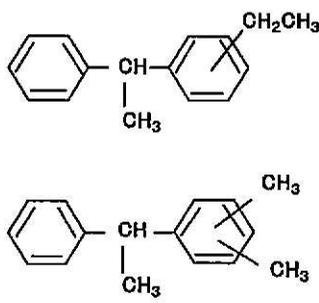


ほ乳類を用いる28日間の反復投与毒性試験結果報告書

1. 一般的事項

新規化学物質の名称 (IUPAC命名法による)	1-フェニル-1-キシリルエタン				
別名	ステリルキシレン	物理化学的性状	分子量	210	
構造式又は示性式			常温における性状	無色透明液体	
			安定性		
融点	-47.5°C				
沸点	蒸留範囲 初留点 : 291.5°C 95% : 297.0°C 終点 : 303.5°C				
試験に供した新規化学物質の純度	91.5wt%		蒸気圧	0.1Pa以下	
不純物の名称及び濃度	① 1,1-Diphenylethane : 0.2mass% ② Indan, 1-methyl-3-phenyl : 5.6mass% ③ その他一成分1mass%未満の構造不明炭化水素類合計 : 2.7mass%		分配係数	-	
			溶解性		
試験に供した新規化学物質のロット番号	██████████		溶解度	水	不溶
CAS番号	40766-31-2			DMSO	溶解
		アセトン	溶解		
		その他 (炭化水素系溶剤等)	溶解		

## 2. 急性毒性試験

試験 No.	試験の種類及び期間	動物種	投与経路	投与量および各群の動物数	結果の要約
1	投与量決定試験(14日間)	ラット	強制経口	1000mg/kg/day: 雌雄各5匹  500mg/kg/day: 雌雄各4匹  250mg/kg/day: 雌雄各4匹  100mg/kg/day: 雌雄各4匹  0mg/kg/day: 雌雄各3匹	死亡: 投与5日までに雌雄全例死亡 一般状態: 流涎, よろめき歩行, 運動性低下, 排糞減少 体重: 減少あるいは増加抑制 摂餌量: 減少  死亡: 投与4日に雌1例死亡 一般状態: 流涎, よろめき歩行, 運動性低下, 排糞減少 体重: 減少あるいは増加抑制 摂餌量: 減少 器官重量: 肝臓の増加傾向  一般状態: 流涎, よろめき歩行 体重: 減少あるいは増加抑制 摂餌量: 減少 器官重量: 肝臓の増加傾向  異常なし(NOEL#)  異常なし
実験場所	株式会社 イナリサーチ				

#: No-observed-adverse-effect level (NOEL)

3. 28日間反復投与毒性試験

被験物質投与期間		自 平成 12 年 12 月 21 日 至 平成 13 年 1 月 17 日											
使用動物種・系統		ラット, Crj:CD(SD)IGS系				1群当たり動物数〔( )内は回復群用の動物数〕							
投与経路		強制経口投与				対照群, 高用量群				低用量群, 中用量群			
被験物質の純度 91.5(%)	投与量 mg/kg	対照群		低用量群		中用量群		高用量群		回復群			
		0		30		100		300		0		300	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
一般状態													
	流涎	-	-	-	-	2	-	11	11	-	-	-	-
	よろめき歩行	-	-	-	-	-	-	7	4	-	-	-	-
	脱毛	-	-	-	-	-	-	1	7	-	-	1	5
	排糞量の減少	-	-	-	-	-	-	-	6	-	-	-	-
	軟便	-	-	-	-	-	-	1	-	-	-	-	-
	運動性の低下	-	-	-	-	-	-	-	1	-	-	-	-
	腹臥位	-	-	-	-	-	-	-	1	-	-	-	-
詳細な症状観察													
	流涎			-	-	-	-	↑↑	↑↑			-	-
	排尿回数			↑	-	-	-	-	-			-	-
機能検査				-	-	-	-	-	-			-	-
自発運動量				-	-	-	-	-	-			-	↑↑
体重				-	-	-	-	↓	↓↓			-	↓
摂餌量				-	-	-	-	↓↓	↓↓			-	↑
尿検査													
	飲水量			-	-	-	-	-	↑↑			-	-
	尿量			-	-	-	-	-	↑			-	-
	尿比重			-	-	-	-	-	↓			-	-
	強度の潜血反応	-	-	-	1	-	-	-	-	-	-	-	-
血液学的検査													
	APTT			-	-	↑↑	-	↑↑	-			-	-
	PT			-	-	-	-	↑↑	-			-	-
	リンパ球比			-	-	-	↑	-	↑			-	-
	好中球分節核球比			-	-	-	-	-	↓			-	-
	ヘモグロビン量			-	-	-	-	-	-			↓	-
	血小板数			-	-	-	-	-	-			-	↑
血液生化学的検査													
	GPT活性			-	-	-	-	↑	-			-	-
	中性脂肪			-	-	-	-	-	↑↑			-	-
	グルコース			-	-	-	-	-	↓			-	-
	総コレステロール			-	-	-	-	↑↑	↑↑			-	-
	総ビリルビン			-	-	↓	-	-	-			↓↓	-
	GOT活性			-	-	-	-	-	-			↓	-

- ↑: 対照群に比べ有意に増加 (p < 0.05)
- ↑↑: 対照群に比べ有意に増加 (p < 0.01)
- ↓: 対照群に比べ有意に減少 (p < 0.05)
- ↓↓: 対照群に比べ有意に減少 (p < 0.01)
- : 変化なし

投与量	mg/kg	対照群		低用量群		中用量群		高用量群		回復群			
		0		30		100		300		0		300	
		♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
剖検所見													
脾臓 膨隆, 境界不明 瞭および剖面か ら濾胞増生		-	-	1	-	-	-	-	-	-	-	-	-
臓器重量変化 実重量													
肝臓				-	↑	↑↑	↑↑	↑↑	↑↑			-	-
胸腺				-	-	-	-	-	-			-	↑
肺				-	-	-	-	-	↓			-	-
心臓				-	-	-	-	↓	-			-	-
副腎				-	-	-	-	↓	-			-	-
精巣				-	*	-	*	-	*			↓↓	*
精巣上体				-	*	-	*	-	*			↓↓	*
体重比重量													
肝臓				-	-	↑↑	↑	↑↑	↑↑			-	↑
腎臓				-	-	-	-	↑	↑↑			↑	-
胸腺				-	-	-	-	-	-			-	↑↑
脾臓				-	-	-	-	-	-			-	↑
組織学的所見													
肝臓													
小葉中心性肝細胞の肥大													
(軽度)		-	-	6	6	5	6	1	3	-	-	-	1
(中等度)		-	-	-	-	1	-	6	3	-	-	-	-
腎臓													
好塩基性尿細管													
(軽度)		-	-	-	-	1	-	4	2	-	-	5	-
(中等度)		-	-	-	-	-	-	1	-	-	-	1	-
蛋白円柱(軽度)		-	-	-	-	-	-	3	-	-	-	1	-
近位尿細管上皮の空胞化(軽度)		-	-	-	3	1	2	2	6	-	-	-	-
甲状腺													
濾胞上皮の過形成/肥大													
(軽度)		-	-	3	3	4	2	1	4	-	-	4	2
(中等度)		-	-	1	-	-	1	5	2	-	-	-	-

↑: 対照群に比べ有意に増加(p < 0.05)

↑↑: 対照群に比べ有意に増加(p < 0.01)

↓: 対照群に比べ有意に減少(p < 0.05)

↓↓: 対照群に比べ有意に減少(p < 0.01)

-: 変化なし

\*: 検査せず

NOAEL <sup>#</sup> (mg/kg)	30mg/kg
NOAEL <sup>#</sup> の推定根拠とした変化	100mg/kgにおいて認められた症状観察における流涎, 血液学的検査におけるAPTTの延長, 病理組織学的検査における腎臓の好塩基性尿細管所見 [参考事項] 肝臓および甲状腺における変化は、薬物代謝酵素の誘導に起因した変化と判断され、毒性変化とはしなかった。また、腎臓における近位尿細管上皮の空胞化については、何らかの物質が尿細管に貯留されているものと推察されるが、いずれも軽度な変化であり、他の検査項目に腎機能への影響を示唆する変動はないことから、毒性変化とはしなかった。

#: No-observed-adverse-effect level (NOAEL)

4. その他

反復投与毒性試験実施機関	名 称	株式会社 イナリサーチ	
	所 在 地	長野県伊那市西箕輪8047番地(〒399-4501)	TEL:0265-72-6616 FAX:0265-72-6657
試験責任者	職 氏 名	[REDACTED]	
	経 験 年 数	[REDACTED]	
	連 絡 先	長野県伊那市西箕輪2148番地(〒399-4501) 株式会社 イナリサーチ 第2研究所	TEL:0265-73-8611 FAX:0265-73-8612
試験番号	2000TT278		
試験実施年月日	平成12年12月4日から平成13年3月14日まで		

1-フェニル-1-キシリルエタンのラットにおける 28 日間反復経口投与毒性試験

最終報告書  
(報告日: 2001 年 3 月 14 日)



1 表題および試験番号

表題 : 1-フェニル-1-キシリルエタンのラットにおける 28 日間反復経口投与  
毒性試験

試験番号: 2000TT278

2 試験目的

1-フェニル-1-キシリルエタンをラットに 28 日間連日経口投与して, その反復投与  
毒性ならびにその後 14 日間の休薬による回復性を調べた。

3 試験委託者

所在地: 東京都渋谷区西原 2-49-10

名称: 経済産業省(旧 通商産業省) 製品評価技術センター  
化学物質安全管理センター

4 試験施設

所在地: 長野県伊那市西箕輪 8047 番地

名称: 株式会社 イナ リサーチ

5 試験実施場所

第 2 研究所(長野県伊那市西箕輪 2148 番地)

動物飼育, 被験物質調製, 投与液の分析, 投与, 臨床観察, 体重および摂餌量測  
定, 血液検査, 剖検, 器官重量測定等の実験操作ならびにデータ解析

本社研究所(長野県伊那市西箕輪 8047 番地)

病理組織標本作製, 資料および標本の保存

高崎分室(群馬県群馬郡群馬町福島 97)

病理組織学的検査

6 試験期間

試験開始日 : 2000年12月4日  
動物入手日 : 2000年12月5日  
実験(投与)開始日 : 2000年12月21日  
投与期間終了時の剖検日: 2001年1月18日  
休菜期間終了時の剖検日: 2001年2月1日  
実験(組織検査)終了日 : 2001年3月1日  
試験終了日 : 2001年3月14日

7 試験責任者

所属: 株式会社 イナ リサーチ  
[Redacted]

8 試験従事者

業務分担	担当者
[Redacted]	[Redacted]
[Redacted]	[Redacted]
[Redacted]	[Redacted]

a) 担当責任者

9 試験計画書, 被験物質のサンプル, 生データ, 標本および最終報告書の保存

保存機関: 株式会社 イナ リサーチ  
保存番号: 2000278  
保存期間: 最終報告書提出後 10 年間

目次

	ページ
I 要約.....	1
II 緒言.....	1
III 材料および方法.....	2
1 被験物質.....	2
2 使用動物および飼育条件.....	2
2.1 使用動物.....	2
2.2 飼育条件.....	2
3 投与.....	2
3.1 投与量.....	2
3.2 使用動物数および群分け.....	2
3.3 被験物質の調製.....	3
3.4 投与条件下における被験物質の安定性.....	3
3.5 投与液の分析(濃度確認).....	3
3.6 投与経路, 投与方法および投与期間.....	3
4 観察, 測定および検査.....	3
4.1 症状観察および機能検査.....	4
4.1.1 一般状態.....	4
4.1.2 詳細な症状観察.....	4
4.1.3 機能検査.....	4
4.1.4 自発運動量.....	4
4.2 体重.....	4
4.3 摂餌量.....	4
4.4 尿検査.....	4
4.5 血液学的検査.....	5
4.6 血液生化学的検査.....	5
4.7 剖検.....	6
4.8 器官重量.....	6
4.9 病理組織学的検査(光学顕微鏡による検査).....	6
5 統計学的解析方法.....	7
IV 成績.....	10
1 症状観察および機能検査.....	10
1.1 一般状態.....	10
1.2 詳細な症状観察.....	10
1.3 機能検査.....	10
1.4 自発運動量.....	10
2 体重.....	10

3	摂餌量.....	11
4	尿検査.....	11
5	血液学的検査.....	11
6	血液生化学的検査.....	11
7	剖検.....	11
8	器官重量.....	11
9	病理組織学的検査.....	12
V	考察.....	13
	文献.....	14
	その他の事項.....	14
1	飼育環境.....	14
2	予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態 および試験計画書に従わなかったこと.....	14

添付資料

- 付表 : Supplement 1~4
- 図 : Figure 1~4
- 総括表 : Table 1~24
- 個別表 : Appendix 1~24

## I 要約

1-フェニル-1-キシリルエタンの 30, 100 および 300 mg/kg/day をラットに 28 日間反復経口投与し、その反復投与毒性ならびにその後 14 日間の休薬による回復性を調べた。

- 1) 症状観察では、100 mg/kg 群の雄および 300 mg/kg 群の雌雄で流涎がみられ、300 mg/kg 群の雌雄でよるめき歩行および脱毛、雄で軟便、雌で運動性の低下、腹臥位および排糞量の減少が認められた。
- 2) 体重および摂餌量では、300 mg/kg 群の雌雄で減少が認められた。
- 3) 尿検査では、300 mg/kg 群の雌で尿量および飲水量の増加、尿比重の低下が認められた。
- 4) 血液学的検査では、100 mg/kg 以上の群の雄で活性化部分トロンボプラスチン時間の延長、300 mg/kg 群の雄ではさらにプロトロンビン時間の延長が認められた。
- 5) 血液生化学的検査では、300 mg/kg 群の雌雄で総コレステロールの増加、雄で GPT 活性の上昇、雌でグルコースの減少および中性脂肪の増加が認められた。
- 6) 器官重量では、100 mg/kg 以上の群の雄および 30 mg/kg 以上の群の雌で肝臓重量の増加、300 mg/kg 群の雌雄で腎臓重量の増加傾向が認められた。
- 7) 病理組織学的検査では、腎臓において、好塩基性尿細管が 100 mg/kg 群の雄および 300 mg/kg 群の雌雄で、蛋白円柱が 300 mg/kg 群の雄で認められた。その他、30 mg/kg 以上の群の雌雄で小葉中心性の肝細胞の肥大、甲状腺の濾胞上皮の過形成/肥大がみられたが、いずれも代謝酵素の誘導に関連した変化と推察され、毒性変化とは判断しなかった。
- 8) 機能検査、自発運動量および剖検では、被験物質投与の影響は認められなかった。
- 9) 14 日間の休薬により、脱毛および腎臓の好塩基性尿細管には回復性が認められなかった。その他の投与期間中あるいは投与期間終了時における変化は、いずれも回復あるいは回復傾向が認められた。
- 10) 以上の結果から、本試験条件下における 1-フェニル-1-キシリルエタンの無毒性量は 30 mg/kg/day と判断された。

## II 緒言

1-フェニル-1-キシリルエタンのラットにおける 28 日間反復経口投与毒性試験を実施し、その結果が得られたので報告する。なお、本試験は OECD GLP(1997)および OECD ガイドライン「Repeated Dose 28-day Oral Toxicity Study in Rodents(#407)」(1995)に従って実施した。

### III 材料および方法

#### 1 被験物質

1-フェニル-1-キシリルエタンは無色透明の液体である。本試験に用いた1-フェニル-1-キシリルエタン [redacted] 提供され、その品質は Supplement 1 に示すとおりである。入手時から返却時まで、本剤を室温で保存した。なお、本剤の投与期間中の安定性は [redacted] において確認されている (Supplement 2)。

#### 2 使用動物および飼育条件

##### 2.1 使用動物

日本チャールス・リバー株式会社で生産された Crj : CD(SD) IGS 系ラットの雌雄各 42 匹を 5 週齢で入手し、7 日間の検疫を含め 16 日間の馴化飼育を行った後、雌雄各 36 匹を 7 週齢で試験に供した。投与開始時の体重は雄が 258~303 g、雌が 178~217 g であった。

##### 2.2 飼育条件

試験実施期間中、温度 21~25℃、湿度 40~70%、換気回数 16 回/時間および照明 12 時間 (7~19 時)/日と設定した飼育室 (実測値は、温度 23~25℃、湿度 43~67%) で、動物を 29W×22D×21H(cm) のステンレス製ワイヤーケージに個別に収容し、飼育した。その間、高圧蒸気滅菌 (121℃, 5 分) した固型飼料 (CRF-1, オリエンタル酵母工業株式会社) と上水道水を自由摂取させた。

#### 3 投与

##### 3.1 投与量

当施設で実施した 2 週間反復投与毒性試験 (投与量 100, 250, 500 および 1000 mg/kg)<sup>1)</sup> の結果、250 mg/kg 以上の群の雌雄で流涎、体重の減少あるいは増加抑制、肝臓重量の増加傾向が、250 mg/kg 群の雄および 500 mg/kg 以上の群の雌雄でよろめき歩行、摂餌量の減少が認められた。また、500 mg/kg 以上の群の雌雄で運動性の低下、排糞量の減少がみられ、500 mg/kg 群の雌 4 例中 1 例と 1000 mg/kg 群の雌雄各 5 例全例が投与 3~5 日に死亡した。以上の結果から、一般状態、体重あるいは肝臓への影響が予想される 300 mg/kg を高用量とし、以下、公比約 3 で 100 および 30 mg/kg をそれぞれ中間用量および低用量とした。以上の 3 群に加え、対照として Corn oil を投与する群を設け、計 4 群で試験を実施した。

##### 3.2 使用動物数および群分け

投与開始 4 日前に、投与開始前の一般状態および体重推移を考慮して健常な動物を選抜し、雌雄別に平均体重に近い 36 匹について、コンピュータを用いた総無作為化法により群分けし、対照群 (I 群) を 12 匹、低用量群 (II 群) および中間用量群 (III 群) を各 6 匹、高用量群 (IV 群) を 12 匹とした。また、I 群および IV 群の雌雄各 12 例中 6 例を回復性試験に供した。

### 3.3 被験物質の調製

投与当日、各用量群ごとに、被験物質の所定量を純度換算(換算係数:1.093)して秤量し、Corn oil(ロット番号 89H0149, Sigma)に溶解した。なお、投与液は調製後6時間以内に使用した。

### 3.4 投与条件下における被験物質の安定性

1-フェニル-1-キシリルエタンをCorn oilに60, 20および6 mg/mL濃度となるよう溶解した場合、室温で6時間安定であることが確認されている(Supplement 3)。

### 3.5 投与液の分析(濃度確認)

初回調製時および最終調製時に、対照群を除く各群の投与液について濃度確認を行った結果、表示値の97.9~101.7%であった(Supplement 4)。

### 3.6 投与経路、投与方法および投与期間

28日間連日、1日1回、9時から14時の間に、1~3 mLのガラス製注射筒およびラット用経口ゾンデを用いて、投与液を強制経口投与した。投与容量は体重1 kgあたり5 mLとし、各個体の投与液量は投与日に最も近い測定日の体重を基準として算出した。

回復性試験用動物については、投与期間終了後14日間の休薬を行った。

#### 【投与量および群構成】

群	投与物質名	投与量 (mg/kg/day)	濃度 (mg/mL)	投与容量 (mL/kg)
I	Corn oil	—	—	5
II	1-フェニル-1-キシリルエタン	30	6	5
III	1-フェニル-1-キシリルエタン	100	20	5
IV	1-フェニル-1-キシリルエタン	300	60	5

群	個体番号	
	雄	雌
I	001~006, 007~012	401~406, 407~412
II	101~106	501~506
III	201~206	601~606
IV	301~306, 307~312	701~706, 707~712

アンダーライン部は回復性試験群

## 4 観察、測定および検査

投与および休薬の日数は投与開始日を投与1日、休薬開始日を休薬1日として、以降の日を表した。また、投与1~7日を投与1週、休薬1~7日を休薬1週として、以降の週

を表した。なお、以下に示す観察、測定および検査は、特に記載のない限り全例を対象とした。

#### 4.1 症状観察および機能検査

##### 4.1.1 一般状態

投与開始前3日から剖検日まで、一般状態を毎日観察した。観察頻度は、投与期間中は投与前と投与後約1時間の1日2回、その他の期間は1日1回とした。

##### 4.1.2 詳細な症状観察

投与開始前3日、投与1, 7, 14, 21 および28日ならびに休薬7および14日に、当施設で規定したスコアリングシステムを用いて動物の症状を観察した。観察時刻は、投与期間中は投与後30分~2時間、その他の期間は午後とした。詳細を別表Iに示した。

##### 4.1.3 機能検査

投与4週および休薬2週に、感覚反応(瞳孔反応、視覚性置き直し反応、聴覚反応、痛覚反応)、空中正向反射、握力(前肢)および着地開脚幅について検査した。詳細を別表IIに示した。

##### 4.1.4 自発運動量

投与4週および休薬2週に、自発運動量測定装置(ACTY303, バイオメディカ)を用いて、60分間の運動量を測定した。

#### 4.2 体重

投与開始前3日、投与1, 3, 8, 15, 22 および28日ならびに休薬1, 8 および14日に体重を測定した。

#### 4.3 摂餌量

投与開始前3日から投与開始前日まで、投与1~3, 3~8, 8~15, 15~22 および22~28日ならびに休薬1~8 および8~14日に摂取量を測定し、いずれも1日あたりの摂餌量を算出した。

#### 4.4 尿検査

投与4週および休薬2週に、排尿後4時間以内の尿および16時間蓄積尿(17時~翌朝の9時)を採取して尿検査を行った。検査項目とその略語、測定方法および使用機種を以下に示した。なお、投与4週における排尿後4時間以内の尿の採取は投与前に行った。

