.0	21.8	34.8
	953	18.5	29.6	22.9	36.7
	954	15.9	28.6	17.6	31.7
	955	14.6	24.1	18.8	31.0
	956	15.6	27.7	17.8	31.6
5 mg/kg	963	16.6	28.8	16.5	28.6
	964	20.3	32.2	15.6	24.8
	965	16.1	26.5	15.1	24.9
	966	14.5	25.7	17.3	30.6
	967	15.5	26.1	23.1	38.8
	968	16.4	27.3	16.0	26.6
20 mg/kg	975	15.3	29.3	12.7	24.3
	976	19.2	30.7	19.5	31.2
	977	19.6	32.7	13.9	23.2
	978	13.7	26.4	12.8	24.7
	979	15.2	27.7	16.2	29.5
	980	15.6	25.9	18.2	30.2
80 mg/kg	987	16.0	27.4	21.3	36.5
	988	20.0	30.2	17.7	26.7
	989	14.2	22.7	21.2	33.9
	990	14.1	27.8	18.1	35.6
	991	15.6	27.9	17.5	31.3
	992	16.8	28.3	18.2	30.7

Appendix 25 Individual organ weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Final body weight	Brain		Pituitary		Thyroids		Heart	
		(g)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	907	526.8	2.49	0.47	16.4	3.1	21.8	4.1	1853.7	351.9
	908	422.5	2.04	0.48	13.3	3.1	15.3	3.6	1427.6	337.9
	909	487.1	2.46	0.51	14.1	2.9	25.8	5.3	1481.1	304.1
	910	428.8	2.11	0.49	12.3	2.9	22.9	5.3	1639.2	382.3
	911	484.9	2.23	0.46	15.5	3.2	21.5	4.4	1670.4	344.5
	912	526.3	2.31	0.44	15.4	2.9	25.1	4.8	1558.5	296.1
5 mg/kg	919	426.9	2.17	0.51	12.5	2.9	18.7	4.4	1491.1	349.3
	920	471.3	2.23	0.47	15.9	3.4	23.2	4.9	1722.6	365.5
	921	410.5	2.12	0.52	12.0	2.9	25.2	6.1	1432.8	349.0
	922	452.5	2.22	0.49	12.4	2.7	16.1	3.6	1743.9	385.4
	923	508.3	2.26	0.44	13.0	2.6	26.6	5.2	1592.7	313.3
	924	520.6	2.41	0.46	17.4	3.3	23.6	4.5	1805.5	346.8
20 mg/kg	931	470.1	2.37	0.50	15.9	3.4	18.4	3.9	1481.0	315.0
	932	428.3	2.27	0.53	12.5	2.9	18.5	4.3	1492.5	348.5
	933	431.7	1.98	0.46	11.2	2.6	18.9	4.4	1459.6	338.1
	934	459.5	2.29	0.50	13.3	2.9	16.6	3.6	1559.9	339.5
	935	469.8	2.29	0.49	17.1	3.6	29.9	6.4	1613.8	343.5
	936	505.3	2.16	0.43	15.0	3.0	21.1	4.2	1569.9	310.7
80 mg/kg	943	441.2	2.17	0.49	12.4	2.8	17.4	3.9	1484.6	336.5
	944	481.9	2.24	0.46	13.2	2.7	24.1	5.0	1663.1	345.1
	945	432.3	2.18	0.50	12.5	2.9	22.9	5.3	1526.6	353.1
	946	435.5	2.27	0.52	13.3	3.1	20.2	4.6	1444.1	331.6
	947	527.0	2.24	0.43	12.6	2.4	25.5	4.8	1655.1	314.1
	948	442.9	2.18	0.49	12.1	2.7	21.8	4.9	1476.2	333.3