項目	略語	測定方法	使用機種
飲水量 <sup>a)</sup>	—	重量差	電子天秤メトラーPM4800
尿量 <sup>a)</sup>	Vol.	計量	25 mL メスシリンダー
色調 <sup>a)</sup>	Col.	目視	—
比重 <sup>a)</sup>	S.G.	屈折法	アタゴ蛋白屈折計

pH <sup>b)</sup>	—	試験紙法 <sup>c)</sup>	—
蛋白 <sup>b)</sup>	Pro.	同上	—
糖 <sup>b)</sup>	Glu.	同上	—
ケトン体 <sup>b)</sup>	Ket.	同上	—
ビリルビン <sup>b)</sup>	Bil.	同上	—
潜血 <sup>b)</sup>	Occ.	同上	—
ウロビリノーゲン <sup>b)</sup>	Uro.	同上	—

a) 16 時間蓄積尿で測定，飲水量は 16 時間蓄積尿採取時に測定

b) 排尿後 4 時間以内の尿で測定

c) 試験紙：マルティスティックス<sup>®</sup>，バイエル メディカル株式会社

#### 4.5 血液学的検査

投与期間終了時(最終投与翌日の剖検時)および休薬期間終了時(休薬 15 日目の剖検時)に，16 時間以上絶食させた動物をエーテルで麻酔し，後大静脈から採取した血液を用いて，血液学的検査を行った。検査項目とその略語，測定方法および使用機種を以下に示した。

項目	略語	測定方法	使用機種
赤血球数 <sup>a)</sup>	RBC	自動計数法	東亜多項目自動血球計数装置 K-4500
ヘモグロビン量 <sup>a)</sup>	Hb	SLS- ヘモグロビン法	同上
ヘマトクリット値 <sup>a)</sup>	Ht	電気抵抗法	同上
プロトロンビン時間 <sup>b)</sup>	PT	凝固法	アメルング KC-10A
活性化部分トロンボ プラスチン時間 <sup>b)</sup>	APTT	同上	同上
血小板数 <sup>a)</sup>	Plate.	自動計数法	東亜多項目自動血球計数装置 K-4500
白血球数 <sup>a)</sup>	WBC	同上	同上
白血球百分率 <sup>a)</sup>	WBC differential count	May-Giemsa 染色後鏡検	オリンパス顕微鏡

抗凝固剤: <sup>a)</sup> EDTA-2K

<sup>b)</sup> 3.8 w/v%クエン酸ナトリウム液

#### 4.6 血液生化学的検査

投与期間終了時(最終投与翌日の剖検時)および休薬期間終了時(休薬 15 日目の剖検時)に，16 時間以上絶食させた動物をエーテルで麻酔し，後大静脈から採取した血液をヘパリン(ノボ・ヘパリン注 1000，ノボ・ノルディスク A/S)処理し，遠心分離(約・1600×g，10 分，4℃)して得た血漿を用いて，血液生化学的検査を行った。検査項目とその略語，測定方法および使用機種を以下に示した。

項目	略語	測定方法	使用機種
グルタミン酸・オキザロ 酢酸トランスアミナーゼ	GOT	UV 法	日立 7150 形自動分析装置
グルタミン酸・ピルピン酸 トランスアミナーゼ	GPT	同上	同上
グルコース	GLU	ヘキソキナーゼ・ G-6-PDH 法	同上
総ビリルビン	BIL	アゾビリルビン法	同上
尿素窒素	UN	ウレアーゼ・イン ドフェノール法	同上
クレアチニン	CRE	Jaffé 法	同上
総コレステロール	CHO	酵素法	同上
中性脂肪	TG	同上	同上
総蛋白	TP	ビウレット法	同上
アルブミン	ALB	BCG 法	同上

#### 4.7 剖検

投与期間終了時(最終投与の翌日)および休薬期間終了時(休薬 15 日目)に、16 時間以上絶食させた動物をエーテルで麻酔し、血液サンプルを採取した後、後大静脈および腹大動脈を切断して放血致死させ、剖検を行った。

#### 4.8 器官重量

剖検後、脳、胸腺、肺、心臓、肝臓、脾臓、副腎、腎臓、精巣、精巣上体、卵巣および子宮の重量を測定した。副腎、腎臓、精巣、精巣上体および卵巣については左右別々に測定した。また、剖検前の体重を基にそれぞれの器官体重比重量を算出した。

#### 4.9 病理組織学的検査(光学顕微鏡による検査)

肺・気管支、気管、心臓、腎臓、膀胱、肝臓、顎下腺、舌下腺、舌・咽喉頭、食道、胃、十二指腸、空腸、回腸、盲腸、結腸、直腸、胸腺、脾臓、下顎リンパ節、腸間膜リンパ節、甲状腺、上皮小体、下垂体、副腎、精巣上体、精囊、凝固腺、前立腺、卵巣、子宮、膣、大脳、小脳、延髄、脊髄(胸部)、坐骨神経、骨および骨髄(胸骨と大腿骨)ならびに剖検で異常の認められた器官・組織を 10 vol% 中性緩衝ホルマリンで固定した。また、精巣はブアン液で固定した。対照群および高用量群では固定したすべての器官・組織について、その他の群では被験物質投与に起因すると思われる変化が認められた肝臓、腎臓、甲状腺および剖検で異常の認められた器官・組織について、常法に従ってヘマトキシリン・エオジン(HE)染色標本作製し、鏡検した。

なお、上記の器官・組織のうち、肺・気管支では左右について、腎臓、顎下腺、舌下腺、甲状腺、上皮小体、副腎、精巣、精巣上体、卵巣、坐骨神経および大腿骨では左右いずれか片側について標本作製を行った。

5 統計学的解析方法

対照群と被験物質投与各群との間の有意差検定を以下のとおり行った。すなわち、投与期間終了時までには得られた各数値データについて、Bartlett 法による分散の一様性の検定(有意水準 5%)を行い、分散が一樣の場合は Dunnett 法により平均値の検定を行った。一方、分散が一樣でない場合は平均順位の違いについて Dunnett 型の検定を行った。また、休業期間中あるいは休業期間終了時に得られたデータについては、対照群と高用量群との間で F 検定による等分散性の検定を行い、2 群間の平均値の違いについて分散が等しい場合は Student の t 検定を、分散が等しくない場合は Aspin-Welch の t 検定を行った。検定はいずれも両側で行い、成績評価にあたっては有意水準 5% で対照群との間に差が認められた場合に有意な変動とし、表中には 5% と 1% に区別して示した。

別表 I 詳細な症状観察法

項目	方法および判定基準(スコア)
1. ケージ内での観察	ケージ内の動物について、以下の項目を観察した。
① 姿勢 Posture	0: 正常 1: 異常(腹臥位, 横臥位, 背臥位, 立位, 座位, うずくまり, 四肢分離位など)
② 痙攣 Convulsions	0: なし 1: 攣縮, 振戦 2: 間代性痙攣 3: 強直性屈曲痙攣 4: 強直性伸展痙攣, 窒息性痙攣
③ 呼吸 Respiration	0: 正常 1: 軽度の異常(浅速呼吸, 頻呼吸, 軽度な不規則呼吸など) 2: 重度の異常(呼吸困難, 重度の不規則呼吸など)
④ 常同行動 Stereotype	0: なし 1: あり(旋回, 毛づくろい増加, 頭振り, 嗅ぎ行動, 立ち上がり, ケージ噛みなど)
⑤ 異常行動 Abnormal behavior	0: なし 1: あり(自傷行為, 追尾反応, 後ずさり, 身悶え, 発声など)
2. 手に取っての観察	動物をケージから取り出して、以下の項目を観察した。
① ケージからの出し易さ/扱い易さ Handling difficulty	0: 簡単 1: 困難(走り回る, 硬直) 2: 非常に困難(攻撃することがある)
② 異常発声 Abnormal vocalization	0: なし 1: あり
③ 筋緊張 Muscle tone	-1: 低下 0: 正常 1: 亢進

④ 被毛の状態 Fur appearance	0: 正常 1: わずかに, 局所的に汚れている 2: 全身的に汚れている
⑤ 立毛 Piloerection	0: なし 1: あり
⑥ 皮膚/可視粘膜 Skin/visual mucosa	-1: 蒼白い 0: 正常 1: 赤い
⑦ 瞳孔径 Pupil size	-1: 大きい(散瞳) 0: 正常 1: 小さい(縮瞳)
⑧ 流涎 Salivation	0: なし 1: あり
⑨ 流涙 Lacrimation	0: なし 1: あり
3. オープンフィールド 内での観察	動物をオープンフィールド(縦横 90 cm, 高さ 30 cm の木製の箱)に置き, 以下の項目を観察した。なお, 正向反射はオープンフィールドに置く時に観察した。残りの項目は 2 分間の観察時間とした。
① 正向反射 Righting reflex	0: あり 1: なし
② 覚醒状態 Consciousness	-1: 低い(昏迷, 昏睡, 反応なし) 0: 正常(警戒, 探索行動あり) 1: 高い(興奮, 緊張, 警戒過多, 突発的な動き)
③ 歩行 Gait	-1: 動かない 0: 正常 1: 異常(よろめき, 爪先立ち, 後肢伸展, 前肢伸展, 四肢伸展など)
④ 脱糞回数 Defecation	実測値
⑤ 排尿回数 Urination	実測値
⑥ 立ち上がり回数 Rearing	実測値

別表Ⅱ 機能検査法

項目	方法および判定基準(スコア)
1. 瞳孔反応 Pupillary reflex	暗所でペンライトを横から照らし、瞳孔の収縮、拡張を調べた。 -1: 散瞳(収縮が認められない) 0: 正常 1: 縮瞳(拡張が認められない)
2. 視覚性置き直し反応 Visual placing response	動物の尾を持って吊り下げ、約 15 cm の距離からテーブル面に近づけて行き、ひげがテーブルに接触する前に頭を持ち上げ、前肢を伸ばして物をつかもうとする反応を観察した。 -1: 反応なし 0: 反応あり(頭を持ち上げ前肢を伸ばす)
3. 聴覚反応 Auditory response	動物の頭上で指を鳴らし、動物の反応を調べた。 -1: 反応なし 0: 正常(尻込む、耳をピクリと動かす) 1: 過敏な反応(跳躍、暴力的な反応を示す)
4. 痛覚反応 Pain response	クレンメで動物の尾を挟み、動物の反応を調べた。 -1: 反応なし 0: 正常(身を固くする、直ちに振り返る、噛む) 1: 過敏な反応(啼鳴、急激に振り返る、攻撃する)
5. 空中正向反射 Aerial righting	約 32 cm の高さから動物を背面位で自由落下させた時、空中で立ち直り、正常の立位で着地する反応を調べた。 -1: 反応なし(立位で着地できない) 0: 反応あり
6. 握力 Grip strength	CPU ゲージ(モデル 9502, アイコーエンジニアリング株式会社)を作業台に固定し、動物が握り易いように網状のものを CPU ゲージに取り付けた。その網に左右前肢を握せ、尾を持ってゲージの反対側に動物を引っ張った。動物が離れた時の数値(負荷値)を記録した。2 回測定し、平均値を算出した。
7. 着地開脚幅 Randing foot-splay	左右の後肢うらに色素を塗り、約 32 cm の高さから半紙上に動物を落下させた。半紙に付着した色素の左右足跡(中央部)間の距離を測定した。2 回測定し、平均値を算出した。

## IV 成績

### 1 症状観察および機能検査

#### 1.1 一般状態(Table 1~2)

投与期間中、100 mg/kg 群の雄 6 例中 2 例および 300 mg/kg 群の雌雄各 12 例中 11 例で流涎が認められた。流涎の発現頻度は、100 mg/kg 群では投与 21~27 日の間に 1~3 日、300 mg/kg 群では投与 7~28 日の間に雄は 2~21 日、雌は 1~21 日であった。300 mg/kg 群ではさらに、雄 7 例および雌 4 例で投与 3~4 日によるめき歩行、雄 1 例および雌 7 例で投与 4 日以降に脱毛、雌 6 例で投与 4 日以降に排糞量の減少がみられ、雄 1 例で投与 3 日に軟便、雌 1 例で投与 7~8 日に運動性の低下および腹臥位が認められた。

休薬期間中、300 mg/kg 群の雌雄各 6 例中、雄 1 例および雌 5 例で脱毛が認められた。なお、脱毛は雌 1 例を除き、投与期間に引き続き休薬期間を通じて認められた。

#### 1.2 詳細な症状観察(Table 3~4)

投与期間中、300 mg/kg 群の雌雄において、投与 14、21 および 28 日の観察で対照群と比較して流涎のスコアに有意な増加が認められた。なお、30 mg/kg 群の雄で投与 21 日の排尿回数に有意な増加がみられたが、用量に伴わない変化であることから、被験物質投与との関連はないと判断した。

休薬 7 および 14 日の観察では、300 mg/kg 群の雌雄とも対照群と比較して有意差は認められなかった。

#### 1.3 機能検査(Table 5~6)

投与 4 週および休薬 2 週の検査では、瞳孔反応、視覚性置き直し反応、聴覚反応、痛覚反応、空中正向反射、握力および着地開脚幅とも、いずれの被験物質投与群にも対照群と比較して有意差は認められなかった。

#### 1.4 自発運動量(Table 7~8)

投与 4 週の検査では、いずれの被験物質投与群にも対照群と比較して有意差は認められなかった。

休薬 2 週の検査では、対照群と比較して、300 mg/kg 群の雌の自発運動量に有意な増加が認められた。

### 2 体重(Fig. 1~2, Table 9~10)

投与期間中、300 mg/kg 群の雌雄で投与 3 日の体重に減少がみられ、その後いずれも増加がみられたが、対照群と比較して、雄では投与 3 日および 8 日の体重に、雌では投与 8~28 日の体重に有意な低値が認められた。

休薬期間中、300 mg/kg 群の雌で投与期間に引き続き休薬 1 日の体重に有意な減少がみられたが、その後は有意差が認められなかった。

### 3 摂餌量(Fig. 3~4, Table 11~12)

投与期間中, 300 mg/kg 群の雌雄で投与1~8日の摂餌量に, 対照群と比較して有意な減少が認められた。

休薬期間中, 300 mg/kg 群の雌で休薬1~8日の摂餌量に, 対照群と比較して有意な増加が認められたが, 休薬期間終了時には対照群とほぼ同様の値となった。

### 4 尿検査(Table 13~14)

投与4週の検査では, 対照群と比較して, 300 mg/kg 群の雌で飲水量および尿量に有意な増加, 尿比重に有意な低下が認められた。なお, 30 mg/kg 群の雌1例で強度の潜血陽性反応がみられたが, 用量に伴わない変動であることから, 被験物質投与との関連はないと判断した。

休薬2週の検査では, 300 mg/kg 群の雌雄とも特記すべき異常は認められなかった。

### 5 血液学的検査(Table 15~16)

投与期間終了時の検査では, 対照群と比較して, 100 mg/kg 以上の群の雄で活性化部分トロンボプラスチン時間の有意な延長がみられ, 300 mg/kg 群の雄ではプロトロンビン時間の有意な延長も認められた。また, 100 mg/kg 以上の群の雌でリンパ球比の有意な上昇がみられ, 300 mg/kg 群の雌では好中球分節核球比の有意な低下が認められた。

休薬期間終了時の検査では, 対照群と比較して, 300 mg/kg 群の雄でヘモグロビン量の有意な減少, 同群の雌で血小板数の有意な増加が認められた。

### 6 血液生化学的検査(Table 17~18)

投与期間終了時の検査では, 対照群と比較して, 300 mg/kg 群の雄でGPT活性の有意な上昇, 雌で中性脂肪の有意な増加およびグルコースの有意な減少が認められた。さらに, 同群の雌雄で総コレステロールの有意な増加も認められた。その他, 100 mg/kg 群の雄で総ビリルビンの有意な減少がみられたが, 用量に伴わない変動であることから, 被験物質投与との関連はないと判断した。

休薬期間終了時の検査では, 300 mg/kg 群の雄でGOT活性の有意な低下および総ビリルビンの有意な減少が認められた。

### 7 剖検(Table 19~20)

投与期間終了時の剖検では, いずれの群にも被験物質投与の影響は認められなかった。なお, 30 mg/kg 群の雄1例で脾臓の表面に膨隆, 境界不明瞭および割面から濾胞増生が認められたが, 用量に伴わない1例のみの変化であり, 被験物質投与との関連はないと判断した。

休薬期間終了時の剖検では, いずれの群の動物にも異常は認められなかった。

### 8 器官重量(Table 21~22)

投与期間終了時の検査では, 対照群と比較して, 100 mg/kg 以上の群の雌雄で肝臓の実重量および体重比重量に有意な増加がみられ, 30 mg/kg 群の雌では実重量のみであった

が、有意な増加が認められた。また、300 mg/kg 群の雌雄で腎臓の体重比重量に有意な増加が認められた。

休薬期間終了時の検査では、対照群と比較して、300 mg/kg 群の雌で胸腺の実重量および体重比重量に有意な増加が認められた。また、同群の雄で腎臓、雌で肝臓の体重比重量にそれぞれ有意な増加が認められた。

その他、投与期間終了時に300 mg/kg 群の雄で心臓および副腎、同群の雌で肺、休薬期間終了時に300 mg/kg 群の雄で精巣および精巣上体、同群の雌で脾臓に有意な変動がみられたが、いずれも実重量あるいは体重比重量のみの変動であり、剖検時の体重差に起因した変動あるいは偶発的な変動と判断した。

## 9 病理組織学的検査 (Table 23~24)

### 1) 肝臓

投与期間終了時の検査において、小葉中心性の肝細胞の肥大が30 mg/kg 以上の群の雌雄各6例全例で軽度~中等度に認められ、用量の増加とともに程度が増強して観察された。

休薬期間終了時の検査では、小葉中心性の肝細胞の肥大が300 mg/kg 群の雌6例中1例で軽度にみられ、投与期間終了時と比較して、発現例数および程度が減弱した。

### 2) 腎臓

投与期間終了時の検査において、好塩基性尿細管が100 mg/kg 群の雄1例で軽度に、300 mg/kg 群の雄5例および雌2例で軽度~中等度にみられ、300 mg/kg 群の雄3例ではさらに蛋白円柱が軽度に認められた。また、近位尿細管上皮の空胞化が30 mg/kg 群の雌3例、100 mg/kg 群の雄1例および雌2例ならびに300 mg/kg 群の雄2例および雌6例で軽度に認められた。

休薬期間終了時の検査では、好塩基性尿細管が300 mg/kg 群の雄6例全例で軽度~中等度にみられ、投与期間終了時と比較して、回復性は認められなかった。また、蛋白円柱が300 mg/kg 群の雄1例で軽度にみられたが、投与期間終了時よりも発現例数が減少した。

### 3) 甲状腺

投与期間終了時の検査において、濾胞上皮の過形成/肥大が30および100 mg/kg 群の各雄4例および雌3例、300 mg/kg 群の雌雄各6例全例で軽度~中等度に認められた。

休薬期間終了時の検査では、濾胞上皮の過形成/肥大が300 mg/kg 群の雄4例および雌2例で軽度にみられ、投与期間終了時と比較して、発現例数および程度が減弱した。

その他、投与期間終了時あるいは休薬期間終了時にみられた変化は、対照群にも認められる変化あるいは少数例のみにみられた自然発生的な変化であり、被験物質投与との関連はないと判断した。

## V 考察

投与期間中、いずれの投与群にも死亡は認められなかった。症状観察では、100 mg/kg 群の雄および 300 mg/kg 群の雌雄で流涎がみられ、300 mg/kg 群の雌雄でよろめき歩行および脱毛、雄で軟便、雌で運動性の低下、腹臥位および排糞量の減少が認められた。このうち流涎は投与 7 日以降に散見された。よろめき歩行は投与 3~4 日のみであり、軟便も同時期に認められた。その後脱毛あるいは排糞量の減少がみられ、投与 7~8 日に運動性の低下と腹臥位が認められた。また、300 mg/kg 群では、摂餌量の減少が投与 1~8 日にみられ、呼応して体重減少が認められた。以上のように、被験物質投与による全身への影響は投与期間初期に強く発現した。なお、週 1 回の頻度で実施した詳細な症状観察では、上記以外の症状は観察されず、機能検査、自発運動量および剖検においても被験物質投与の影響は認められなかった。また、尿検査において、300 mg/kg 群の雌で尿量の増加および尿比重の低下が認められた。同時に測定した飲水量が増加しており、上述の流涎とも関連して、被験物質の刺激により飲水量が増加し、その結果として尿量増加、尿比重低下が生じたものと判断された。

1-フェニル-1-キシリルエタンの反復投与により腎臓、肝臓および甲状腺への影響が認められた。腎臓では、好塩基性尿細管が 100 mg/kg 群の雄および 300 mg/kg 群の雌雄で、蛋白円柱が 300 mg/kg 群の雄でみられ、300 mg/kg 群では腎臓重量の増加傾向が認められた。なお、近位尿細管上皮の空胞化が 30 mg/kg 以上の群の雌および 100 mg/kg 以上の群の雄でみられ、何らかの物質が尿細管に貯留されているものと推察されるが、いずれも軽度な変化であり、他の検査項目に腎機能への影響を示唆する変動が認められないことから、毒性学的意義はないと判断した。

肝臓では、30 mg/kg 以上の群の雌雄で小葉中心性の肝細胞の肥大がみられ、100 mg/kg 以上の群の雄および 30 mg/kg 以上の群の雌で肝臓重量の増加が認められた。被験物質の代謝酵素に及ぼす影響について検討していないが、フェノバルビタールなどの酵素誘導作用を有する物質の反復投与で同様の変化が観察されており、上述のように被験物質投与による全身への影響は投与期間初期に強く認められていることから、これらの変化は代謝酵素の誘導に関連したものと推察された。また、甲状腺では、30 mg/kg 以上の群の雌雄で濾胞上皮の過形成/肥大が認められた。肝臓の薬物代謝酵素を誘導することによって甲状腺の機能が変化し、甲状腺ホルモン(T4)の分泌が亢進されることが確認されており<sup>2)3)</sup>、この甲状腺における変化も酵素誘導に起因したものと判断された。なお、血液学的検査では、100 mg/kg 以上の群の雄で活性化部分トロンボプラスチン時間の延長、300 mg/kg 群の雄でプロトロンビン時間の延長が、血液生化学的検査では、300 mg/kg 群の雌雄で総コレステロールの増加、雄で GPT 活性の上昇、雌でグルコースの減少および中性脂肪の増加が認められ、いずれも軽度な変動であるものの肝機能への影響が示唆された。

その他、血液学的検査において、100 mg/kg 以上の群の雌でリンパ球比の上昇、300 mg/kg 群の雌で好中球分節核球比の低下が認められた。この原因は明らかでないが、総白血球数に変動はなく、毒性学的意義はないと判断した。

投与期間終了後 14 日間の休薬期間を設け、上述の変化の回復性について検討した。その結果、脱毛および腎臓の好塩基性尿細管には回復性が認められなかった。その他の投与

期間中あるいは投与期間終了時における変化は、いずれも回復あるいは回復傾向が認められた。なお、自発運動量、血液学的検査、血液生化学的検査および器官重量で有意差がみられた項目があったが、いずれも投与期間終了時には認められていない軽度な変動であり、血液検査および器官重量における変動については器官・組織に関連する変化が認められなかったことから、被験物質投与の影響ではないと判断した。

以上の結果から、本試験条件下における1-フェニル-1-キシリルエタンの無毒性量は30 mg/kg/day と判断された。

## 文 献

- 1) 佐藤伸一 他(未発表)：1-フェニル-1-キシリルエタンのラットにおける28日間反復経口投与毒性試験の投与量設定試験(14日間反復投与試験)[試験番号：2000TT277]。
- 2) McClain, R. M. (1989) : The significance of hepatic microsomal enzyme induction and altered thyroid function in rats: Implications for thyroid gland neoplasia, *Toxicol. Pathol.* 17, 294~306.
- 3) Bookstaff, R. C. *et al* (1996) : Effects of Doxylamine succinate on thyroid hormone balance and enzyme induction in mice. *Toxicol. Appl. Pharmacol.* 141, 584~594.