Appendix 25 - continued

Individual organ weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Lungs		Thymus		Liver		Spleen		Kidneys	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)
Control	907	1838.3	349.0	440.2	83.6	16.99	3.23	1005.4	190.9	3.82	0.73
	908	1446.0	342.2	473.5	112.1	13.05	3.09	744.0	176.1	3.12	0.74
	909	1555.8	319.4	495.2	101.7	15.46	3.17	900.3	184.8	3.43	0.70
	910	1308.6	305.2	518.3	120.9	12.73	2.97	972.8	226.9	2.74	0.64
	911	1573.5	324.5	701.8	144.7	14.96	3.09	868.9	179.2	3.66	0.75
	912	1758.6	334.1	417.5	79.3	15.05	2.86	837.8	159.2	3.66	0.70
5 mg/kg	919	1373.6	321.8	461.3	108.1	11.46	2.68	748.9	175.4	2.84	0.67
	920	1531.9	325.0	418.1	88.7	13.12	2.78	927.5	196.8	2.85	0.60
	921	1402.4	341.6	540.5	131.7	11.94	2.91	792.8	193.1	2.83	0.69
	922	1548.8	342.3	433.8	95.9	15.11	3.34	777.7	171.9	3.17	0.70
	923	1525.6	300.1	655.6	129.0	12.64	2.49	903.9	177.8	2.76	0.54
	924	1642.3	315.5	742.2	142.6	15.46	2.97	1092.3	209.8	3.48	0.67
20 mg/kg	931	1416.8	301.4	651.9	138.7	15.94	3.39	864.7	183.9	3.66	0.78
	932	1487.0	347.2	438.1	102.3	14.17	3.31	839.2	195.9	2.86	0.67
	933	1222.4	283.2	637.5	147.7	11.50	2.66	684.4	158.5	2.86	0.66
	934	1413.5	307.6	474.1	103.2	15.93	3.47	885.6	192.7	3.03	0.66
	935	1545.0	328.9	807.7	171.9	13.68	2.91	901.4	191.9	3.60	0.77
	936	1642.2	325.0	433.6	85.8	15.35	3.04	822.5	162.8	3.09	0.61
80 mg/kg	943	1476.2	334.6	444.4	100.7	13.49	3.06	743.4	168.5	2.91	0.66
	944	1535.6	318.7	490.6	101.8	15.10	3.13	978.8	203.1	3.02	0.63
	945	1373.6	317.7	607.8	140.6	11.70	2.71	834.9	193.1	2.81	0.65
	946	1469.5	337.4	623.2	143.1	14.92	3.43	928.5	213.2	3.06	0.70
	947	1690.5	320.8	707.9	134.3	17.62	3.34	1356.3	257.4	3.23	0.61
	948	1354.4	305.8	427.2	96.5	12.40	2.80	704.6	159.1	2.86	0.65

Appendix 25 - continued

Individual organ weights in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Adrenals		Epididymides		Testes	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	907	77.0	14.6	1469.3	278.9	3873.5	735.3
	908	50.3	11.9	1297.9	307.2	3797.8	898.9
	909	67.7	13.9	1166.8	239.5	3713.2	762.3
	910	52.1	12.2	1103.3	257.3	3693.7	861.4
	911	64.3	13.3	1325.7	273.4	3531.9	728.4
	912	59.1	11.2	1135.6	215.8	5104.0	969.8
5 mg/kg	919	57.8	13.5	1171.5	274.4	3453.0	808.9
	920	73.9	15.7	1256.5	266.6	3449.1	731.8
	921	63.5	15.5	1267.2	308.7	3696.8	900.6
	922	59.5	13.1	1179.5	260.7	3303.2	730.0
	923	83.5	16.4	995.6	195.9	3248.5	639.1
	924	89.1	17.1	1404.9	269.9	3938.6	756.6
20 mg/kg	931	59.4	12.6	1300.6	276.7	3632.0	772.6
	932	67.3	15.7	662.8	154.8	1499.2	350.0
	933	58.4	13.5	1076.5	249.4	3627.8	840.4
	934	67.0	14.6	539.1	117.3	1086.3	236.4
	935	65.6	14.0	1368.6	291.3	3732.2	794.4
	936	83.7	16.6	1260.2	249.4	3656.4	723.6
80 mg/kg	943	52.6	11.9	1116.1	253.0	3301.3	748.3
	944	80.1	16.6	1158.6	240.4	3599.5	746.9
	945	59.3	13.7	1203.8	278.5	3308.8	765.4
	946	49.4	11.3	1100.3	252.7	3084.9	708.4
	947	63.3	12.0	1250.3	237.2	3846.2	729.8
	948	56.4	12.7	971.9	219.4	2976.5	672.0

Appendix 26 Individual organ weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Final body weight	Brain		Pituitary		Thyroids		Heart	
		(g)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	957	295.7	2.16	0.73	15.3	5.2	24.2	8.2	1072.1	362.6
	958	277.6	2.00	0.72	13.3	4.8	17.9	6.4	930.4	335.2
	959	290.4	2.01	0.69	15.6	5.4	13.3	4.6	1015.0	349.5
	960	278.2	2.03	0.73	16.2	5.8	18.8	6.8	901.2	323.9
	961	238.1	1.93	0.81	13.9	5.8	15.1	6.3	858.6	360.6
	962	290.7	1.98	0.68	15.2	5.2	20.6	7.1	1020.9	351.2
5 mg/kg	969	264.6	2.11	0.80	14.9	5.6	15.0	5.7	942.9	356.3
	970	273.6	2.15	0.79	17.5	6.4	21.6	7.9	1104.1	403.5
	971	270.8	2.00	0.74	17.4	6.4	17.0	6.3	911.2	336.5
	972	269.4	2.06	0.76	14.9	5.5	15.3	5.7	937.9	348.1
	973	322.4	2.04	0.63	16.8	5.2	17.5	5.4	1066.3	330.7
	974	298.2	2.19	0.73	17.4	5.8	17.6	5.9	1078.7	361.7
20 mg/kg	981	238.6	1.94	0.81	14.0	5.9	14.0	5.9	922.3	386.5
	982	246.3	1.92	0.78	15.0	6.1	16.1	6.5	1003.5	407.4
	983	267.7	2.07	0.77	14.8	5.5	15.5	5.8	939.7	351.0
	984	235.1	2.03	0.86	17.1	7.3	13.8	5.9	865.2	368.0
	985	257.2	2.07	0.80	15.0	5.8	12.2	4.7	1001.2	389.3
	986	252.7	2.05	0.81	15.2	6.0	17.8	7.0	1104.1	436.9
80 mg/kg	993	247.1	1.98	0.80	11.9	4.8	15.5	6.3	863.7	349.5
	994	260.6	1.90	0.73	13.2	5.1	17.4	6.7	1050.4	403.1
	995	284.7	1.87	0.66	15.3	5.4	22.0	7.7	920.5	323.3
	996	257.7	1.93	0.75	16.8	6.5	17.1	6.6	1051.3	408.0
	997	241.5	1.91	0.79	13.0	5.4	11.9	4.9	924.7	382.9
	998	249.8	1.97	0.79	13.9	5.6	17.2	6.9	981.1	392.8