## その他の事項

### 1 飼育環境

飼育室内の環境は許容範囲内に維持されており、また、飼料および飲料水中には試験に影響を及ぼすような濃度の夾雑物は認められなかった。

### 2 予見することができなかった試験の信頼性に影響を及ぼす疑いのある事態および試験計画書に従わなかったこと

以下のような事例があったが、試験評価に影響を及ぼすものではなかった。

- 1) 雄の使用時体重範囲は、「170~270 g」と規定されていたが、実際は「258~303 g」であり、上限を上回った個体(36例中31例)を使用した。

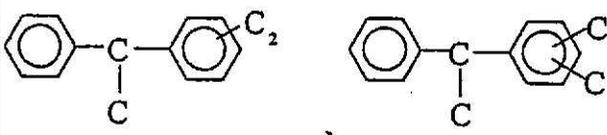
一般的事項

サンプルの名称	1-フェニル-1-キシリルエタン					
別名	スチリルキシレン					
構造式又は示性式 (いずれも不明の場合は、その製法の概要)						
サンプルの純度	91.5	wt%	サンプルのLot No.	[REDACTED]		
不純物の名称及び濃度	1,1-Diphenyethane:0.2mass%, Indan, 1-methyl-3-phenyl:5.6mass% その他 一成分1mass%未満の構造不明炭化水素類合計:2.7mass% wt%					
C A S 番号	40766-31-2		蒸気圧	0.1Pa以下		
分子量	210		分配係数	-		
融点	流動点: -47.5°C °C		常温における性状	無色透明液体		
沸点	蒸留範囲 初留点: 291.5°C 95% : 297.0°C 終点 : 303.5°C °C					
定性						
溶媒に対する溶解度等	溶媒	溶解度	溶媒中の安定性	溶媒	溶解度	溶媒中の安定性
	水	不溶	安定	DMSO	溶解	安定
	アセトン	溶解	安定	その他 ( )	炭化水素系 溶剤等によく 溶ける	安定

【備考】

1. 「安定性」の欄には、温度、光等に対する安定性を記入して下さい。
2. 「蒸気圧」の欄には、サンプルの蒸気圧を記入して下さい。
3. 「分配係数」の欄には、分配係数、測定温度及び分配係数の測定に用いた溶媒名を記入して下さい。
4. 「溶媒に対する溶解度等」の欄には、サンプルの溶媒に対する溶解度及びその溶媒中での安定性を記入して下さい。

## 一般的事項

サンプルの名称	1-フェニル-1-キシリルエタン (試験終了後の試料)					
別名	スチリルキシレン					
構造式又は示性式 (いずれも不明の場合 は、その製法の概要)						
サンプルの純度*1	90.9	mass%	サンプルのLot No.	[REDACTED]		
不純物の名称及び濃度*1	1,1-Diphenylethane:0.2mass%, Indan, 1-methyl-3-phenyl:5.6mass% その他 一成分1mass%未満の構造不明炭化水素類合計:3.3mass%					
C A S 番号	40766-31-2		蒸気圧	-		
分子量	210		分配係数	-		
融点	流動点: -	°C	常温における性状	無色透明液体		
沸点	-					
安定性						
溶媒に対する溶解度等	溶媒	溶解度	溶媒中の安定性	溶媒	溶解度	溶媒中の安定性
	水	-	-	DMSO	-	-
	アセトン	-	-	その他( )	-	-

## 〔備考〕

- 「安定性」の欄には、温度、光等に対する安定性を記入して下さい。
- 「蒸気圧」の欄には、サンプルの蒸気圧を記入して下さい。
- 「分配係数」の欄には、分配係数、測定温度及び分配係数の測定に用いた溶媒名を記入して下さい。
- 「溶媒に対する溶解度等」の欄には、サンプルの溶媒に対する溶解度及びその溶媒中での安定性を記入して下さい。

注1 サンプル純度および不純物濃度：ガスクロマトーグラフ測定

測定条件 カラム；OV-1701

カラム温度；200℃一定

注入口温度；300℃

検出器温度；300℃

No. 2000TT278-S1-1

CERTIFICATE OF ANALYSIS  
(STABILITY)

Study No.: 2000TT278  
 Test article: 1-phenyl-1-xylylethane [REDACTED]  
 Vehicle: Corn oil  
 Storage container: Glass container  
 Storage conditions: A: at preparation  
 B: for 6-hour storage at room temperature  
 Date of preparation: December 19, 2000  
 Dates of determination: A: December 19, 2000  
 B: December 19, 2000  
 Analyst: [REDACTED]

## Results:

Nominal conc. (mg/mL)		Conc. (mg/mL)	Mean conc. (mg/mL)	Remaining (%)	Judgement
6	A	6.107	6.077	-	-
		6.047			
	B	6.088	6.028	99.2	Conforms
		5.967			
20	A	19.95	19.85	-	-
		19.75			
	B	19.89	19.84	99.9	Conforms
		19.79			
60	A	58.64	58.80	-	-
		58.95			
	B	58.14	57.84	98.4	Conforms
		57.54			

Judgment criterion: The remaining percentages to the values at preparation ranging from 90-110 % are acceptable.

Conclusion: 1-phenyl-1-xylylethane solutions in corn oil at 6, 20 and 60 mg/mL are stable for 6-hour storage at room temperature.

Chief investigator:  
 [REDACTED]

Analytical Services Dept.  
 Ina Research Inc.

No. 2000TT278-C1-1

CERTIFICATE OF ANALYSIS  
(CONCENTRATIONS)

Study No.: 2000TT278  
Test article: 1-phenyl-1-xylylethane [REDACTED]  
Vehicle: Corn oil  
Date of preparation: December 21, 2000  
Date of determination: December 21, 2000  
Analyst: [REDACTED]

## Result

Nominal Conc. (mg/mL)	Conc. (mg/mL)	Mean conc. (mg/mL)	Percentage to nominal conc.	Judgement
6	6.251 5.952	6.102	101.7	Conforms
20	19.94 20.64	20.29	101.5	Conforms
60	58.93 59.82	59.38	99.0	Conforms

Judgment criterion: The percentages to nominal concentrations ranging from 90-110% are acceptable.

Chief investigator:  
[REDACTED]

Analytical Services Dept.  
Ina Research Inc.

No. 2000TT278-C1-2

CERTIFICATE OF ANALYSIS  
(CONCENTRATIONS)

Study No. : 2000TT278  
Test article: 1-phenyl-1-xylylethane [REDACTED]  
Vehicle: Corn oil  
Date of preparation: January 17, 2001  
Date of determination: January 17, 2001  
Analyst: [REDACTED]

## Result

Nominal Conc. (mg/mL)	Conc. (mg/mL)	Mean conc. (mg/mL)	Percentage to nominal conc.	Judgement
6	5.952	5.907	98.5	Conforms
	5.861			
20	19.74	19.69	98.5	Conforms
	19.64			
60	58.30	58.76	97.9	Conforms
	59.22			

Judgment criterion: The percentages to nominal concentrations ranging from 90-110% are acceptable.

Chief investigator: [REDACTED]

Analytical Services Dept.  
Ina Research Inc.

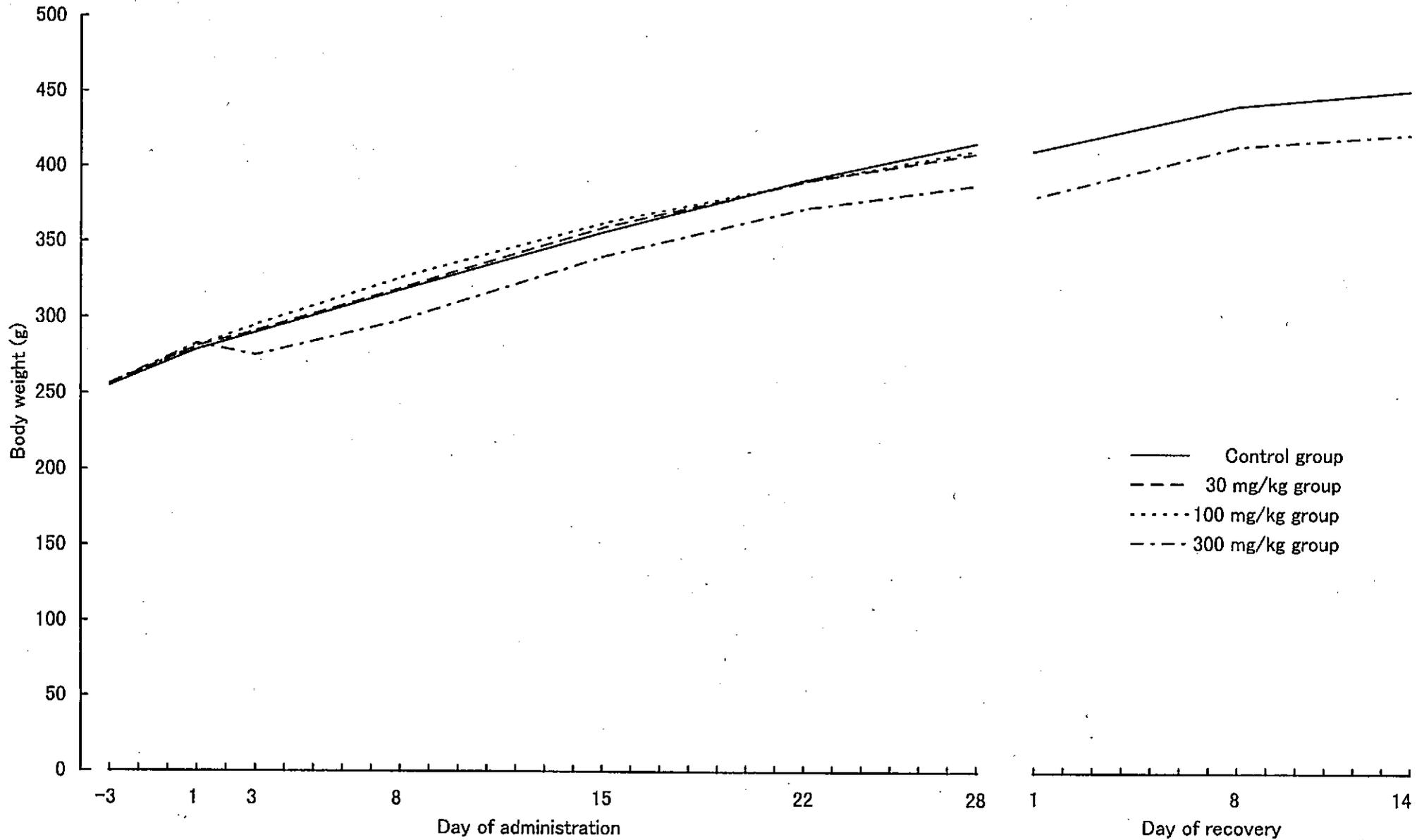


Fig. 1 Mean body weight in male rats administered 1-phenyl-1-xylylethane orally for 28 days

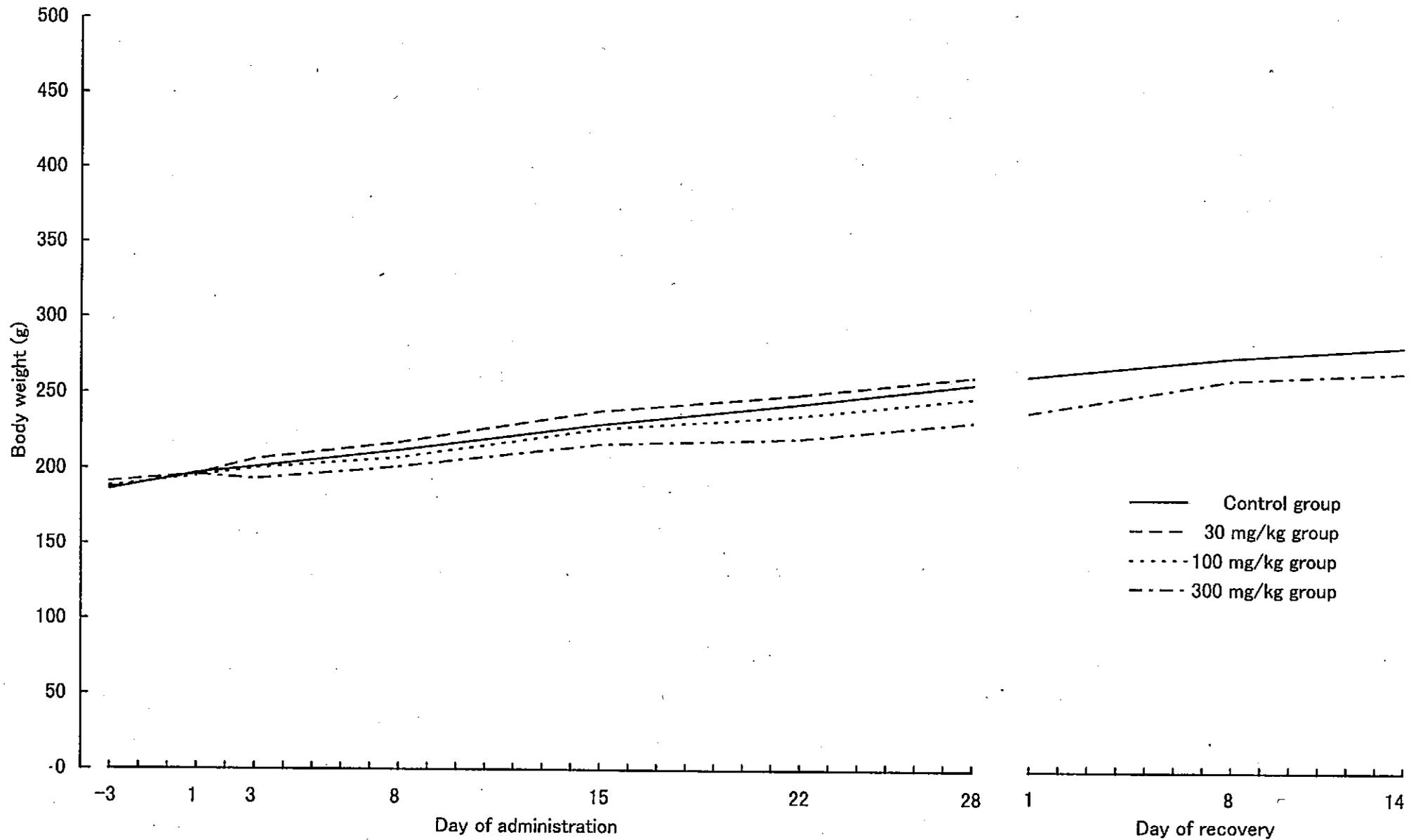


Fig. 2 Mean body weight in female rats administered 1-phenyl-1-xylyethane orally for 28 days

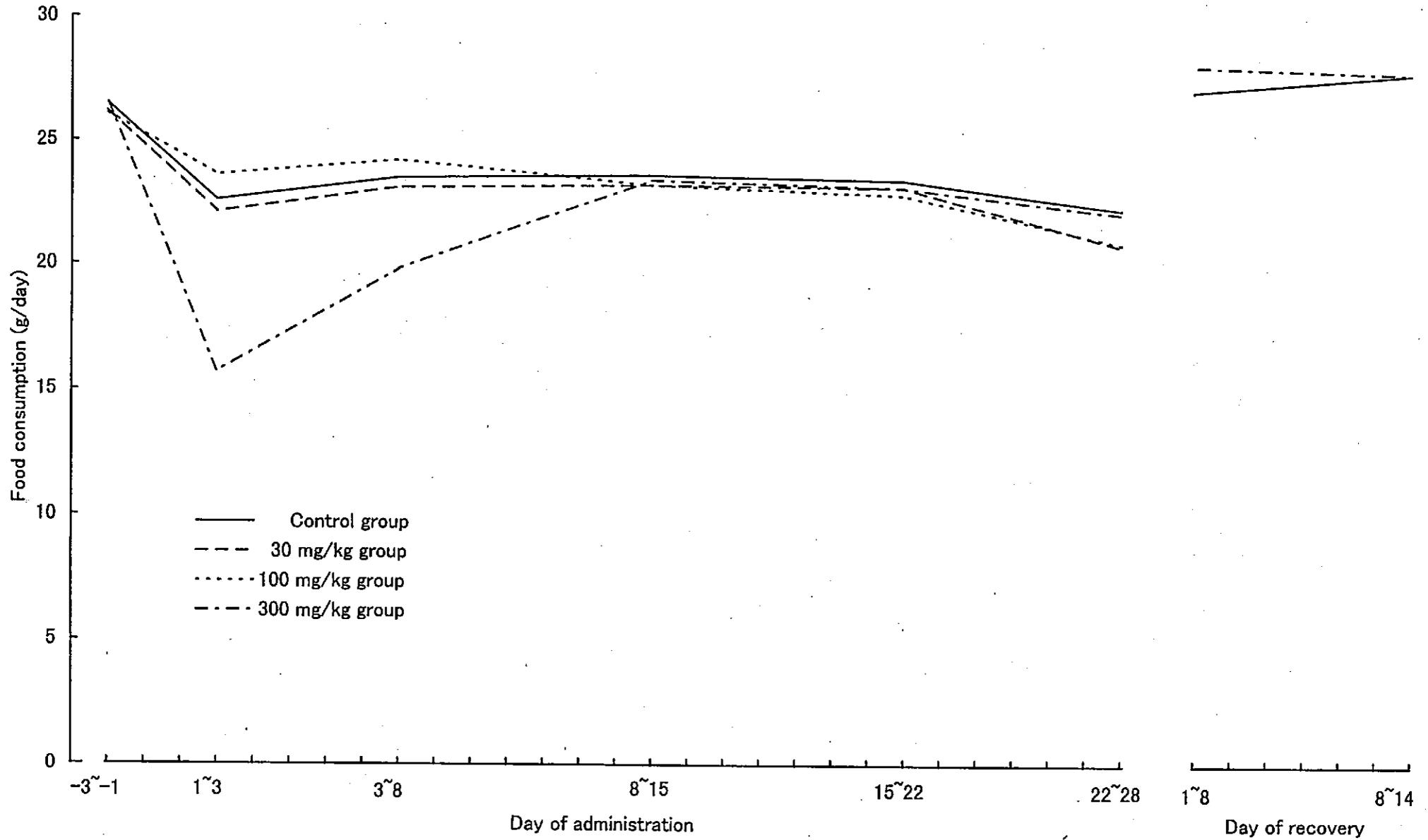


Fig. 3 Mean food consumption in male rats administered 1-phenyl-1-xylene orally for 28 days