Appendix 26 - continued

Individual organ weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Lungs		Thymus		Liver		Spleen		Kidneys	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)	(mg)	(mg/100gB.W.)	(g)	(g/100gB.W.)
Control	957	1261.8	426.7	573.2	193.8	7.80	2.64	770.0	260.4	1.95	0.66
	958	1132.6	408.0	528.6	190.4	7.37	2.65	507.9	183.0	1.79	0.64
	959	1207.2	415.7	509.1	175.3	7.45	2.57	573.6	197.5	2.07	0.71
	960	1096.9	394.3	474.9	170.7	7.72	2.77	672.8	241.8	1.94	0.70
	961	916.4	384.9	371.1	155.9	6.45	2.71	473.3	198.8	1.70	0.71
	962	1148.9	395.2	549.0	188.9	7.93	2.73	548.6	188.7	1.85	0.64
5 mg/kg	969	1039.4	392.8	554.4	209.5	7.12	2.69	551.7	208.5	2.08	0.79
	970	1231.7	450.2	515.2	188.3	7.63	2.79	691.2	252.6	1.97	0.72
	971	1025.5	378.7	531.9	196.4	7.23	2.67	512.2	189.1	1.71	0.63
	972	1093.4	405.9	395.9	147.0	6.96	2.58	503.4	186.9	1.86	0.69
	973	1374.0	426.2	552.6	171.4	9.79	3.04	781.8	242.5	2.16	0.67
	974	1261.8	423.1	676.5	226.9	7.75	2.60	673.1	225.7	1.92	0.64
20 mg/kg	981	1032.8	432.9	364.2	152.6	6.47	2.71	549.9	230.5	1.74	0.73
	982	1045.2	424.4	427.7	173.7	7.74	3.14	497.3	201.9	1.83	0.74
	983	1058.8	395.5	587.6	219.5	6.74	2.52	593.9	221.9	1.67	0.62
	984	1069.7	455.0	401.0	170.6	6.96	2.96	533.9	227.1	1.72	0.73
	985	1017.2	395.5	326.5	126.9	6.72	2.61	561.7	218.4	1.82	0.71
	986	1020.3	403.8	474.2	187.7	6.71	2.66	504.6	199.7	1.62	0.64
80 mg/kg	993	945.6	382.7	302.7	122.5	6.28	2.54	399.1	161.5	1.67	0.68
	994	976.4	374.7	574.1	220.3	6.85	2.63	563.1	216.1	1.64	0.63
	995	1127.1	395.9	363.5	127.7	8.08	2.84	493.3	173.3	1.86	0.65
	996	955.4	370.7	556.4	215.9	6.97	2.70	592.1	229.8	1.82	0.71
	997	983.9	407.4	474.7	196.6	6.67	2.76	550.6	228.0	1.72	0.71
	998	962.8	385.4	479.1	191.8	7.11	2.85	643.4	257.6	1.87	0.75

Appendix 26 - continued

Individual organ weights in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Group and dose	Animal No.	Adrenals		Ovaries	
		(mg)	(mg/100gB.W.)	(mg)	(mg/100gB.W.)
Control	957	91.0	30.8	107.2	36.3
	958	68.5	24.7	72.2	26.0
	959	86.8	29.9	86.9	29.9
	960	61.1	22.0	90.7	32.6
	961	65.4	27.5	74.5	31.3
	962	72.0	24.8	95.8	33.0
5 mg/kg	969	76.6	28.9	69.7	26.3
	970	85.7	31.3	94.1	34.4
	971	73.3	27.1	71.8	26.5
	972	60.6	22.5	93.7	34.8
	973	84.6	26.2	86.5	26.8
	974	83.1	27.9	89.8	30.1
20 mg/kg	981	64.4	27.0	71.8	30.1
	982	75.8	30.8	63.0	25.6
	983	68.0	25.4	60.9	22.7
	984	89.0	37.9	80.9	34.4
	985	68.1	26.5	102.0	39.7
	986	74.1	29.3	71.9	28.5
80 mg/kg	993	60.7	24.6	61.3	24.8
	994	60.2	23.1	59.8	22.9
	995	68.8	24.2	89.3	31.4
	996	66.7	25.9	73.3	28.4
	997	67.4	27.9	74.1	30.7
	998	74.4	29.8	72.7	29.1

Appendix 27 Individual histopathological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings \ Group and dose	Control						5 mg/kg					
Animal No.	901	902	903	904	905	906	913	914	915	916	917	918
Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system												
Kidney							*	*	*	*	*	*
Dilatation, tubule, focal	-	-	+	-	-	-						

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, testis, epididymis, pituitary, thyroid, adrenal and brain in all animals of control group.

Appendix 27 - continued Individual histopathological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days

Study No.49816

Organs and findings	Group and dose	20 mg/kg						80 mg/kg					
	Animal No.	925	926	927	928	929	930	937	938	939	940	941	942
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system													
Kidney		*	*	*	*	*	*						
Dilatation, tubule, focal								-	+	-	-	-	+

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, testis, epididymis, pituitary, thyroid, adrenal, brain and integument in all animals of 80 mg/kg group.