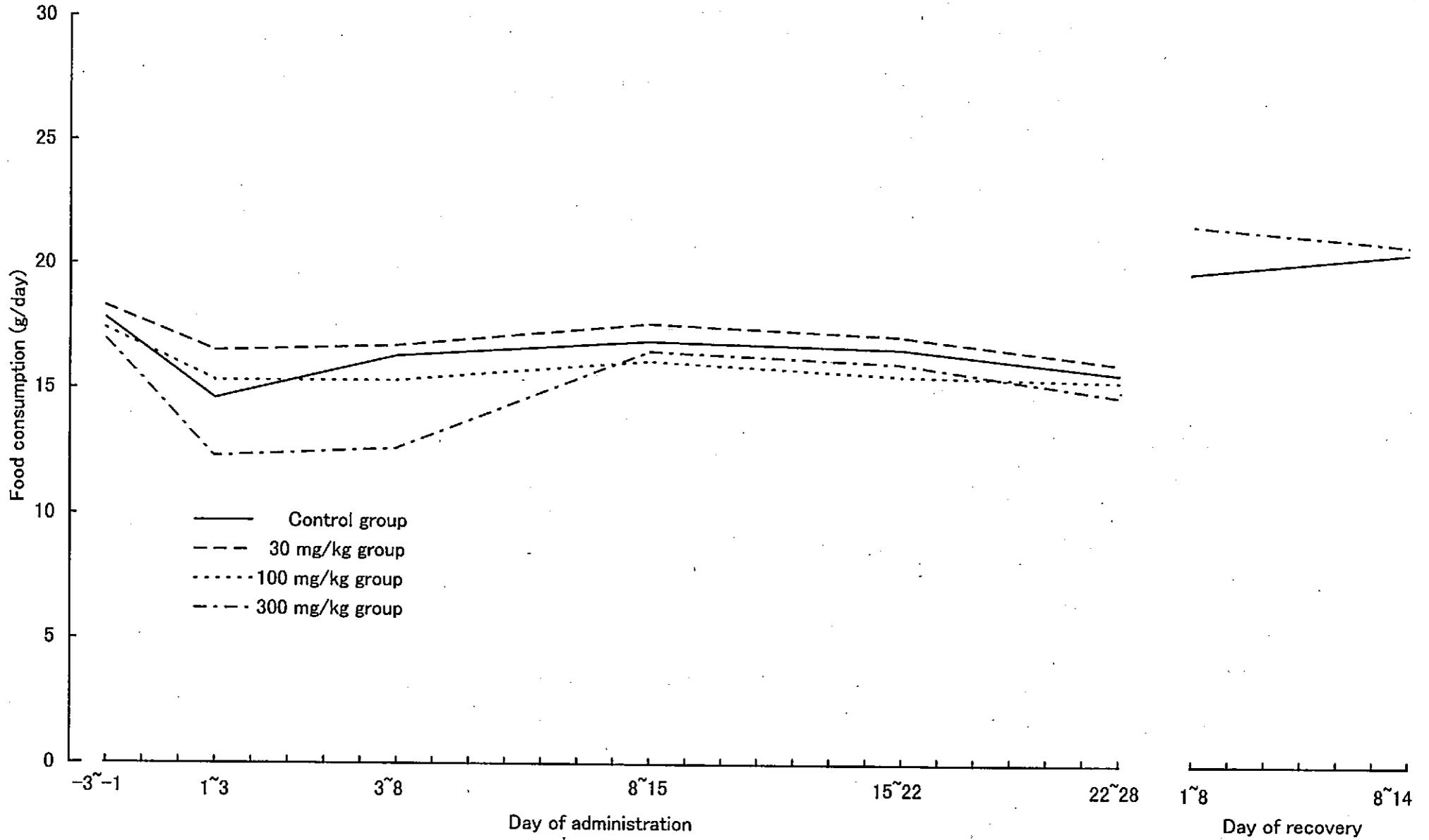


Fig. 4 Mean food consumption in female rats administered 1-phenyl-1-xilylethane orally for 28 days

Table 1 General condition in male rats administered 1-phenyl-1-xylylethane orally for 28 days

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
<b>Administration period</b>				
Number of animals observed	12	6	6	12
Number of animals with abnormal signs	0	0	2	12
Number of animals with the following signs				
Salivation	0	0	2	11
Staggering gait	0	0	0	7
Loose stool	0	0	0	1
Loss of fur	0	0	0	1
<b>Recovery period</b>				
Number of animals observed	6	.	.	6
Number of animals with abnormal signs	0	.	.	1
Number of animals with the following signs				
Loss of fur	0	.	.	1

Table 2 General condition in female rats administered 1-phenyl-1-xylylethane orally for 28 days

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
Administration period				
Number of animals observed	12	6	6	12
Number of animals with abnormal signs	0	0	0	12
Number of animals with the following signs				
Decrease in movement	0	0	0	1
Prone position	0	0	0	1
Salivation	0	0	0	11
Staggering gait	0	0	0	4
Loss of fur	0	0	0	7
Scant feces	0	0	0	6
Recovery period				
Number of animals observed	6	.	.	6
Number of animals with abnormal signs	0	.	.	5
Number of animals with the following signs				
Loss of fur	0	.	.	5

Table 3 Functional observational battery in male rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control	30		100		300		
Posture :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
Convulsions :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
Respiration :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
Stereotype :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	

Each value represents Mean ± S.D. (scores)

B : Before administration

D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 3 (Continued-1) Functional observational battery in male rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control	30		100		300		
Abnormal behavior :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
Handling difficulty :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
Abnormal vocalization :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
Muscle tone :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	

Each value represents Mean ± S.D. (scores)

B : Before administration

D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 3 (Continued-2)

Functional observational battery in male rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control		30		100		300	
Fur appearance :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
Piloerection :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
Skin/visual mucosa :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
Pupil size :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)

Each value represents Mean ± S.D. (scores)

B : Before administration

D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 3 (Continued-3)

Functional observational battery in male rats administered 1-phenyl-1-xylethane orally for 28 days

		Control		1-phenyl-1-xylethane (mg/kg)							
				30		100		300			
Salivation :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.1 ± 0.3	(12)		
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.8 ± 0.5 **	(12)		
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.2 ± 0.4	(6)	0.7 ± 0.5 **	(12)		
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.2 ± 0.4	(6)	0.8 ± 0.5 **	(12)		
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
Lacrimation :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
Righting reflex :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
Consciousness :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)		
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		

Each value represents Mean ± S.D. (scores)

B : Before administration      D : Day of administration

R : Day of recovery

( ) : Number of animals

\*\* Significantly different from control (P&lt;0.01)

Table 3 (Continued-4)

Functional observational battery in male rats administered 1-phenyl-1-xylylethane orally for 28 days

		Control		1-phenyl-1-xylylethane (mg/kg)							
				30		100		300			
Gait <sup>a)</sup> :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
Defecation <sup>b)</sup> : (counts / 2 min)	B3	0.0 ± 0.0	(12)	1.0 ± 1.3 *	(6)	0.2 ± 0.4	(6)	0.3 ± 0.5	(12)		
	D1	0.6 ± 1.7	(12)	0.8 ± 1.0	(6)	0.2 ± 0.4	(6)	0.5 ± 0.9	(12)		
	D7	0.3 ± 0.5	(12)	0.5 ± 0.8	(6)	0.3 ± 0.8	(6)	0.3 ± 0.7	(12)		
	D14	0.3 ± 0.8	(12)	0.7 ± 1.0	(6)	0.2 ± 0.4	(6)	0.3 ± 0.6	(12)		
	D21	0.2 ± 0.4	(12)	0.5 ± 0.8	(6)	0.2 ± 0.4	(6)	0.2 ± 0.6	(12)		
	D28	0.5 ± 1.2	(12)	0.0 ± 0.0	(6)	0.3 ± 0.8	(6)	0.2 ± 0.6	(12)		
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)		
Urination <sup>b)</sup> : (counts / 2 min)	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.2 ± 0.4	(6)	0.2 ± 0.4	(12)		
	D1	0.0 ± 0.0	(12)	0.2 ± 0.4	(6)	0.0 ± 0.0	(6)	0.2 ± 0.4	(12)		
	D7	0.0 ± 0.0	(12)	0.2 ± 0.4	(6)	0.0 ± 0.0	(6)	0.3 ± 0.7	(12)		
	D14	0.2 ± 0.4	(12)	0.2 ± 0.4	(6)	0.5 ± 0.5	(6)	0.4 ± 0.5	(12)		
	D21	0.2 ± 0.4	(12)	0.8 ± 0.4 *	(6)	0.5 ± 0.5	(6)	0.3 ± 0.5	(12)		
	D28	0.3 ± 0.6	(12)	0.3 ± 0.5	(6)	0.3 ± 0.5	(6)	0.1 ± 0.3	(12)		
	R7	0.5 ± 0.5	(6)	.	.	.	.	0.0 ± 0.0	(6)		
	R14	0.2 ± 0.4	(6)	.	.	.	.	0.2 ± 0.4	(6)		
Rearing <sup>b)</sup> : (counts / 2 min)	B3	3.0 ± 1.5	(12)	2.3 ± 3.0	(6)	1.3 ± 1.0	(6)	2.0 ± 1.5	(12)		
	D1	4.9 ± 3.7	(12)	3.8 ± 3.2	(6)	1.8 ± 1.9	(6)	3.8 ± 2.7	(12)		
	D7	1.3 ± 1.4	(12)	0.7 ± 1.0	(6)	0.5 ± 0.8	(6)	1.3 ± 2.2	(12)		
	D14	3.2 ± 3.0	(12)	2.8 ± 3.4	(6)	1.5 ± 1.8	(6)	2.0 ± 2.4	(12)		
	D21	3.8 ± 2.8	(12)	2.5 ± 3.4	(6)	3.2 ± 2.6	(6)	3.1 ± 3.9	(12)		
	D28	3.6 ± 3.4	(12)	3.5 ± 4.2	(6)	2.0 ± 2.5	(6)	2.4 ± 2.5	(12)		
	R7	3.2 ± 1.2	(6)	.	.	.	.	3.5 ± 2.3	(6)		
	R14	3.2 ± 1.9	(6)	.	.	.	.	3.7 ± 1.9	(6)		

<sup>a)</sup> Each value represents Mean ± S.D. (scores)

<sup>b)</sup> Each value represents Mean ± S.D. (frequencies)

B : Before administration      D : Day of administration

R : Day of recovery

( ) : Number of animals

\* Significantly different from control (P<0.05)

Table 4 Functional observational battery in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control		30		100		300	
Posture :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.1 ± 0.3	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
Convulsions :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
Respiration :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
Stereotype :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	0.0 ± 0.0	(6)

Each value represents Mean ± S.D. (scores)

B : Before administration

D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 4 (Continued-1) Functional observational battery in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control	30		100		300		
Abnormal behavior :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
Handling difficulty :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
Abnormal vocalization :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
Muscle tone :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	

Each value represents Mean ± S.D. (scores)

B : Before administration      D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 4 (Continued-2)

Functional observational battery in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control	30		100		300		
Fur appearance :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
Piloerection :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
Skin/visual mucosa :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
Pupil size :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)	
	R7	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	
	R14	0.0 ± 0.0 (6)	.	.	.	.	.	0.0 ± 0.0 (6)	

Each value represents Mean ± S.D. (scores)

B : Before administration

D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 4 (Continued-3)

Functional observational battery in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		Control		1-phenyl-1-xylylethane (mg/kg)							
				30		100		300			
Salivation :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.2 ± 0.4	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.4 ± 0.5 *	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.5 ± 0.5 **	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.7 ± 0.5 **	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
Lacrimation :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
Righting reflex :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
Consciousness :	B3	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D1	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D7	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D14	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D21	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	D28	0.0 ± 0.0	(12)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(6)	0.0 ± 0.0	(12)
	R7	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)
	R14	0.0 ± 0.0	(6)	.	.	.	.	.	.	0.0 ± 0.0	(6)

Each value represents Mean ± S.D. (scores)

B : Before administration    D : Day of administration

R : Day of recovery

( ) : Number of animals

\* Significantly different from control (P&lt;0.05)

\*\* Significantly different from control (P&lt;0.01)

Table 4 (Continued-4) Functional observational battery in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control	30		100		300		
Gait <sup>a)</sup> :	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)		
	D1	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)			
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	R7	0.0 ± 0.0 (6)	.	.	0.0 ± 0.0 (6)				
	R14	0.0 ± 0.0 (6)	.	.	0.0 ± 0.0 (6)				
Defecation <sup>b)</sup> : (counts / 2 min)	B3	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)			
	D1	0.1 ± 0.3 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D7	0.2 ± 0.6 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	R7	0.0 ± 0.0 (6)	.	.	0.0 ± 0.0 (6)				
	R14	0.0 ± 0.0 (6)	.	.	0.0 ± 0.0 (6)				
Urination <sup>b)</sup> : (counts / 2 min)	B3	0.0 ± 0.0 (12)	0.2 ± 0.4 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D1	0.1 ± 0.3 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.1 ± 0.3 (12)				
	D7	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D14	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D21	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	D28	0.0 ± 0.0 (12)	0.0 ± 0.0 (6)	0.0 ± 0.0 (6)	0.0 ± 0.0 (12)				
	R7	0.0 ± 0.0 (6)	.	.	0.0 ± 0.0 (6)				
	R14	0.0 ± 0.0 (6)	.	.	0.0 ± 0.0 (6)				
Rearing <sup>b)</sup> : (counts / 2 min)	B3	7.0 ± 4.3 (12)	5.2 ± 2.6 (6)	5.7 ± 2.5 (6)	6.4 ± 3.7 (12)				
	D1	9.7 ± 4.1 (12)	7.2 ± 4.3 (6)	11.2 ± 5.1 (6)	7.7 ± 3.3 (12)				
	D7	8.3 ± 4.0 (12)	7.0 ± 3.8 (6)	9.2 ± 7.4 (6)	4.7 ± 3.7 (12)				
	D14	10.3 ± 4.8 (12)	7.0 ± 3.7 (6)	10.2 ± 8.5 (6)	6.9 ± 4.3 (12)				
	D21	11.5 ± 2.6 (12)	13.2 ± 4.0 (6)	9.5 ± 7.9 (6)	7.9 ± 5.4 (12)				
	D28	11.7 ± 3.8 (12)	10.7 ± 3.7 (6)	10.3 ± 6.7 (6)	8.3 ± 4.1 (12)				
	R7	11.2 ± 3.2 (6)	.	.	9.5 ± 6.3 (6)				
	R14	11.0 ± 2.5 (6)	.	.	7.7 ± 2.9 (6)				

<sup>a)</sup> Each value represents Mean ± S.D. (scores)

<sup>b)</sup> Each value represents Mean ± S.D. (frequencies)

B : Before administration      D : Day of administration

R : Day of recovery

( ) : Number of animals

Table 5-1 Functional tests in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 4th week of administration -

	Control	1-phenyl-1-xylylethane (mg/kg)			
		30	100	300	
Number of animals	12	6	6	12	
Score : Pupillary reflex	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Visual placing response	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Auditory response	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Pain response	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Aerial righting	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Grip strength (kg) :					
I	1.035 ± 0.229	1.061 ± 0.314	1.027 ± 0.205	1.035 ± 0.180	
II	1.089 ± 0.209	1.113 ± 0.312	0.989 ± 0.117	1.061 ± 0.151	
Mean	1.062 ± 0.204	1.087 ± 0.306	1.008 ± 0.144	1.048 ± 0.141	
Landing foot-splay (cm) :					
I	6.8 ± 1.9	7.4 ± 2.3	7.9 ± 2.5	7.0 ± 1.6	
II	6.5 ± 2.4	6.8 ± 3.0	7.9 ± 2.2	6.1 ± 1.4	
Mean	6.7 ± 2.1	7.1 ± 2.6	8.0 ± 2.3	6.6 ± 1.5	

Each value represents Mean ± S.D.

I : First trial      II : Second trial

Table 5-2 Functional tests in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 2nd week of recovery -

		Control	1-phenyl-1-xylylethane (mg/kg)
			300
Number of animals		6	6
Score : Pupillary reflex		0.0 ± 0.0	0.0 ± 0.0
Visual placing response		0.0 ± 0.0	0.0 ± 0.0
Auditory response		0.0 ± 0.0	0.0 ± 0.0
Pain response		0.0 ± 0.0	0.0 ± 0.0
Aerial righting		0.0 ± 0.0	0.0 ± 0.0
Grip strength (kg) :	I	1.545 ± 0.290	1.608 ± 0.114
	II	1.662 ± 0.252	1.462 ± 0.133
	Mean	1.604 ± 0.252	1.536 ± 0.096
Landing foot-splay (cm) :	I	4.8 ± 2.2	5.3 ± 1.2
	II	4.7 ± 1.9	5.1 ± 0.9
	Mean	4.8 ± 2.0	5.2 ± 1.0

Each value represents Mean ± S.D.

I : First trial      II : Second trial

Table 6-1 Functional tests in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 4th week of administration -

	Control	1-phenyl-1-xylylethane (mg/kg)			
		30	100	300	
Number of animals	12	6	6	12	
Score : Pupillary reflex	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Visual placing response	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Auditory response	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Pain response	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Aerial righting	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Grip strength (kg) :					
I	0.871 ± 0.196	0.833 ± 0.218	0.769 ± 0.174	0.818 ± 0.175	
II	0.858 ± 0.191	0.867 ± 0.154	0.868 ± 0.143	0.849 ± 0.153	
Mean	0.865 ± 0.191	0.851 ± 0.176	0.819 ± 0.149	0.834 ± 0.160	
Landing foot-splay (cm) :					
I	5.5 ± 1.5	5.1 ± 0.6	5.8 ± 1.9	4.3 ± 1.5	
II	5.1 ± 1.5	4.4 ± 1.0	5.7 ± 1.4	4.3 ± 1.2	
Mean	5.3 ± 1.5	4.8 ± 0.7	5.8 ± 1.6	4.3 ± 1.3	

Each value represents Mean ± S.D.

I : First trial      II : Second trial

Table 6-2 Functional tests in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 2nd week of recovery -

		Control		1-phenyl-1-xylylethane (mg/kg)	
		6		300	
Number of animals		6		6	
Score : Pupillary reflex		0.0 ± 0.0		0.0 ± 0.0	
Visual placing response		0.0 ± 0.0		0.0 ± 0.0	
Auditory response		0.0 ± 0.0		0.0 ± 0.0	
Pain response		0.0 ± 0.0		0.0 ± 0.0	
Aerial righting		0.0 ± 0.0		0.0 ± 0.0	
Grip strength (kg) :	I	1.251 ± 0.218		1.298 ± 0.100	
	II	1.197 ± 0.260		1.250 ± 0.159	
	Mean	1.224 ± 0.216		1.275 ± 0.120	
Landing foot-splay (cm) :	I	5.0 ± 2.1		5.4 ± 1.2	
	II	5.2 ± 1.7		4.8 ± 1.0	
	Mean	5.2 ± 1.9		5.1 ± 1.0	

Each value represents Mean ± S.D.

I : First trial      II : Second trial

Table 7 Spontaneous motor activity in male rats administered 1-phenyl-1-xylylethane orally for 28 days

	Control	1-phenyl-1-xylylethane (mg/kg)					
		30		100		300	
Motor activity (counts / 60 min)							
The 4th week of administration	387 ± 263 (12)	227 ± 138 (6)	226 ± 148 (6)	227 ± 124 (12)			
The 2nd week of recovery	266 ± 115 (6)			388 ± 233 (6)			

Each value represents Mean ± S.D.

( ): Number of animals

Table 8 Spontaneous motor activity in female rats administered 1-phenyl-1-xylylethane orally for 28 days

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
Motor activity (counts / 60 min)				
The 4th week of administration	286 ± 82 (12)	287 ± 190 (6)	253 ± 155 (6)	249 ± 107 (12)
The 2nd week of recovery	193 ± 87 (6)	.	.	503 ± 201 ** (6)

Each value represents Mean ± S.D.

( ): Number of animals

\*\* Significantly different from control (P<0.01)

Table 9 Body weight in male rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control	30		100		300		
Day of administration	-3	255 ± 9	(12)	256 ± 9	(6)	256 ± 8	(6)	256 ± 10	(12)
	1	279 ± 10	(12)	281 ± 9	(6)	281 ± 10	(6)	283 ± 12	(12)
	3	290 ± 13	(12)	291 ± 8	(6)	295 ± 12	(6)	275 ± 17 *	(12)
	8	318 ± 19	(12)	319 ± 11	(6)	326 ± 16	(6)	298 ± 21 *	(12)
	15	356 ± 21	(12)	359 ± 16	(6)	362 ± 19	(6)	340 ± 26	(12)
	22	391 ± 28	(12)	390 ± 18	(6)	390 ± 27	(6)	372 ± 30	(12)
	28	416 ± 32	(12)	409 ± 22	(6)	411 ± 29	(6)	388 ± 31	(12)
Day of recovery	1	411 ± 39	(6)	.	.	.	.	380 ± 19	(6)
	8	441 ± 39	(6)	.	.	.	.	414 ± 21	(6)
	14	451 ± 36	(6)	.	.	.	.	422 ± 20	(6)

Each value represents Mean ± S.D. (g)

( ): Number of animals

\* Significantly different from control (P<0.05)

Table 10 Body weight in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control		30		100		300	
Day of administration	-3	186 ± 8	(12)	191 ± 10	(6)	188 ± 9	(6)	187 ± 9	(12)
	1	197 ± 10	(12)	196 ± 12	(6)	195 ± 12	(6)	196 ± 10	(12)
	3	201 ± 6	(12)	206 ± 11	(6)	200 ± 12	(6)	193 ± 10	(12)
	8	212 ± 9	(12)	217 ± 10	(6)	207 ± 14	(6)	201 ± 11 *	(12)
	15	229 ± 10	(12)	238 ± 13	(6)	226 ± 18	(6)	216 ± 14 *	(12)
	22	243 ± 13	(12)	249 ± 16	(6)	235 ± 22	(6)	220 ± 15 **	(12)
	28	256 ± 14	(12)	261 ± 13	(6)	247 ± 22	(6)	231 ± 17 **	(12)
Day of recovery	1	262 ± 10	(6)	.	.	.	.	238 ± 18 *	(6)
	8	275 ± 14	(6)	.	.	.	.	260 ± 22	(6)
	14	282 ± 15	(6)	.	.	.	.	265 ± 20	(6)

Each value represents Mean ± S.D. (g)

( ): Number of animals

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 11 Food consumption in male rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control		30		100		300	
Day of administration	-3~-1	26.5 ± 1.9	(12)	26.2 ± 2.1	(6)	26.1 ± 2.0	(6)	26.5 ± 1.3	(12)
	1~3	22.6 ± 2.0	(12)	22.1 ± 1.3	(6)	23.6 ± 1.9	(6)	15.7 ± 3.8 **	(12)
	3~8	23.5 ± 1.7	(12)	23.1 ± 2.3	(6)	24.2 ± 1.9	(6)	19.8 ± 2.5 **	(12)
	8~15	23.6 ± 1.7	(12)	23.2 ± 2.3	(6)	23.2 ± 1.3	(6)	23.4 ± 2.2	(12)
	15~22	23.4 ± 1.8	(12)	23.1 ± 2.0	(6)	22.8 ± 1.3	(6)	23.1 ± 2.6	(12)
	22~28	22.2 ± 2.2	(12)	20.7 ± 2.0	(6)	20.8 ± 1.4	(6)	22.0 ± 1.7	(12)
Day of recovery	1~8	27.0 ± 2.2	(6)					28.0 ± 1.9	(6)
	8~14	27.7 ± 1.1	(6)					27.7 ± 1.8	(6)

Each value represents Mean ± S.D. (g/day)

( ): Number of animals

\*\* Significantly different from control (P<0.01)

Table 12 Food consumption in female rats administered 1-phenyl-1-xylylethane orally for 28 days

		1-phenyl-1-xylylethane (mg/kg)							
		Control		30		100		300	
Day of administration	-3~-1	17.8 ± 1.6	(12)	18.3 ± 1.4	(6)	17.4 ± 1.8	(6)	16.9 ± 1.5	(12)
	1~3	14.6 ± 1.5	(12)	16.5 ± 1.8	(6)	15.3 ± 1.5	(6)	12.3 ± 2.2 **	(12)
	3~8	16.3 ± 1.0	(12)	16.7 ± 1.2	(6)	15.3 ± 0.9	(6)	12.6 ± 1.7 **	(12)
	8~15	16.9 ± 1.0	(12)	17.6 ± 1.8	(6)	16.1 ± 1.1	(6)	16.5 ± 1.5	(12)
	15~22	16.6 ± 1.1	(12)	17.1 ± 2.3	(6)	15.5 ± 1.5	(6)	16.0 ± 2.1	(12)
	22~28	15.6 ± 0.9	(12)	16.0 ± 1.9	(6)	15.3 ± 1.2	(6)	14.7 ± 2.1	(12)
Day of recovery	1~8	19.7 ± 1.4	(6)					21.6 ± 1.3 *	(6)
	8~14	20.5 ± 0.7	(6)					20.8 ± 1.0	(6)

Each value represents Mean ± S.D. (g/day)

( ): Number of animals

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Table 13 and 14      Urinary findings  
- List of abbreviations -

Abbreviation	Expansion
Vol.	Volume
Col.	Colour
S.G.	Specific gravity
Pro.	Protein
Glu.	Glucose
Ket.	Ketone bodies
Bil.	Bilirubin
Occ.	Occult blood
Uro.	Urobilinogen
Y	Yellow
LY	Light yellow
Grade	
-	Negative
+-	Trace
+	Slight
+++	Considerable

Table 13-1 Urinary findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 4th week of administration -

	Control	1-phenyl-1-xylylethane (mg/kg)			
		30	100	300	
Number of animals	12	6	6	12	
Water intake <sup>a)</sup> (mL/16hr)	31.1 ± 9.0	26.1 ± 5.3	25.9 ± 6.1	32.4 ± 6.0	
Vol. <sup>a)</sup> (mL/16hr)	16.2 ± 7.0	12.7 ± 4.6	11.4 ± 3.2	13.8 ± 4.7	
Col. <sup>b)</sup> : Y	12	6	6	12	
S.G. <sup>a)</sup>	1.038 ± 0.008	1.042 ± 0.008	1.042 ± 0.007	1.042 ± 0.007	
pH <sup>b)</sup> : ~8.0	6	3	1	8	
~9.0	6	3	5	4	
Pro. <sup>b)</sup> : -	6	3	1	10	
+	6	2	4	2	
+	0	1	1	0	
Glu. <sup>b)</sup> : -	12	6	6	12	
Ket. <sup>b)</sup> : -	5	0	2	10	
+	2	4	3	2	
+	5	2	1	0	
Bil. <sup>b)</sup> : -	12	6	6	12	
Occ. <sup>b)</sup> : -	12	5	6	12	
+	0	1	0	0	
Uro. <sup>b)</sup> : 0.1 (Ehrlich unit/dL)	12	6	6	12	

<sup>a)</sup> Each value represents Mean ± S.D.

<sup>b)</sup> Each value represents the number of animals with each finding.

Table 13-2 Urinary findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 2nd week of recovery -

	Control		1-phenyl-1-xylylethane (mg/kg)	
			300	
Number of animals	6		6	
Water intake <sup>a)</sup> (mL/16hr)	35.7 ± 10.7		29.5 ± 8.1	
Vol. <sup>a)</sup> (mL/16hr)	19.0 ± 9.4		14.1 ± 5.2	
Col. <sup>b)</sup> : Y	6		6	
S.G. <sup>a)</sup>	1.038 ± 0.009		1.044 ± 0.007	
pH <sup>b)</sup> : ~8.0	2		2	
~9.0	4		4	
Pro. <sup>b)</sup> : -	4		4	
+-	2		1	
+	0		1	
Glu. <sup>b)</sup> : -	6		6	
Ket. <sup>b)</sup> : -	5		3	
+-	0		1	
+	1		2	
Bil. <sup>b)</sup> : -	6		6	
Occ. <sup>b)</sup> : -	6		5	
: +-	0		1	
Uro. <sup>b)</sup> : 0.1 (Ehrlich unit/dL)	6		6	

<sup>a)</sup> Each value represents Mean ± S.D.

<sup>b)</sup> Each value represents the number of animals with each finding.

Table 14-1 Urinary findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 4th week of administration -

	1-phenyl-1-xylylethane (mg/kg)			
	Control	30	100	300
Number of animals	12	6	6	12
Water intake <sup>a)</sup> (mL/16hr)	17.8 ± 5.9	20.9 ± 5.2	21.8 ± 5.4	28.6 ± 12.6 **
Vol. <sup>a)</sup> (mL/16hr)	8.8 ± 4.4	11.2 ± 4.6	11.2 ± 3.3	17.0 ± 9.9 *
Col. <sup>b)</sup> : Y	12	6	6	11
LY	0	0	0	1
S.G. <sup>a)</sup>	1.044 ± 0.011	1.040 ± 0.010	1.038 ± 0.006	1.033 ± 0.009 *
pH <sup>b)</sup> : ~7.0	1	1	0	2
~8.0	6	3	2	5
~9.0	5	2	4	5
Pro. <sup>b)</sup> : -	8	3	4	12
+-	4	3	2	0
Glu. <sup>b)</sup> : -	12	6	6	12
Ket. <sup>b)</sup> : -	12	6	6	12
Bil. <sup>b)</sup> : -	12	6	6	12
Occ. <sup>b)</sup> : -	12	5	5	12
+	0	0	1	0
+++	0	1	0	0
Uro. <sup>b)</sup> : 0.1 (Ehrlich unit/dL)	12	6	6	12

<sup>a)</sup> Each value represents Mean ± S.D.

<sup>b)</sup> Each value represents the number of animals with each finding.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 14-2 Urinary findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- The 2nd week of recovery -

	Control		1-phenyl-1-xylylethane (mg/kg)	
			300	
Number of animals	6		6	
Water intake <sup>a)</sup> (mL/16hr)	24.1 ± 8.5		19.5 ± 4.8	
Vol. <sup>a)</sup> (mL/16hr)	14.1 ± 6.6		9.0 ± 3.3	
Col. <sup>b)</sup> : Y	6		6	
S.G. <sup>a)</sup>	1.040 ± 0.009		1.048 ± 0.005	
pH <sup>b)</sup> : ~8.0	6		6	
Pro. <sup>b)</sup> : -	6		6	
Glu. <sup>b)</sup> : -	6		6	
Ket. <sup>b)</sup> : -	6		6	
Bil. <sup>b)</sup> : -	6		6	
Occ. <sup>b)</sup> : -	5		6	
+	1		0	
Uro. <sup>b)</sup> : 0.1 (Ehrlich unit/dL)	6		6	

<sup>a)</sup> Each value represents Mean ± S.D.

<sup>b)</sup> Each value represents the number of animals with each finding.

Table 15 and 16

Hematological findings  
- List of abbreviations -

2000TT278

Abbreviation	Expansion
RBC	Red blood cell count
Hb	Hemoglobin concentration
Ht	Hematocrit
PT	Prothrombin time
APTT	Activated partial thromboplastin time
Plate.	Platelet count
WBC	White blood cell count
St.	Staff form of neutrocyte
Seg.	Segment form of neutrocyte
Eo.	Eosinocyte
Ba.	Basocyte
Ly.	Lymphocyte
Mo.	Monocyte

Table 15-1 Hematological findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
Number of animals	6	6	6	6
RBC (10 <sup>4</sup> /μL)	803 ± 36	811 ± 32	796 ± 37	801 ± 18
Hb (g/dL)	16.3 ± 0.8	16.4 ± 1.0	16.1 ± 0.5	16.4 ± 0.6
Ht (%)	46.5 ± 2.2	46.6 ± 2.6	45.6 ± 1.3	46.4 ± 1.8
PT (sec.)	12.0 ± 0.5	14.7 ± 3.0	16.8 ± 1.9	22.4 ± 1.7 **
APTT (sec.)	21.8 ± 1.7	25.4 ± 5.0	29.2 ± 2.9 **	32.6 ± 2.6 **
Plate. (10 <sup>4</sup> /μL)	106.7 ± 30.2	91.8 ± 11.9	96.4 ± 5.6	97.7 ± 7.7
WBC (10 <sup>2</sup> /μL)	97 ± 26	84 ± 26	82 ± 17	104 ± 26
WBC differential count (%)				
St.	0.1 ± 0.2	0.1 ± 0.2	0.0 ± 0.0	0.0 ± 0.0
Seg.	7.3 ± 4.7	6.3 ± 3.6	5.6 ± 1.3	5.6 ± 2.2
Eo.	0.3 ± 0.4	0.3 ± 0.4	0.1 ± 0.2	0.2 ± 0.3
Ba.	0.0 ± 0.0	0.1 ± 0.2	0.0 ± 0.0	0.0 ± 0.0
Ly.	91.8 ± 4.8	92.9 ± 3.6	93.9 ± 1.4	94.0 ± 2.1
Mo.	0.6 ± 0.2	0.3 ± 0.3	0.4 ± 0.5	0.3 ± 0.3

Each value represents Mean ± S.D.

\*\* Significantly different from control (P<0.01)

2000TT278

Table 15-2 Hematological findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

	Control	1-phenyl-1-xylylethane (mg/kg)	
		300	
Number of animals	6	6	
RBC (10 <sup>4</sup> /μL)	825 ± 18	801 ± 29	
Hb (g/dL)	16.3 ± 0.5	15.7 ± 0.4 *	
Ht (%)	46.5 ± 1.5	45.8 ± 1.6	
PT (sec.)	11.7 ± 1.4	12.2 ± 0.8	
APTT (sec.)	20.2 ± 4.5	20.8 ± 3.0	
Plate. (10 <sup>4</sup> /μL)	104.9 ± 10.0	103.2 ± 8.2	
WBC (10 <sup>2</sup> /μL)	99 ± 17	96 ± 16	
WBC differential count (%)			
St.	0.2 ± 0.3	0.0 ± 0.0	
Seg.	9.3 ± 5.6	12.8 ± 4.2	
Eo.	0.4 ± 0.2	0.6 ± 0.4	
Ba.	0.0 ± 0.0	0.1 ± 0.2	
Ly.	89.9 ± 5.7	86.3 ± 3.9	
Mo.	0.3 ± 0.3	0.3 ± 0.3	

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

Table 16-1 Hematological findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
Number of animals	6	6	6	6
RBC (10 <sup>4</sup> /μL)	745 ± 56	739 ± 53	750 ± 36	753 ± 68
Hb (g/dL)	15.2 ± 0.7	15.1 ± 0.8	15.6 ± 0.8	15.6 ± 1.3
Ht (%)	42.1 ± 2.7	41.4 ± 2.8	43.2 ± 2.4	42.0 ± 3.4
PT (sec.)	9.5 ± 0.4	9.4 ± 0.3	9.6 ± 0.2	10.2 ± 1.4
APTT (sec.)	13.9 ± 2.5	14.1 ± 2.5	15.3 ± 3.1	18.0 ± 6.4
Plate. (10 <sup>4</sup> /μL)	106.6 ± 15.4	111.7 ± 7.6	97.0 ± 9.6	107.6 ± 9.3
WBC (10 <sup>2</sup> /μL)	74 ± 19	82 ± 32	68 ± 13	74 ± 22
WBC differential count (%)				
St.	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Seg.	5.9 ± 2.1	3.3 ± 1.2	3.3 ± 2.1	2.6 ± 2.0 *
Eo.	0.3 ± 0.4	0.3 ± 0.3	0.3 ± 0.4	0.3 ± 0.3
Ba.	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Ly.	93.4 ± 2.4	96.2 ± 1.2	96.3 ± 2.2 *	96.9 ± 1.8 *
Mo.	0.3 ± 0.4	0.3 ± 0.4	0.0 ± 0.0	0.3 ± 0.3

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

2000TT278

Table 16-2 Hematological findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

	Control	1-phenyl-1-xylylethane (mg/kg)	
		300	
Number of animals	6	6	
RBC (10 <sup>4</sup> /μL)	742 ± 38	759 ± 30	
Hb (g/dL)	15.2 ± 0.6	15.5 ± 0.5	
Ht (%)	42.3 ± 2.0	43.8 ± 1.7	
PT (sec.)	9.3 ± 0.6	9.4 ± 0.5	
APTT (sec.)	12.8 ± 2.2	13.0 ± 1.5	
Plate. (10 <sup>4</sup> /μL)	102.3 ± 10.8	115.8 ± 9.1 *	
WBC (10 <sup>2</sup> /μL)	69 ± 15	67 ± 17	
WBC differential count (%)			
St.	0.0 ± 0.0	0.0 ± 0.0	
Seg.	11.6 ± 7.2	9.6 ± 4.3	
Eo.	0.6 ± 0.6	0.9 ± 0.7	
Ba.	0.0 ± 0.0	0.2 ± 0.3	
Ly.	87.1 ± 7.9	89.0 ± 3.9	
Mo.	0.8 ± 0.9	0.3 ± 0.4	

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

2000TT278

Table 17 and 18      Blood chemistry findings  
- List of abbreviations -

Abbreviation	Expansion
GOT	Glutamic oxaloacetic transaminase
GPT	Glutamic pyruvic transaminase
GLU	Glucose
BIL	Total bilirubin
UN	Urea nitrogen
CRE	Creatinine
CHO	Total cholesterol
TG	Triglyceride
TP	Total protein
ALB	Albumin

Table 17-1 Blood chemistry findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

		Control	1-phenyl-1-xylylethane (mg/kg)		
			30	100	300
Number of animals		6	6	6	6
GOT	(IU/L)	67.9 ± 9.1	67.6 ± 4.5	65.5 ± 4.6	74.2 ± 7.7
GPT	(IU/L)	23.2 ± 4.7	24.0 ± 2.5	30.1 ± 6.5	32.2 ± 5.0 *
GLU	(mg/dL)	129 ± 19	127 ± 9	125 ± 8	122 ± 18
BIL	(mg/dL)	0.05 ± 0.01	0.05 ± 0.01	0.04 ± 0.01 *	0.06 ± 0.01
UN	(mg/dL)	12.9 ± 1.1	12.4 ± 1.3	12.9 ± 1.1	14.3 ± 2.2
CRE	(mg/dL)	0.37 ± 0.05	0.35 ± 0.04	0.33 ± 0.06	0.37 ± 0.05
CHO	(mg/dL)	50 ± 4	59 ± 8	59 ± 10	70 ± 17 **
TG	(mg/dL)	23.0 ± 12.3	29.0 ± 16.2	35.7 ± 22.7	19.3 ± 5.1
TP	(g/dL)	5.89 ± 0.19	5.87 ± 0.27	5.71 ± 0.27	5.86 ± 0.41
ALB	(g/dL)	2.45 ± 0.12	2.42 ± 0.12	2.49 ± 0.18	2.49 ± 0.17

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Table 17-2 Blood chemistry findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

		1-phenyl-1-xylylethane (mg/kg)	
		Control	300
Number of animals		6	6
GOT	(IU/L)	81.5 ± 7.0	73.5 ± 3.7 *
GPT	(IU/L)	29.2 ± 5.6	28.8 ± 6.3
GLU	(mg/dL)	143 ± 9	134 ± 10
BIL	(mg/dL)	0.07 ± 0.01	0.06 ± 0.01 **
UN	(mg/dL)	17.4 ± 2.9	18.2 ± 1.7
CRE	(mg/dL)	0.46 ± 0.03	0.42 ± 0.06
CHO	(mg/dL)	60 ± 15	67 ± 11
TG	(mg/dL)	32.9 ± 10.1	28.3 ± 7.6
TP	(g/dL)	5.94 ± 0.23	5.87 ± 0.32
ALB	(g/dL)	2.37 ± 0.09	2.40 ± 0.12

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 18-1 Blood chemistry findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

		Control	1-phenyl-1-xylylethane (mg/kg)		
			30	100	300
Number of animals		6	6	6	6
GOT	(IU/L)	67.9 ± 6.4	61.8 ± 7.2	60.4 ± 5.1	59.9 ± 3.5
GPT	(IU/L)	19.9 ± 2.6	21.4 ± 4.6	20.3 ± 2.8	22.3 ± 0.9
GLU	(mg/dL)	122 ± 12	131 ± 12	121 ± 14	99 ± 16 *
BIL	(mg/dL)	0.06 ± 0.02	0.05 ± 0.01	0.05 ± 0.01	0.06 ± 0.01
UN	(mg/dL)	14.9 ± 1.7	14.1 ± 2.0	15.6 ± 1.6	13.7 ± 2.1
CRE	(mg/dL)	0.38 ± 0.04	0.41 ± 0.03	0.41 ± 0.05	0.34 ± 0.04
CHO	(mg/dL)	51 ± 11	65 ± 17	73 ± 12	89 ± 28 **
TG	(mg/dL)	5.3 ± 2.5	8.6 ± 4.6	10.0 ± 3.2	16.6 ± 5.3 **
TP	(g/dL)	5.76 ± 0.24	5.92 ± 0.41	6.07 ± 0.23	5.78 ± 0.40
ALB	(g/dL)	2.56 ± 0.15	2.58 ± 0.17	2.64 ± 0.16	2.42 ± 0.17

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Table 18-2 Blood chemistry findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

		1-phenyl-1-xylylethane (mg/kg)	
		Control	300
Number of animals		6	6
GOT	(IU/L)	77.0 ± 12.0	67.8 ± 10.4
GPT	(IU/L)	27.2 ± 6.6	22.5 ± 3.4
GLU	(mg/dL)	130 ± 15	124 ± 13
BIL	(mg/dL)	0.08 ± 0.02	0.06 ± 0.01
UN	(mg/dL)	19.2 ± 0.4	18.8 ± 1.9
CRE	(mg/dL)	0.51 ± 0.07	0.48 ± 0.05
CHO	(mg/dL)	75 ± 14	88 ± 16
TG	(mg/dL)	19.6 ± 12.1	21.2 ± 13.6
TP	(g/dL)	6.22 ± 0.21	6.24 ± 0.20
ALB	(g/dL)	2.71 ± 0.15	2.72 ± 0.05

Each value represents Mean ± S.D.