Appendix 28 Individual histopathological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Organs and findings \ Group and dose	Control						5 mg/kg					
Animal No.	951	952	953	954	955	956	963	964	965	966	967	968
Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system												
Kidney							*	*	*	*	*	*
Dilatation, tubule, focal	-	-	-	+	-	+						

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, ovary, pituitary, thyroid, adrenal and brain in all animals of control group.

Appendix 28 - continued Individual histopathological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days

Study No.49816

Organs and findings	Group and dose	20 mg/kg						80 mg/kg					
	Animal No.	975	976	977	978	979	980	987	988	989	990	991	992
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system													
Kidney		*	*	*	*	*	*						
Dilatation, tubule, focal								-	-	+	-	-	-

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, ovary, pituitary, thyroid, adrenal, brain and integument in all animals of 80 mg/kg group.

Appendix 29 Individual histopathological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings \ Group and dose	Control						5 mg/kg					
Animal No.	907	908	909	910	911	912	919	920	921	922	923	924
Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Genital system												
Testis							*	*	*	*	*	*
Atrophy, seminiferous tubule	-	-	-	-	-	-						
Dilatation, seminiferous tubule	-	-	-	-	-	+						
Epididymis							*	*	*	*	*	*
Decrease, sperm, lumen	-	-	-	-	-	-						
Debris, germ cell, lumen	-	-	-	-	-	-						
Granuloma, spermatic	-	-	-	-	-	-						
Nervous system												
Cerebrum							*	*	*	*	*	*
Dilatation, ventricle	-	-	-	-	+	-						

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, kidney, pituitary, thyroid, adrenal and cerebellum in all animals of control group.

Appendix 29 - continued

Individual histopathological findings in juvenile male rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings \ Group and dose	20 mg/kg						80 mg/kg					
Animal No.	931	932	933	934	935	936	943	944	945	946	947	948
Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Genital system												
Testis	*		*		*	*						
Atrophy, seminiferous tubule		+++		+++			-	-	-	-	-	-
Dilatation, seminiferous tubule		-		-			-	-	-	-	-	-
Epididymis	*	*	*		*	*						
Decrease, sperm, lumen				+++			-	-	-	-	-	-
Debris, germ cell, lumen				+			-	-	-	-	-	-
Granuloma, spermatic				-			-	+	-	-	-	-
Nervous system												
Cerebrum	*	*	*	*	*	*						
Dilatation, ventricle							-	-	-	-	-	-

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, kidney, pituitary, thyroid, adrenal, cerebellum and integument in all animals of 80 mg/kg group.

Appendix 30 Individual histopathological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings \ Group and dose	Control						5 mg/kg					
Animal No.	957	958	959	960	961	962	969	970	971	972	973	974
Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system												
Kidney								*	*	*	*	*
Dilatation, pelvic cavity	-	-	-	-	-	-	+					
Mineralization	+	+	+	-	-	-	-					

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, ovary, pituitary, thyroid, adrenal and brain in all animals of control group.

Study No. 49816

Appendix 30 - continued

Individual histopathological findings in juvenile female rats treated orally with 2,4,6-Trinitrophenol for 18 days followed by 63-day withdrawal period

Organs and findings	Group and dose	20 mg/kg						80 mg/kg					
	Animal No.	981	982	983	984	985	986	993	994	995	996	997	998
	Necropsy timing	S	S	S	S	S	S	S	S	S	S	S	S
Urinary system													
Kidney		*	*	*	*	*	*						
Dilatation, pelvic cavity								-	-	-	-	-	-
Mineralization								-	-	-	-	-	-

Abbreviation: S, scheduled.
Grade sign: -, none; +, mild; ++, moderate; +++, marked.
*, not examined.
There are no remarkable changes in the liver, lung, thymus, spleen, heart, ovary, pituitary, thyroid, adrenal, brain and integument in all animals of 80 mg/kg group.