Table 19 Gross pathological findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
Number of animals necropsied at the end of administration period	6	6	6	6
Number of animals with abnormalities	0	1	0	0
Number of animals with the following abnormalities				
Spleen : Elevated area, from surface, Local, Indistinct boundary, Increase in number of the follicles from cut-surface	0	1	0	0
Number of animals necropsied at the end of recovery period	6	.	.	6
Number of animals with abnormalities	0	.	.	0

Table 20 Gross pathological findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days

	Control	1-phenyl-1-xylylethane (mg/kg)		
		30	100	300
Number of animals necropsied at the end of administration period	6	6	6	6
Number of animals with abnormalities	0	0	0	0
Number of animals necropsied at the end of recovery period	6	.	.	6
Number of animals with abnormalities	0	.	.	0

Table 21-1-1 Absolute organ weights in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

		1-phenyl-1-xylylethane (mg/kg)			
		Control	30	100	300
Number of animals		6	6	6	6
Body weight	(g)	386 ± 27	381 ± 20	386 ± 25	355 ± 39
Brain	(g)	2.04 ± 0.06	2.05 ± 0.04	2.04 ± 0.08	1.96 ± 0.08
Thymus	(mg)	477 ± 110	477 ± 89	461 ± 43	374 ± 44
Lungs	(g)	1.33 ± 0.07	1.29 ± 0.16	1.32 ± 0.09	1.19 ± 0.11
Heart	(g)	1.229 ± 0.037	1.209 ± 0.077	1.212 ± 0.105	1.074 ± 0.124 *
Liver	(g)	11.2 ± 1.2	12.0 ± 1.5	14.3 ± 0.9 **	15.1 ± 1.7 **
Spleen	(g)	0.680 ± 0.064	0.616 ± 0.187	0.606 ± 0.079	0.526 ± 0.082
Adrenal :					
Left	(mg)	32.7 ± 4.2	30.2 ± 3.3	28.0 ± 2.1	27.0 ± 4.0 *
Right	(mg)	31.3 ± 6.7	28.0 ± 2.5	26.0 ± 2.8	27.5 ± 5.0
Kidney :					
Left	(g)	1.28 ± 0.11	1.38 ± 0.08	1.39 ± 0.12	1.32 ± 0.17
Right	(g)	1.31 ± 0.10	1.44 ± 0.11	1.43 ± 0.12	1.33 ± 0.18
Testis :					
Left	(g)	1.57 ± 0.05	1.61 ± 0.11	1.55 ± 0.10	1.54 ± 0.14
Right	(g)	1.57 ± 0.03	1.63 ± 0.10	1.55 ± 0.08	1.57 ± 0.12
Epididymis :					
Left	(g)	0.51 ± 0.02	0.54 ± 0.05	0.52 ± 0.03	0.49 ± 0.04
Right	(g)	0.53 ± 0.01	0.56 ± 0.07	0.55 ± 0.04	0.50 ± 0.05

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 21-1-2 Relative organ weights in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

		1-phenyl-1-xylylethane (mg/kg)			
		Control	30	100	300
Number of animals		6	6	6	6
Brain	(g%)	0.529 ± 0.030	0.539 ± 0.025	0.529 ± 0.031	0.557 ± 0.057
Thymus	(mg%)	124 ± 26	125 ± 21	120 ± 11	107 ± 23
Lungs	(g%)	0.346 ± 0.024	0.339 ± 0.032	0.343 ± 0.022	0.335 ± 0.011
Heart	(g%)	0.320 ± 0.017	0.317 ± 0.015	0.315 ± 0.023	0.302 ± 0.009
Liver	(g%)	2.90 ± 0.19	3.14 ± 0.22	3.72 ± 0.13 **	4.25 ± 0.16 **
Spleen	(g%)	0.177 ± 0.017	0.161 ± 0.041	0.157 ± 0.019	0.149 ± 0.021
Adrenal :					
Left	(mg%)	8.50 ± 1.19	7.94 ± 1.00	7.29 ± 0.83	7.61 ± 0.84
Right	(mg%)	8.15 ± 1.82	7.38 ± 0.97	6.78 ± 1.04	7.73 ± 1.01
Kidney :					
Left	(g%)	0.333 ± 0.026	0.362 ± 0.023	0.360 ± 0.027	0.371 ± 0.021 *
Right	(g%)	0.340 ± 0.028	0.379 ± 0.026	0.372 ± 0.028	0.374 ± 0.026
Testis :					
Left	(g%)	0.409 ± 0.028	0.423 ± 0.028	0.403 ± 0.028	0.439 ± 0.060
Right	(g%)	0.408 ± 0.029	0.428 ± 0.034	0.402 ± 0.030	0.447 ± 0.056
Epididymis :					
Left	(g%)	0.132 ± 0.012	0.142 ± 0.012	0.134 ± 0.013	0.139 ± 0.013
Right	(g%)	0.138 ± 0.011	0.146 ± 0.015	0.142 ± 0.012	0.143 ± 0.021

Each value represents Mean ± S.D.

Relative organ weights were calculated based upon the body weight.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 21-2-1 Absolute organ weights in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

		Control		1-phenyl-1-xylylethane (mg/kg)	
		6		300	
Number of animals		6		6	
Body weight	(g)	423 ± 38		394 ± 20	
Brain	(g)	2.05 ± 0.09		1.98 ± 0.07	
Thymus	(mg)	482 ± 86		432 ± 102	
Lungs	(g)	1.38 ± 0.07		1.26 ± 0.15	
Heart	(g)	1.270 ± 0.120		1.278 ± 0.084	
Liver	(g)	11.3 ± 1.1		10.9 ± 0.8	
Spleen	(g)	0.751 ± 0.093		0.688 ± 0.059	
Adrenal :					
Left	(mg)	32.2 ± 4.9		32.3 ± 6.6	
Right	(mg)	29.8 ± 2.3		31.0 ± 5.5	
Kidney :					
Left	(g)	1.30 ± 0.10		1.44 ± 0.19	
Right	(g)	1.31 ± 0.08		1.42 ± 0.16	
Testis :					
Left	(g)	1.66 ± 0.11		1.54 ± 0.06 *	
Right	(g)	1.70 ± 0.09		1.56 ± 0.04 **	
Epididymis :					
Left	(g)	0.61 ± 0.04		0.54 ± 0.04 **	
Right	(g)	0.61 ± 0.05		0.56 ± 0.05	

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 21-2-2 Relative organ weights in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

		Control	1-phenyl-1-xylylethane (mg/kg)
		6	300
Number of animals		6	6
Brain	(g%)	0.487 ± 0.043	0.505 ± 0.033
Thymus	(mg%)	113 ± 12	109 ± 24
Lungs	(g%)	0.328 ± 0.022	0.321 ± 0.037
Heart	(g%)	0.301 ± 0.029	0.325 ± 0.022
Liver	(g%)	2.68 ± 0.25	2.77 ± 0.12
Spleen	(g%)	0.178 ± 0.021	0.175 ± 0.016
Adrenal :			
Left	(mg%)	7.60 ± 0.99	8.22 ± 1.61
Right	(mg%)	7.06 ± 0.45	7.89 ± 1.43
Kidney :			
Left	(g%)	0.308 ± 0.017	0.365 ± 0.048 *
Right	(g%)	0.309 ± 0.016	0.362 ± 0.043 *
Testis :			
Left	(g%)	0.396 ± 0.045	0.392 ± 0.028
Right	(g%)	0.404 ± 0.045	0.398 ± 0.024
Epididymis :			
Left	(g%)	0.146 ± 0.018	0.136 ± 0.006
Right	(g%)	0.145 ± 0.016	0.141 ± 0.010

Each value represents Mean ± S.D.

Relative organ weights were calculated based upon the body weight.

\* Significantly different from control (P<0.05)

Table 22-1-1 Absolute organ weights in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

		Control	1-phenyl-1-xylylethane (mg/kg)			
			30	100	300	
Number of animals		6	6	6	6	
Body weight	(g)	233 ± 13	244 ± 15	228 ± 20	204 ± 9	**
Brain	(g)	1.92 ± 0.06	1.89 ± 0.10	1.93 ± 0.09	1.83 ± 0.06	
Thymus	(mg)	418 ± 62	486 ± 122	424 ± 67	378 ± 107	
Lungs	(g)	1.04 ± 0.07	1.04 ± 0.08	1.02 ± 0.05	0.92 ± 0.05	*
Heart	(g)	0.773 ± 0.049	0.838 ± 0.092	0.768 ± 0.045	0.701 ± 0.058	
Liver	(g)	6.7 ± 0.5	7.8 ± 0.5 *	8.0 ± 0.9 **	9.2 ± 0.7 **	
Spleen	(g)	0.486 ± 0.065	0.535 ± 0.081	0.436 ± 0.089	0.408 ± 0.060	
Adrenal :						
Left	(mg)	33.7 ± 4.3	35.3 ± 5.6	37.5 ± 5.9	34.8 ± 5.2	
Right	(mg)	37.0 ± 8.3	32.5 ± 4.3	34.8 ± 5.1	35.0 ± 3.2	
Kidney :						
Left	(g)	0.82 ± 0.02	0.83 ± 0.06	0.82 ± 0.06	0.81 ± 0.06	
Right	(g)	0.83 ± 0.06	0.84 ± 0.05	0.84 ± 0.08	0.84 ± 0.04	
Ovary :						
Left	(mg)	50.5 ± 5.4	49.8 ± 7.3	46.0 ± 16.5	38.7 ± 6.2	
Right	(mg)	47.7 ± 10.7	50.8 ± 8.8	47.7 ± 9.2	42.2 ± 8.9	
Uterus	(g)	0.61 ± 0.27	0.57 ± 0.13	0.65 ± 0.28	0.55 ± 0.17	

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 22-1-2 Relative organ weights in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

		Control	1-phenyl-1-xylylethane (mg/kg)			
			30	100	300	
Number of animals		6	6	6	6	
Brain	(g%)	0.826 ± 0.058	0.776 ± 0.054	0.849 ± 0.063	0.901 ± 0.018	
Thymus	(mg%)	180 ± 29	199 ± 43	186 ± 23	184 ± 44	
Lungs	(g%)	0.445 ± 0.028	0.429 ± 0.026	0.447 ± 0.025	0.455 ± 0.036	
Heart	(g%)	0.332 ± 0.019	0.343 ± 0.020	0.338 ± 0.026	0.345 ± 0.029	
Liver	(g%)	2.89 ± 0.14	3.19 ± 0.07	3.52 ± 0.15 *	4.53 ± 0.36 **	
Spleen	(g%)	0.210 ± 0.036	0.221 ± 0.038	0.191 ± 0.036	0.200 ± 0.030	
Adrenal :	Left	(mg%)	14.48 ± 1.86	14.61 ± 2.71	16.43 ± 1.97	17.22 ± 3.19
	Right	(mg%)	15.89 ± 3.49	13.43 ± 2.21	15.25 ± 1.54	17.24 ± 1.96
Kidney :	Left	(g%)	0.351 ± 0.013	0.343 ± 0.028	0.361 ± 0.016	0.398 ± 0.037 *
	Right	(g%)	0.357 ± 0.013	0.343 ± 0.017	0.366 ± 0.023	0.411 ± 0.023 **
Ovary :	Left	(mg%)	21.8 ± 2.9	20.4 ± 2.1	19.9 ± 5.5	19.0 ± 2.8
	Right	(mg%)	20.6 ± 5.3	20.8 ± 2.9	20.7 ± 2.3	20.7 ± 4.2
Uterus	(g%)	0.260 ± 0.119	0.235 ± 0.060	0.284 ± 0.125	0.273 ± 0.090	

Each value represents Mean ± S.D.

Relative organ weights were calculated based upon the body weight.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Table 22-2-1 Absolute organ weights in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

		Control		1-phenyl-1-xylylethane (mg/kg)	
		6		300	
Number of animals		6		6	
Body weight	(g)	265 ±	14	245 ±	20
Brain	(g)	1.92 ±	0.12	1.93 ±	0.07
Thymus	(mg)	354 ±	59	435 ±	27 *
Lungs	(g)	1.10 ±	0.06	1.10 ±	0.09
Heart	(g)	0.871 ±	0.044	0.856 ±	0.060
Liver	(g)	7.4 ±	0.7	7.4 ±	0.6
Spleen	(g)	0.512 ±	0.052	0.534 ±	0.057
Adrenal :	Left (mg)	39.0 ±	3.2	38.3 ±	3.9
	Right (mg)	38.3 ±	6.5	37.0 ±	4.5
Kidney :	Left (g)	0.86 ±	0.07	0.84 ±	0.10
	Right (g)	0.90 ±	0.06	0.85 ±	0.10
Ovary :	Left (mg)	45.8 ±	7.7	41.8 ±	3.5
	Right (mg)	51.5 ±	10.3	48.3 ±	2.8
Uterus	(g)	0.53 ±	0.12	0.59 ±	0.20

Each value represents Mean ± S.D.

\* Significantly different from control (P<0.05)

Table 22-2-2 Relative organ weights in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

		Control	1-phenyl-1-xylylethane (mg/kg)
		6	300
Number of animals		6	6
Brain	(g%)	0.728 ± 0.072	0.788 ± 0.059
Thymus	(mg%)	134 ± 19	178 ± 17 **
Lungs	(g%)	0.415 ± 0.047	0.451 ± 0.045
Heart	(g%)	0.329 ± 0.024	0.349 ± 0.014
Liver	(g%)	2.80 ± 0.14	3.01 ± 0.10 *
Spleen	(g%)	0.194 ± 0.021	0.218 ± 0.010 *
Adrenal :			
Left	(mg%)	14.73 ± 1.27	15.72 ± 2.11
Right	(mg%)	14.56 ± 3.04	15.17 ± 2.26
Kidney :			
Left	(g%)	0.324 ± 0.034	0.342 ± 0.017
Right	(g%)	0.341 ± 0.034	0.347 ± 0.018
Ovary :			
Left	(mg%)	17.3 ± 2.7	17.1 ± 1.2
Right	(mg%)	19.5 ± 4.2	19.9 ± 2.5
Uterus	(g%)	0.200 ± 0.048	0.245 ± 0.104

Each value represents Mean ± S.D.

Relative organ weights were calculated based upon the body weight.

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Table 23-1 Histopathological findings in male rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

Organ and tissue	Findings	Group Grade	Control			1-phenyl-1-xylylethane (mg/kg)								
			-	+	++	30			100			300		
						-	+	++	-	+	++	-	+	++
Liver	Hypertrophy of centrilobular hepatocyte		6	0	0	0	6	0	0	5	1	0	1	5
	Microgranuloma		1	5	0	1	5	0	1	5	0	3	3	0
	Apoptotic necrosis of hepatocyte		2	4	0	1	5	0	1	5	0	3	3	0
	Brown pigmentation		6	0	0	6	0	0	6	0	0	5	1	0
Kidney	Basophilic tubule		6	0	0	6	0	0	5	1	0	1	4	1
	Vacuolation of tubular epithelium, proximal		6	0	0	6	0	0	5	1	0	4	2	0
	Protein cast		6	0	0	6	0	0	6	0	0	3	3	0
	Mononuclear cell infiltration, cortex		4	2	0	4	2	0	4	2	0	5	1	0
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		6	0	0	2	3	1	2	4	0	0	1	5
	Ectopic thymus		6	0	0	6	0	0	6	0	0	5	1	0
Spleen	Follicular hyperplasia of lymphocyte		6	0	0	0	0	1	.	.	.	6	0	0
Lungs(Bronchi)	Foam cell accumulation, alveolar space		2	4	0	.	.	.	.	.	.	1	5	0
	Mononuclear cell infiltration, perivascular		3	3	0	.	.	.	.	.	.	3	3	0
	Microgranuloma		6	0	0	.	.	.	.	.	.	5	1	0
	Osseous metaplasia of alveolar wall		6	0	0	.	.	.	.	.	.	5	1	0
	Calcification in artery		3	3	0	.	.	.	.	.	.	2	4	0
	Hemorrhage		5	1	0	.	.	.	.	.	.	5	1	0
	Bronchiolar/alveolar hyperplasia		6	0	0	.	.	.	.	.	.	5	1	0
Trachea	Mononuclear cell infiltration, submucosa		5	1	0	.	.	.	.	.	.	5	1	0
Heart	Fibrosis of myocardium, septum		6	0	0	.	.	.	.	.	.	5	1	0
	Mononuclear cell infiltration		5	1	0	.	.	.	.	.	.	4	2	0
Stomach	Mononuclear cell infiltration, glandular submucosa		6	0	0	.	.	.	.	.	.	5	1	0
Epididymis	Mononuclear cell infiltration, interstitium		5	1	0	.	.	.	.	.	.	6	0	0
Prostate	Mononuclear cell infiltration, interstitium		4	2	0	.	.	.	.	.	.	4	2	0
Laryngopharynx, Urinary bladder, Thymus, Mandibular lymph node, Mesenteric lymph node, Submaxillary gland, Sublingual gland, Tongue, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Testis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities			Not examined						No abnormalities		

Each value represents the number of animals with each finding.

- : No change      + : Slight change      ++ : Moderate change      . : Not examined

Table 23-2 Histopathological findings in male rats administered 1-phenyl-1-xylethane orally for 28 days  
- End of recovery -

Organ and tissue	Findings	Group Grade	Control			1-phenyl-1-xylethane 300 mg/kg		
			-	+	++	-	+	++
Kidney	Basophilic tubule		6	0	0	0	5	1
	Protein cast		6	0	0	5	1	0
	Mononuclear cell infiltration, cortex		3	3	0	2	4	0
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		6	0	0	2	4	0
	Remnant of ultimobranchial body		6	0	0	5	1	0
Lungs(Bronchi)	Foam cell accumulation, alveolar space		3	3	0	1	5	0
	Mononuclear cell infiltration, perivascular		4	2	0	3	3	0
	Osseous metaplasia of alveolar wall		6	0	0	5	1	0
	Calcification in artery		4	2	0	5	1	0
	Hemorrhage		5	1	0	6	0	0
Heart	Fibrosis of myocardium, septum		5	1	0	5	1	0
	Mononuclear cell infiltration		6	0	0	5	1	0
Sublingual gland	Mononuclear cell infiltration, interstitium		6	0	0	5	1	0
Cecum	Mononuclear cell infiltration, mucosa		5	1	0	6	0	0
Epididymis	Mononuclear cell infiltration, interstitium		6	0	0	5	1	0
Prostate	Mononuclear cell infiltration, interstitium		4	2	0	6	0	0
Skin	Significant lesion		.	.	.	1	0	0
Laryngopharynx, Trachea, Urinary bladder, Thymus, Spleen, Mandibular lymph node, Mesenteric lymph node, Liver, Submaxillary gland, Tongue, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Rectum, Testis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities					

Each value represents the number of animals with each finding.

- : No change    + : Slight change    ++ : Moderate change    . : Not examined

Table 24-1 Histopathological findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of administration -

Organ and tissue	Findings	Group Grade	Control			1-phenyl-1-xylylethane (mg/kg)								
			-	+	++	30			100			300		
			-	+	++	-	+	++	-	+	++	-	+	++
Liver	Hypertrophy of centrilobular hepatocyte		6	0	0	0	6	0	0	6	0	0	3	3
	Microgranuloma		2	4	0	1	5	0	3	3	0	2	4	0
	Apoptotic necrosis of hepatocyte		4	2	0	1	5	0	3	3	0	2	4	0
Kidney	Basophilic tubule		6	0	0	6	0	0	6	0	0	4	2	0
	Vacuolation of tubular epithelium, proximal		6	0	0	3	3	0	4	2	0	0	6	0
	Mononuclear cell infiltration, cortex		3	3	0	4	2	0	4	2	0	6	0	0
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		6	0	0	3	3	0	3	2	1	0	4	2
	Ectopic thymus		6	0	0	6	0	0	5	1	0	6	0	0
	Remnant of ultimobranchial body		4	2	0	6	0	0	5	1	0	6	0	0
	Mononuclear cell infiltration		6	0	0	6	0	0	5	1	0	6	0	0
Lungs(Bronchi)	Foam cell accumulation, alveolar space		5	1	0	.	.	.	.	.	.	2	4	0
	Mononuclear cell infiltration, perivascular		1	5	0	.	.	.	.	.	.	5	1	0
	Osseous metaplasia of alveolar wall		6	0	0	.	.	.	.	.	.	4	2	0
Laryngopharynx	Neutrophil infiltration, submucosa		5	1	0	.	.	.	.	.	.	6	0	0
Heart	Mononuclear cell infiltration		5	1	0	.	.	.	.	.	.	6	0	0
Thymus	Epithelial tubule		5	1	0	.	.	.	.	.	.	5	1	0
Mandibular lymph node	Lymphocytic hyperplasia		6	0	0	.	.	.	.	.	.	5	1	0
Esophagus	Degeneration of muscle fiber		5	1	0	.	.	.	.	.	.	4	2	0
	Mononuclear cell infiltration, muscular		5	1	0	.	.	.	.	.	.	4	2	0
Ovary	Luteal cyst		5	1	0	.	.	.	.	.	.	5	1	0
Sciatic nerve	Inflammatory cell infiltration, paraneurium		5	1	0	.	.	.	.	.	.	6	0	0
Skin	Significant lesion		.	.	.	.	.	.	.	.	.	3	0	0
Trachea, Urinary bladder, Spleen, Mesenteric lymph node, Submaxillary gland, Sublingual gland, Tongue, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Uterus, Vagina, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities			Not examined						No abnormalities		

Each value represents the number of animals with each finding.

- : No change      + : Slight change      ++ : Moderate change      • : Not examined

Table 24-2 Histopathological findings in female rats administered 1-phenyl-1-xylylethane orally for 28 days  
- End of recovery -

Organ and tissue	Findings	Group Grade	Control			1-phenyl-1-xylylethane 300 mg/kg		
			-	+	++	-	+	++
Liver	Hypertrophy of centrilobular hepatocyte		6	0	0	5	1	0
Kidney	Mononuclear cell infiltration, cortex		6	0	0	4	2	0
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		6	0	0	4	2	0
Lungs(Bronchi)	Foam cell accumulation, alveolar space		3	3	0	3	3	0
	Mononuclear cell infiltration, perivascular		0	6	0	2	4	0
	Calcification in artery		5	1	0	6	0	0
Thymus	Epithelial tubule		6	0	0	5	1	0
Mesenteric lymph node	Lymphocytic hyperplasia		5	1	0	6	0	0
Sublingual gland	Ductal hyperplasia		5	1	0	6	0	0
Tongue	Mononuclear cell infiltration, submucosa		5	1	0	6	0	0
Ovary	Luteal cyst		5	1	0	5	1	0
	Follicular cyst		6	0	0	5	1	0
	Corpus albicans		5	1	0	6	0	0
Skin	Significant lesion		.	.	.	5	0	0
Laryngopharynx, Trachea, Heart, Urinary bladder, Spleen, Mandibular lymph node, Submaxillary gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Uterus, Vagina, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities					

Each value represents the number of animals with each finding.

- : No change      + : Slight change      ++ : Moderate change      . : Not examined

2000TT278

List of samples missing

Male	
Organ and tissue	Group
Parathyroid	300 mg/kg
	309

2000TT278

Appendix 1-1-1      General condition in male rats  
- Administration period -

Control group

Animal No.	Findings
001	No abnormalities
002	No abnormalities
003	No abnormalities
004	No abnormalities
005	No abnormalities
006	No abnormalities
007	No abnormalities
008	No abnormalities
009	No abnormalities
010	No abnormalities
011	No abnormalities
012	No abnormalities

2000TT278

Appendix 1-1-2    General condition in male rats  
- Administration period -

30 mg/kg group

Animal	
No.	Findings
101	No abnormalities
102	No abnormalities
103	No abnormalities
104	No abnormalities
105	No abnormalities
106	No abnormalities

2000TT278

Appendix 1-1-3    General condition in male rats  
- Administration period -

100 mg/kg group

Animal	
No.	Findings
201	Salivation on Day 26
202	No abnormalities
203	No abnormalities
204	No abnormalities
205	Salivation on Days 21, 26 and 27
206	No abnormalities

Appendix 1-1-4 General condition in male rats  
- Administration period -

300 mg/kg group

Animal No.	Findings
301	Salivation on Days 12, 14, 15, 17 to 19 and 21 to 28
302	Staggering gait on Day 4 Salivation on Days 13, 14, 18, 19, 21 and 23 to 28
303	Salivation on Days 13 to 27
304	Salivation on Days 10 to 15 and 17 to 28
305	Salivation on Days 13, 14, 20 and 23 to 28
306	Staggering gait on Days 3 and 4 Salivation on Days 7 to 12 and 14 to 28
307	Staggering gait on Days 3 and 4
308	Staggering gait on Day 4 Salivation on Days 14, 18, 20, 22 to 24 and 26 to 28
309	Salivation on Days 13, 14, 18 and 21 to 28
310	Staggering gait on Days 3 and 4 Loose stool on Day 3 Loss of fur in the abdominal region on Days 5 to 28 Salivation on Days 25 and 26
311	Staggering gait on Days 3 and 4 Salivation on Days 9, 11, 12, 14 to 18, 20 to 22 and 24 to 28
312	Staggering gait on Day 3 Salivation on Days 13, 14, 16, 18 and 21 to 28

2000TT278

Appendix 1-2-1    General condition in male rats  
- Recovery period -

Control group

Animal	Findings
007	No abnormalities
008	No abnormalities
009	No abnormalities
010	No abnormalities
011	No abnormalities
012	No abnormalities

2000TT278

Appendix 1-2-2    General condition in male rats  
- Recovery period -

300 mg/kg group

Animal No.	Findings
307	No abnormalities
308	No abnormalities
309	No abnormalities
310	Loss of fur in the abdominal region on Days 1 to 15
311	No abnormalities
312	No abnormalities

Appendix 2-1-1    General condition in female rats  
- Administration period -

Control group

Animal	
No.	Findings
401	No abnormalities
402	No abnormalities
403	No abnormalities
404	No abnormalities
405	No abnormalities
406	No abnormalities
407	No abnormalities
408	No abnormalities
409	No abnormalities
410	No abnormalities
411	No abnormalities
412	No abnormalities

2000TT278

Appendix 2-1-2    General condition in female rats  
- Administration period -

30 mg/kg group

Animal	
No.	Findings
501	No abnormalities
502	No abnormalities
503	No abnormalities
504	No abnormalities
505	No abnormalities
506	No abnormalities

2000TT278

Appendix 2-1-3      General condition in female rats  
- Administration period -

100 mg/kg group

Animal No.	Findings
601	No abnormalities
602	No abnormalities
603	No abnormalities
604	No abnormalities
605	No abnormalities
606	No abnormalities

Appendix 2-1-4 General condition in female rats  
- Administration period -

## 300 mg/kg group

Animal No.	Findings
701	Loss of fur in the abdominal region on Days 9 to 29 Salivation on Day 28
702	Scant feces on Day 4 Decrease in movement on Days 7 and 8 Prone position on Days 7 and 8 Loss of fur in the abdominal region on Days 5 to 29 Loss of fur in the thoracic region on Days 21 to 29 Loss of fur in the femoral region on Days 27 to 29 Salivation on Days 14, 15, 17, 18, 21 to 24, 26 and 27
703	Salivation on Days 9, 14, 19 to 21, 23, 24 and 26 to 28
704	Staggering gait on Day 4 Loss of fur in the abdominal region on Days 4 to 29 Loss of fur in the femoral region on Day 29 Scant feces on Days 4, 5, 12, 18 and 24 to 26 Salivation on Days 24 and 26
705	Salivation on Days 9 to 28
706	Salivation on Days 7 to 16 and 18 to 28 Scant feces on Days 13 and 14
707	Staggering gait on Day 4 Loss of fur in the abdominal region on Days 5 to 28 Salivation on Days 7, 11 to 14, 16 to 19, 21, 23, 24, 26 and 27
708	Salivation on Days 15 to 17, 21 and 27 Scant feces on Days 16 to 19
709	Staggering gait on Day 3 Loss of fur in the abdominal region on Days 4 to 28 Salivation on Days 20, 27 and 28
710	Staggering gait on Day 4 Salivation on Days 10 to 28 Scant feces on Days 22 to 24 Loss of fur in the femoral region on Days 27 and 28
711	Loss of fur in the abdominal region on Days 4 to 28 Scant feces on Days 4, 5, 10, 15 and 16
712	Salivation on Days 14, 16 and 26

2000TT278

Appendix 2-2-1    General condition in female rats  
- Recovery period -

Control group

Animal	Findings
407	No abnormalities
408	No abnormalities
409	No abnormalities
410	No abnormalities
411	No abnormalities
412	No abnormalities

2000TT278

Appendix 2-2-2    General condition in female rats  
- Recovery period -

300 mg/kg group

Animal	
No.	Findings
707	Loss of fur in the abdominal region on Days 1 to 15
708	No abnormalities
709	Loss of fur in the abdominal region on Days 1 to 15
710	Loss of fur in the femoral region on Days 1 to 15
711	Loss of fur in the abdominal region on Days 1 to 15
712	Loss of fur in the forelimbs on Days 14 and 15

Appendix 3-1 Functional observational battery in male rats

Control group																								
Animal No.	Posture								Convulsions								Respiration							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
002	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
004	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
005	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
006	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 3-1 (Continued-1) Functional observational battery in male rats

Control group																
Animal No.	Stereotype								Abnormal behavior							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
002	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
004	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
005	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
006	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration  
 Figures indicate scores

D : Day of administration

R : Day of recovery

## Appendix 3-1 (Continued-2) Functional observational battery in male rats

## Control group

Animal No.	Handling difficulty								Abnormal vocalization								Muscle tone							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
002	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
004	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
005	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
006	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 3-1 (Continued-3) Functional observational battery in male rats

## Control group

Animal No.	Fur appearance								Piloerection								Skin/visual mucosa							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
002	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
004	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
005	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
006	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 3-1 (Continued-4) Functional observational battery in male rats

Control group																								
Animal No.	Pupil size								Salivation								Lacrimation							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
002	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
004	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
005	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
006	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 3-1 (Continued-5) Functional observational battery in male rats

Control group																								
Animal	Righting reflex								Consciousness								Gait							
No.	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
002	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
004	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
005	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
006	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
011	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 3-1 (Continued-6) Functional observational battery in male rats

Control group																								
Animal No.	Defecation (counts / 2 min)								Urination (counts / 2 min)								Rearing (counts / 2 min)							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
001	0	1	1	2	1	3	.	.	0	0	0	0	1	2	.	.	0	5	0	0	2	2	.	.
002	0	0	1	0	0	0	.	.	0	0	0	0	0	0	.	.	3	3	0	0	0	0	.	.
003	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	2	5	1	4	2	3	.	.
004	0	0	0	0	0	0	.	.	0	0	0	1	0	0	.	.	5	9	3	9	5	6	.	.
005	0	0	0	2	1	3	.	.	0	0	0	0	0	0	.	.	3	1	0	3	7	4	.	.
006	0	0	0	0	0	0	.	.	0	0	0	1	1	0	.	.	5	2	3	8	8	7	.	.
007	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	7	0	3	4	2	3	4
008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	2	3	3	0	4	5
009	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	8	1	0	1	2	4	0
010	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	6	1	3	8	4	4	3
011	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	2	12	4	5	4	12	3	5
012	0	6	1	0	0	0	0	0	0	0	0	0	0	0	1	1	4	0	0	0	1	1	1	2
Mean	0.0	0.6	0.3	0.3	0.2	0.5	0.0	0.0	0.0	0.0	0.0	0.2	0.2	0.3	0.5	0.2	3.0	4.9	1.3	3.2	3.8	3.6	3.2	3.2
S.D.	0.0	1.7	0.5	0.8	0.4	1.2	0.0	0.0	0.0	0.0	0.0	0.4	0.4	0.6	0.5	0.4	1.5	3.7	1.4	3.0	2.8	3.4	1.2	1.9
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

## Appendix 3-2 Functional observational battery in male rats

## 30 mg/kg group

Animal No.	Posture						Convulsions						Respiration						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
101	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-2 (Continued-1) Functional observational battery in male rats

30 mg/kg group

Animal No.	Stereotype						Abnormal behavior					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
101	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-2 (Continued-2) Functional observational battery in male rats

## 30 mg/kg group

Animal No.	Handling difficulty						Abnormal vocalization						Muscle tone						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
101	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-2 (Continued-3) Functional observational battery in male rats

## 30 mg/kg group

Animal No.	Fur appearance						Piloerection						Skin/visual mucosa					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
101	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

Figures indicate scores

## Appendix 3-2 (Continued-4) Functional observational battery in male rats

## 30 mg/kg group

Animal No.	Pupil size						Salivation						Lacrimation					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
101	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-2 (Continued-5) Functional observational battery in male rats

## 30 mg/kg group

Animal No.	Righting reflex						Consciousness						Gait						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
101	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

Figures indicate scores

## Appendix 3-2 (Continued-6) Functional observational battery in male rats

## 30 mg/kg group

Animal No.	Defecation (counts / 2 min)						Urination (counts / 2 min)						Rearing (counts / 2 min)					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
101	1	2	0	2	0	0	0	0	0	0	1	0	1	3	2	1	2	4
102	0	2	1	0	2	0	0	0	0	1	1		8	7	0	4	0	0
103	3	0	0	0	0	0	0	0	0	1	0		2	8	2	9	9	11
104	0	0	0	0	0	0	0	0	0	1	1		3	4	0	3	3	1
105	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0
106	2	1	2	2	1	0	0	1	1	1	0		0	1	0	0	1	5
	*						*											
Mean	1.0	0.8	0.5	0.7	0.5	0.0	0.0	0.2	0.2	0.2	0.8	0.3	2.3	3.8	0.7	2.8	2.5	3.5
S.D.	1.3	1.0	0.8	1.0	0.8	0.0	0.0	0.4	0.4	0.4	0.4	0.5	3.0	3.2	1.0	3.4	3.4	4.2
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

\* Significantly different from control (P&lt;0.05)

## Appendix 3-3 Functional observational battery in male rats

## 100 mg/kg group

Animal No.	Posture						Convulsions						Respiration					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
201	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
202	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
203	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
204	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
205	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
206	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-3 (Continued-1) Functional observational battery in male rats

100 mg/kg group

Animal No.	Stereotype						Abnormal behavior					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
201	0	0	0	0	0	0	0	0	0	0	0	0
202	0	0	0	0	0	0	0	0	0	0	0	0
203	0	0	0	0	0	0	0	0	0	0	0	0
204	0	0	0	0	0	0	0	0	0	0	0	0
205	0	0	0	0	0	0	0	0	0	0	0	0
206	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-3 (Continued-2) Functional observational battery in male rats

## 100 mg/kg group

Animal No.	Handling difficulty						Abnormal vocalization						Muscle tone						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
201	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
202	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
203	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
204	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
205	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
206	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

Figures indicate scores

## Appendix 3-3 (Continued-3) Functional observational battery in male rats

## 100 mg/kg group

Animal No.	Fur appearance						Piloerection						Skin/visual mucosa						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
201	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
202	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
203	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
204	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
205	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
206	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-3 (Continued-4) Functional observational battery in male rats

## 100 mg/kg group

Animal No.	Pupil size						Salivation						Lacrimation						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
201	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
202	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
203	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
204	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
205	0	0	0	0	0	0	0	0	0	1	1		0	0	0	0	0	0	0
206	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.2		0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.4		0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-3 (Continued-5) Functional observational battery in male rats

## 100 mg/kg group

Animal No.	Righting reflex						Consciousness						Gait						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
201	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
202	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
203	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
204	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
205	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
206	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 3-3 (Continued-6) Functional observational battery in male rats

## 100 mg/kg group

Animal No.	Defecation (counts / 2 min)						Urination (counts / 2 min)						Rearing (counts / 2 min)					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
201	0	0	0	0	0	0	0	0	0	1	1	0	3	5	2	4	3	4
202	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	2	8	6
203	0	0	0	0	0	0	0	0	0	0	0	0	2	2	0	0	1	0
204	1	1	2	1	1	2	1	0	0	1	0	0	1	0	0	0	1	0
205	0	0	0	0	0	0	0	0	0	1	1	1	1	3	1	3	3	2
206	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	3	0
Mean	0.2	0.2	0.3	0.2	0.2	0.3	0.2	0.0	0.0	0.5	0.5	0.3	1.3	1.8	0.5	1.5	3.2	2.0
S.D.	0.4	0.4	0.8	0.4	0.4	0.8	0.4	0.0	0.0	0.5	0.5	0.5	1.0	1.9	0.8	1.8	2.6	2.5
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

## Appendix 3-4 Functional observational battery in male rats

## 300 mg/kg group

Animal No.	Posture								Convulsions								Respiration							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
302	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
303	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
304	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
306	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
308	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
309	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
310	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
311	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
312	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 3-4 (Continued-1) Functional observational battery in male rats

300 mg/kg group

Animal No.	Stereotype								Abnormal behavior							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
302	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
303	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
304	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
306	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
308	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
309	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
310	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
311	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
312	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 3-4 (Continued-2) Functional observational battery in male rats

## 300 mg/kg group

Animal No.	Handling difficulty								Abnormal vocalization								Muscle tone							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
302	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
303	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
304	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
306	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
308	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
309	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
310	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
311	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
312	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 3-4 (Continued-3) Functional observational battery in male rats

## 300 mg/kg group

Animal No.	Fur appearance								Piloerection								Skin/visual mucosa							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
302	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
303	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
304	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
306	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
308	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
309	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
310	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
311	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
312	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 3-4 (Continued-4) Functional observational battery in male rats

## 300 mg/kg group

Animal No.	Pupil size								Salivation								Lacrimation							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.	0	0	0	0	0	0	.	.
302	0	0	0	0	0	0	.	.	0	0	0	1	0	1	.	.	0	0	0	0	0	0	.	.
303	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.	0	0	0	0	0	0	.	.
304	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.	0	0	0	0	0	0	.	.
306	0	0	0	0	0	0	.	.	0	0	1	1	1	1	.	.	0	0	0	0	0	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
308	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
309	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
310	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
311	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
312	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.8	0.7	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.5	0.5	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery

Figures indicate scores

\*\* Significantly different from control (P&lt;0.01)

Appendix 3-4 (Continued-5) Functional observational battery in male rats

300 mg/kg group

Animal No.	Righting reflex								Consciousness								Gait							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
302	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
303	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
304	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
306	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
308	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
309	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
310	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
311	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
312	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 3-4 (Continued-6) Functional observational battery in male rats

## 300 mg/kg group

Animal No.	Defecation (counts / 2 min)								Urination (counts / 2 min)								Rearing (counts / 2 min)							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
301	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	3	5	7	8	13	9	.	.
302	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	2	2	1	1	1	1	.	.
303	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	2	2	0	2	2	2	.	.
304	1	2	2	2	2	2	.	.	1	0	1	1	1	0	.	.	0	0	0	0	0	0	.	.
305	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.
306	1	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	3	6	4	2	3	0	.	.
307	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	5	5	2	4	0	4	3	6
308	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	5	0	0	2	3	4	3
309	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	7	2	4	5	2	0	2
310	1	2	1	0	0	0	0	0	0	1	0	0	0	0	0	1	2	6	0	0	0	0	2	3
311	1	2	1	1	0	0	0	0	1	1	2	1	1	0	0	0	3	1	0	0	8	4	6	6
312	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	7	0	2	2	3	6	2
Mean	0.3	0.5	0.3	0.3	0.2	0.2	0.0	0.0	0.2	0.2	0.3	0.4	0.3	0.1	0.0	0.2	2.0	3.8	1.3	2.0	3.1	2.4	3.5	3.7
S.D.	0.5	0.9	0.7	0.6	0.6	0.6	0.0	0.0	0.4	0.4	0.7	0.5	0.5	0.3	0.0	0.4	1.5	2.7	2.2	2.4	3.9	2.5	2.3	1.9
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Appendix 4-1 Functional observational battery in female rats

Control group																								
Animal No.	Posture								Convulsions								Respiration							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
408	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 4-1 (Continued-1) Functional observational battery in female rats

Control group																
Animal No.	Stereotype								Abnormal behavior							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
408	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration  
 Figures indicate scores

D : Day of administration

R : Day of recovery

## Appendix 4-1 (Continued-2) Functional observational battery in female rats

Control group																								
Animal No.	Handling difficulty								Abnormal vocalization								Muscle tone							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
408	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 4-1 (Continued-3) Functional observational battery in female rats

Control group																								
Animal No.	Fur appearance								Piloerection								Skin/visual mucosa							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
408	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 4-1 (Continued-4) Functional observational battery in female rats

Control group																								
Animal	Pupil size								Salivation								Lacrimation							
No.	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
408	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 4-1 (Continued-5) Functional observational battery in female rats

Control group																								
Animal No.	Righting reflex								Consciousness								Gait							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
408	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 4-1 (Continued-6) Functional observational battery in female rats

Control group																								
Animal No.	Defecation (counts / 2 min)								Urination (counts / 2 min)								Rearing (counts / 2 min)							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
401	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	7	6	3	2	9	13	.	.
402	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	13	10	12	10	16	13	.	.
403	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	9	10	9	10	12	18	.	.
404	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	3	8	1	8	13	10	.	.
405	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	8	11	11	22	14	17	.	.
406	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	3	5	13	8	10	10	.	.
407	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	5	6	7	8	6	12	12
408	0	1	2	0	0	0	0	0	0	1	0	0	0	0	0	0	16	13	11	9	11	14	10	14
409	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	18	4	12	10	7	8	11
410	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	5	10	9	8	10	11	8
411	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	14	12	13	12	8	9	13
412	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	11	7	14	15	14	17	8
Mean	0.0	0.1	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	7.0	9.7	8.3	10.3	11.5	11.7	11.2	11.0
S.D.	0.0	0.3	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	4.3	4.1	4.0	4.8	2.6	3.8	3.2	2.5
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

## Appendix 4-2 Functional observational battery in female rats

## 30 mg/kg group

Animal No.	Posture						Convulsions						Respiration						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
501	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
502	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
503	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
504	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
505	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
506	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-2 (Continued-1) Functional observational battery in female rats

30 mg/kg group

Animal No.	Stereotype						Abnormal behavior					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
501	0	0	0	0	0	0	0	0	0	0	0	0
502	0	0	0	0	0	0	0	0	0	0	0	0
503	0	0	0	0	0	0	0	0	0	0	0	0
504	0	0	0	0	0	0	0	0	0	0	0	0
505	0	0	0	0	0	0	0	0	0	0	0	0
506	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-2 (Continued-2) Functional observational battery in female rats

## 30 mg/kg group

Animal No.	Handling difficulty						Abnormal vocalization						Muscle tone						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
501	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
502	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
503	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
504	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
505	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
506	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

Figures indicate scores

## Appendix 4-2 (Continued-3) Functional observational battery in female rats

## 30 mg/kg group

Animal No.	Fur appearance						Piloerection						Skin/visual mucosa						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
501	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
502	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
503	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
504	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
505	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
506	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-2 (Continued-4) Functional observational battery in female rats

## 30 mg/kg group

Animal No.	Pupil size						Salivation						Lacrimation						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
501	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
502	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
503	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
504	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
505	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
506	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-2 (Continued-5) Functional observational battery in female rats

## 30 mg/kg group

Animal No.	Righting reflex						Consciousness						Gait						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
501	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
502	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
503	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
504	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
505	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
506	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-2 (Continued-6) Functional observational battery in female rats

## 30 mg/kg group

Animal No.	Defecation (counts / 2 min)						Urination (counts / 2 min)						Rearing (counts / 2 min)					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
501	0	0	0	0	0	0	0	0	0	0	0	0	8	12	7	8	10	12
502	0	0	0	0	0	0	0	0	0	0	0	0	5	12	7	10	18	16
503	0	0	0	0	0	0	0	0	0	0	0	0	7	7	3	2	10	7
504	0	0	0	0	0	0	0	0	0	0	0	0	2	5	7	3	9	6
505	0	0	0	0	0	0	0	0	0	0	0	0	2	6	4	8	17	11
506	0	0	0	0	0	0	1	0	0	0	0	0	7	1	14	11	15	12
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	5.2	7.2	7.0	7.0	13.2	10.7
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	2.6	4.3	3.8	3.7	4.0	3.7
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration

Appendix 4-3 Functional observational battery in female rats

100 mg/kg group

Animal No.	Posture						Convulsions						Respiration						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
601	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
602	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
603	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
604	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
605	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
606	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-3 (Continued-1) Functional observational battery in female rats

100 mg/kg group

Animal No.	Stereotype						Abnormal behavior					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
601	0	0	0	0	0	0	0	0	0	0	0	0
602	0	0	0	0	0	0	0	0	0	0	0	0
603	0	0	0	0	0	0	0	0	0	0	0	0
604	0	0	0	0	0	0	0	0	0	0	0	0
605	0	0	0	0	0	0	0	0	0	0	0	0
606	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-3 (Continued-2) Functional observational battery in female rats

## 100 mg/kg group

Animal No.	Handling difficulty						Abnormal vocalization						Muscle tone					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
601	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
602	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
603	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
604	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
605	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
606	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-3 (Continued-3) Functional observational battery in female rats

## 100 mg/kg group

Animal No.	Fur appearance						Piloerection						Skin/visual mucosa						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
601	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
602	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
603	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
604	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
605	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
606	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-3 (Continued-4) Functional observational battery in female rats

## 100 mg/kg group

Animal No.	Pupil size						Salivation						Lacrimation						
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	
601	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
602	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
603	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
604	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
605	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
606	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

Appendix 4-3 (Continued-5) Functional observational battery in female rats

100 mg/kg group

Animal No.	Righting reflex						Consciousness						Gait					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
601	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
602	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
603	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
604	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
605	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
606	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration      D : Day of administration  
 Figures indicate scores

## Appendix 4-3 (Continued-6) Functional observational battery in female rats

## 100 mg/kg group

Animal No.	Defecation (counts / 2 min)						Urination (counts / 2 min)						Rearing (counts / 2 min)					
	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28	B3	D1	D7	D14	D21	D28
601	0	0	0	0	0	0	0	0	0	0	0	0	7	12	11	5	7	15
602	0	0	0	0	0	0	0	0	0	0	0	0	7	7	6	9	5	9
603	0	0	0	0	0	0	0	0	0	0	0	0	7	17	16	15	16	14
604	0	0	0	0	0	0	0	0	0	0	0	0	3	9	2	3	1	0
605	0	0	0	0	0	0	0	0	0	0	0	0	8	17	19	25	22	18
606	0	0	0	0	0	0	0	0	0	0	0	0	2	5	1	4	6	6
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.7	11.2	9.2	10.2	9.5	10.3
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	5.1	7.4	8.5	7.9	6.7
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

B : Before administration

D : Day of administration

## Appendix 4-4 Functional observational battery in female rats

## 300 mg/kg group

Animal No.	Posture								Convulsions								Respiration							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
702	0	0	1	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
705	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
706	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
707	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
709	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
710	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 4-4 (Continued-1) Functional observational battery in female rats

300 mg/kg group

Animal No.	Stereotype								Abnormal behavior							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
702	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
705	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
706	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
707	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
709	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
710	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration  
 Figures indicate scores

D : Day of administration

R : Day of recovery

## Appendix 4-4 (Continued-2) Functional observational battery in female rats

300 mg/kg group

Animal No.	Handling difficulty								Abnormal vocalization								Muscle tone							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
702	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
705	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
706	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
707	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
709	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
710	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 4-4 (Continued-3) Functional observational battery in female rats

## 300 mg/kg group

Animal No.	Fur appearance								Piloerection								Skin/visual mucosa							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
702	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
705	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
706	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
707	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
709	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
710	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery  
 Figures indicate scores

## Appendix 4-4 (Continued-4) Functional observational battery in female rats

300 mg/kg group

Animal No.	Pupil size								Salivation								Lacrimation							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	0	0	0	0	1	.	.	0	0	0	0	0	0	.	.
702	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.	0	0	0	0	0	0	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	1	1	.	.	0	0	0	0	0	0	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
705	0	0	0	0	0	0	.	.	0	0	0	1	1	1	.	.	0	0	0	0	0	0	.	.
706	0	0	0	0	0	0	.	.	0	0	1	1	1	1	.	.	0	0	0	0	0	0	.	.
707	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
709	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
710	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.4	0.5	0.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.5	0.5	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration      D : Day of administration      R : Day of recovery

Figures indicate scores

\* Significantly different from control (P&lt;0.05)

\*\* Significantly different from control (P&lt;0.01)

## Appendix 4-4 (Continued-5) Functional observational battery in female rats

## 300 mg/kg group

Animal No.	Righting reflex								Consciousness								Gait							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
702	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
705	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
706	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.
707	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
709	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
710	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Figures indicate scores

## Appendix 4-4 (Continued-6) Functional observational battery in female rats

## 300 mg/kg group

Animal No.	Defecation (counts / 2 min)								Urination (counts / 2 min)								Rearing (counts / 2 min)							
	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14	B3	D1	D7	D14	D21	D28	R7	R14
701	0	0	0	0	0	0	.	.	0	1	0	0	0	0	.	.	13	13	14	11	18	14	.	.
702	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	1	10	0	7	1	6	.	.
703	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	4	11	5	6	7	7	.	.
704	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	6	4	3	5	7	9	.	.
705	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	3	7	2	4	7	10	.	.
706	0	0	0	0	0	0	.	.	0	0	0	0	0	0	.	.	9	7	7	10	14	9	.	.
707	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	8	4	1	3	4	7	3
708	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	6	1	7	2	2	5	6
709	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	12	3	8	8	6	8	7
710	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	5	4	4	11	11	9	9
711	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	13	7	6	17	14	16	22	10
712	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	2	7	3	3	5	6	11
Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	6.4	7.7	4.7	6.9	7.9	8.3	9.5	7.7
S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	3.7	3.3	3.7	4.3	5.4	4.1	6.3	2.9
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

B : Before administration

D : Day of administration

R : Day of recovery

Appendix 5-1-1 Functional tests in male rats  
- The 4th week of administration -

## Control group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
001	0	0	0	0	0	0.704	0.873	0.789	9.0	10.2	9.6
002	0	0	0	0	0	1.012	1.266	1.139	10.5	11.7	11.1
003	0	0	0	0	0	0.947	0.831	0.889	5.0	6.5	5.8
004	0	0	0	0	0	0.982	1.157	1.070	8.5	7.3	7.9
005	0	0	0	0	0	1.588	1.360	1.474	6.2	5.3	5.8
006	0	0	0	0	0	1.112	0.933	1.023	5.6	4.7	5.2
007	0	0	0	0	0	1.079	1.065	1.072	6.5	6.6	6.6
008	0	0	0	0	0	0.740	0.722	0.731	4.3	3.5	3.9
009	0	0	0	0	0	0.964	1.112	1.038	5.2	4.6	4.9
010	0	0	0	0	0	1.028	1.185	1.107	6.0	5.1	5.6
011	0	0	0	0	0	1.012	1.192	1.102	6.0	5.2	5.6
012	0	0	0	0	0	1.253	1.369	1.311	8.3	7.2	7.8
Mean	0.0	0.0	0.0	0.0	0.0	1.035	1.089	1.062	6.8	6.5	6.7
S.D.	0.0	0.0	0.0	0.0	0.0	0.229	0.209	0.204	1.9	2.4	2.1
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

I : First trial

II : Second trial

Appendix 5-1-2 Functional tests in male rats  
- The 4th week of administration -

## 30 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
101	0	0	0	0	0	0.880	0.803	0.842	11.2	12.0	11.6
102	0	0	0	0	0	1.474	1.359	1.417	6.0	4.5	5.3
103	0	0	0	0	0	0.679	0.841	0.760	4.5	3.8	4.2
104	0	0	0	0	0	1.164	1.223	1.194	6.4	5.5	6.0
105	0	0	0	0	0	0.828	0.895	0.862	8.0	7.6	7.8
106	0	0	0	0	0	1.341	1.557	1.449	8.2	7.5	7.9
Mean	0.0	0.0	0.0	0.0	0.0	1.061	1.113	1.087	7.4	6.8	7.1
S.D.	0.0	0.0	0.0	0.0	0.0	0.314	0.312	0.306	2.3	3.0	2.6
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 5-1-3 Functional tests in male rats  
- The 4th week of administration -

## 100 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
201	0	0	0	0	0	1.124	1.085	1.105	6.0	7.5	6.8
202	0	0	0	0	0	0.844	0.828	0.836	9.0	8.5	8.8
203	0	0	0	0	0	0.890	1.090	0.990	7.4	6.5	7.0
204	0	0	0	0	0	0.812	0.895	0.854	9.0	9.5	9.3
205	0	0	0	0	0	1.181	0.937	1.059	11.5	10.8	11.2
206	0	0	0	0	0	1.308	1.097	1.203	4.5	4.6	4.6
Mean	0.0	0.0	0.0	0.0	0.0	1.027	0.989	1.008	7.9	7.9	8.0
S.D.	0.0	0.0	0.0	0.0	0.0	0.205	0.117	0.144	2.5	2.2	2.3
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 5-1-4 Functional tests in male rats  
- The 4th week of administration -

## 300 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
301	0	0	0	0	0	0.896	0.964	0.930	5.4	5.2	5.3
302	0	0	0	0	0	1.239	1.102	1.171	9.3	8.2	8.8
303	0	0	0	0	0	0.737	0.873	0.805	5.9	5.7	5.8
304	0	0	0	0	0	1.211	1.384	1.298	7.4	5.7	6.6
305	0	0	0	0	0	0.907	0.995	0.951	8.2	8.3	8.3
306	0	0	0	0	0	1.096	0.994	1.045	6.4	4.8	5.6
307	0	0	0	0	0	0.852	0.905	0.879	5.3	5.1	5.2
308	0	0	0	0	0	1.104	0.991	1.048	8.2	6.3	7.3
309	0	0	0	0	0	0.875	1.161	1.018	8.5	7.3	7.9
310	0	0	0	0	0	1.321	1.007	1.164	8.6	7.5	8.1
311	0	0	0	0	0	1.046	1.285	1.166	4.0	4.0	4.0
312	0	0	0	0	0	1.137	1.072	1.105	6.5	5.5	6.0
Mean	0.0	0.0	0.0	0.0	0.0	1.035	1.061	1.048	7.0	6.1	6.6
S.D.	0.0	0.0	0.0	0.0	0.0	0.180	0.151	0.141	1.6	1.4	1.5
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

I : First trial

II : Second trial

Appendix 5-2-1 Functional tests in male rats  
- The 2nd week of recovery -

## Control group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
007	0	0	0	0	0	1.674	1.947	1.811	2.7	3.2	3.0
008	0	0	0	0	0	1.790	1.638	1.714	5.3	6.2	5.8
009	0	0	0	0	0	1.412	1.477	1.445	2.8	2.9	2.9
010	0	0	0	0	0	1.015	1.319	1.167	5.0	4.0	4.5
011	0	0	0	0	0	1.654	1.949	1.802	8.7	7.9	8.3
012	0	0	0	0	0	1.724	1.643	1.684	4.4	4.2	4.3
Mean	0.0	0.0	0.0	0.0	0.0	1.545	1.662	1.604	4.8	4.7	4.8
S.D.	0.0	0.0	0.0	0.0	0.0	0.290	0.252	0.252	2.2	1.9	2.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 5-2-2 Functional tests in male rats  
- The 2nd week of recovery -

## 300 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
307	0	0	0	0	0	1.542	1.227	1.385	4.1	4.3	4.2
308	0	0	0	0	0	1.591	1.588	1.590	5.6	6.0	5.8
309	0	0	0	0	0	1.752	1.412	1.582	4.2	4.6	4.4
310	0	0	0	0	0	1.748	1.568	1.658	7.4	6.2	6.8
311	0	0	0	0	0	1.506	1.519	1.513	5.7	5.3	5.5
312	0	0	0	0	0	1.510	1.460	1.485	4.8	4.1	4.5
Mean	0.0	0.0	0.0	0.0	0.0	1.608	1.462	1.536	5.3	5.1	5.2
S.D.	0.0	0.0	0.0	0.0	0.0	0.114	0.133	0.096	1.2	0.9	1.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 6-1-1 Functional tests in female rats  
- The 4th week of administration -

## Control group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
401	0	0	0	0	0	0.799	0.699	0.749	4.0	3.9	4.0
402	0	0	0	0	0	0.514	0.478	0.496	6.2	6.0	6.1
403	0	0	0	0	0	0.685	0.709	0.697	4.5	3.2	3.9
404	0	0	0	0	0	0.912	0.864	0.888	6.2	4.2	5.2
405	0	0	0	0	0	0.990	1.002	0.996	5.4	4.7	5.1
406	0	0	0	0	0	0.731	0.835	0.783	6.8	6.2	6.5
407	0	0	0	0	0	0.956	1.031	0.994	5.1	5.0	5.1
408	0	0	0	0	0	0.788	0.737	0.763	3.8	4.7	4.3
409	0	0	0	0	0	0.777	0.789	0.783	5.0	4.5	4.8
410	0	0	0	0	0	1.072	1.002	1.037	6.3	5.4	5.9
411	0	0	0	0	0	0.973	0.970	0.972	4.0	4.2	4.1
412	0	0	0	0	0	1.254	1.180	1.217	9.0	9.1	9.1
Mean	0.0	0.0	0.0	0.0	0.0	0.871	0.858	0.865	5.5	5.1	5.3
S.D.	0.0	0.0	0.0	0.0	0.0	0.196	0.191	0.191	1.5	1.5	1.5
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

I : First trial

II : Second trial

Appendix 6-1-2 Functional tests in female rats  
- The 4th week of administration -

30 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
501	0	0	0	0	0	0.648	0.795	0.722	5.2	4.3	4.8
502	0	0	0	0	0	0.800	0.938	0.869	4.5	3.0	3.8
503	0	0	0	0	0	0.535	0.688	0.612	4.5	4.0	4.3
504	0	0	0	0	0	0.978	0.805	0.892	6.0	6.0	6.0
505	0	0	0	0	0	0.909	0.842	0.876	5.5	4.0	4.8
506	0	0	0	0	0	1.129	1.135	1.132	4.7	5.2	5.0
Mean	0.0	0.0	0.0	0.0	0.0	0.833	0.867	0.851	5.1	4.4	4.8
S.D.	0.0	0.0	0.0	0.0	0.0	0.218	0.154	0.176	0.6	1.0	0.7
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 6-1-3 Functional tests in female rats  
- The 4th week of administration -

100 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
601	0	0	0	0	0	0.700	0.887	0.794	4.5	5.5	5.0
602	0	0	0	0	0	0.640	0.833	0.737	4.5	6.0	5.3
603	0	0	0	0	0	0.656	0.861	0.759	6.8	6.5	6.7
604	0	0	0	0	0	0.806	0.743	0.775	4.5	4.0	4.3
605	0	0	0	0	0	0.707	0.749	0.728	5.3	4.2	4.8
606	0	0	0	0	0	1.104	1.134	1.119	9.2	7.8	8.5
Mean	0.0	0.0	0.0	0.0	0.0	0.769	0.868	0.819	5.8	5.7	5.8
S.D.	0.0	0.0	0.0	0.0	0.0	0.174	0.143	0.149	1.9	1.4	1.6
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 6-1-4 Functional tests in female rats  
- The 4th week of administration -

300 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
701	0	0	0	0	0	0.748	0.849	0.799	5.7	5.4	5.6
702	0	0	0	0	0	0.547	0.688	0.618	3.0	3.7	3.4
703	0	0	0	0	0	0.652	0.750	0.701	3.2	3.8	3.5
704	0	0	0	0	0	0.583	0.600	0.592	4.2	3.5	3.9
705	0	0	0	0	0	0.892	0.801	0.847	3.2	3.8	3.5
706	0	0	0	0	0	0.814	0.911	0.863	3.4	3.2	3.3
707	0	0	0	0	0	0.888	0.791	0.840	6.3	6.0	6.2
708	0	0	0	0	0	0.986	0.989	0.988	2.5	2.7	2.6
709	0	0	0	0	0	0.765	0.801	0.783	4.6	5.1	4.9
710	0	0	0	0	0	1.104	1.184	1.144	7.5	6.5	7.0
711	0	0	0	0	0	0.795	0.841	0.818	4.1	4.0	4.1
712	0	0	0	0	0	1.046	0.980	1.013	3.4	3.8	3.6
Mean	0.0	0.0	0.0	0.0	0.0	0.818	0.849	0.834	4.3	4.3	4.3
S.D.	0.0	0.0	0.0	0.0	0.0	0.175	0.153	0.160	1.5	1.2	1.3
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(12)

I : First trial

II : Second trial

Appendix 6-2-1 Functional tests in female rats  
- The 2nd week of recovery -

## Control group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
407	0	0	0	0	0	1.031	0.915	0.973	4.1	4.5	4.3
408	0	0	0	0	0	1.229	1.210	1.220	4.5	6.0	5.3
409	0	0	0	0	0	1.176	0.880	1.028	4.7	3.9	4.3
410	0	0	0	0	0	1.356	1.232	1.294	5.5	5.8	5.7
411	0	0	0	0	0	1.085	1.413	1.249	2.5	3.2	2.9
412	0	0	0	0	0	1.631	1.529	1.580	8.7	8.0	8.4
Mean	0.0	0.0	0.0	0.0	0.0	1.251	1.197	1.224	5.0	5.2	5.2
S.D.	0.0	0.0	0.0	0.0	0.0	0.218	0.260	0.216	2.1	1.7	1.9
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

Appendix 6-2-2 Functional tests in female rats  
- The 2nd week of recovery -

## 300 mg/kg group

Animal No.	Score					Grip strength (kg)			Landing foot-splay (cm)		
	Pupillary reflex	Visual placing response	Auditory response	Pain response	Aerial righting	I	II	Mean	I	II	Mean
707	0	0	0	0	0	1.339	1.402	1.371	6.2	5.4	5.8
708	0	0	0	0	0	1.396	1.351	1.374	5.3	5.1	5.2
709	0	0	0	0	0	1.141	0.956	1.049	4.3	4.0	4.2
710	0	0	0	0	0	1.292	1.313	1.303	6.5	6.0	6.3
711	0	0	0	0	0	1.228	1.274	1.251	6.3	5.1	5.7
712	0	0	0	0	0	1.392	1.206	1.299	3.7	3.4	3.6
Mean	0.0	0.0	0.0	0.0	0.0	1.298	1.250	1.275	5.4	4.8	5.1
S.D.	0.0	0.0	0.0	0.0	0.0	0.100	0.159	0.120	1.2	1.0	1.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

I : First trial

II : Second trial

## Appendix 7-1 Spontaneous motor activity in male rats

Control group		
Animal No.	Motor activity (counts / 60 min)	
	The 4th week of administration	The 2nd week of recovery
001	56	.
002	280	.
003	155	.
004	279	.
005	308	.
006	877	.
007	907	352
008	308	135
009	372	102
010	545	341
011	255	312
012	298	352
Mean	387	266
S.D.	263	115
(N)	(12)	(6)

2000TT278

Appendix 7-2 Spontaneous motor activity in male rats

30 mg/kg group	
Animal	Motor activity (counts / 60 min)
No.	The 4th week of administration
101	91
102	275
103	224
104	60
105	438
106	275
Mean	227
S.D.	138
(N)	(6)

2000TT278

Appendix 7-3 Spontaneous motor activity in male rats

100 mg/kg group	
Animal	Motor activity (counts / 60 min)
No.	The 4th week of administration
201	304
202	151
203	239
204	93
205	93
206	475
Mean	226
S.D.	148
(N)	(6)

2000TT278

## Appendix 7-4 Spontaneous motor activity in male rats

300 mg/kg group

Animal No.	Motor activity (counts / 60 min)	
	The 4th week of administration	The 2nd week of recovery
301	309	.
302	174	.
303	363	.
304	71	.
305	179	.
306	112	.
307	478	797
308	293	253
309	132	195
310	116	258
311	326	292
312	174	535
Mean	227	388
S.D.	124	233
(N)	(12)	(6)

2000TT278

## Appendix 8-1 Spontaneous motor activity in female rats

Control group		
Animal No.	Motor activity (counts / 60 min)	
	The 4th week of administration	The 2nd week of recovery
401	272	.
402	327	.
403	318	.
404	246	.
405	352	.
406	425	.
407	82	84
408	307	219
409	308	182
410	227	129
411	294	205
412	271	339
Mean	286	193
S.D.	82	87
(N)	(12)	(6)

Appendix 8-2 Spontaneous motor activity in female rats

2000TT278

30 mg/kg group

Animal No.	Motor activity (counts / 60 min) The 4th week of administration
501	341
502	636
503	237
504	89
505	236
506	182
Mean	287
S.D.	190
(N)	(6)

2000TT278

Appendix 8-3 Spontaneous motor activity in female rats

100 mg/kg group

Animal	Motor activity (counts / 60 min)
No.	The 4th week of administration
601	247
602	344
603	517
604	155
605	108
606	148
Mean	253
S.D.	155
(N)	(6)

## Appendix 8-4 Spontaneous motor activity in female rats

2000TT278

300 mg/kg group

Animal No.	Motor activity (counts / 60 min)	
	The 4th week of administration	The 2nd week of recovery
701	267	
702	205	
703	469	
704	192	
705	162	
706	138	
707	110	215
708	192	380
709	350	536
710	261	805
711	264	607
712	383	474
Mean	249	**
S.D.	107	503
(N)	(12)	201
		(6)

## Appendix 9-1 Body weight in male rats

Control group		Unit : g								
Animal No.	Day of administration							Day of recovery		
	-3	1	3	8	15	22	28	1	8	14
001	252	278	288	316	353	387	406	.	.	.
002	264	288	303	337	367	411	443	.	.	.
003	257	285	296	332	375	419	446	.	.	.
004	250	276	290	321	358	401	432	.	.	.
005	258	282	297	324	355	376	386	.	.	.
006	255	283	283	302	336	363	391	.	.	.
007	268	292	307	347	397	444	475	473	504	507
008	239	258	267	292	334	371	389	384	409	425
009	259	284	299	335	372	403	432	430	455	463
010	239	261	265	287	322	348	371	368	403	411
011	257	284	291	321	367	403	430	426	458	469
012	256	278	288	306	337	365	388	383	418	430
Mean	255	279	290	318	356	391	416	411	441	451
S.D.	9	10	13	19	21	28	32	39	39	36
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(6)

2000TT278

## Appendix 9-2 Body weight in male rats

30 mg/kg group

Unit : g

Animal No.	Day of administration						
	-3	1	3	8	15	22	28
101	266	295	304	335	376	413	438
102	244	274	288	317	373	401	418
103	250	273	282	309	345	375	402
104	251	272	284	305	341	370	383
105	261	285	295	328	371	404	427
106	263	287	295	320	348	376	386
Mean	256	281	291	319	359	390	409
S.D.	9	9	8	11	16	18	22
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

## Appendix 9-3 Body weight in male rats

100 mg/kg group

Unit : g

Animal No.	Day of administration						
	-3	1	3	8	15	22	28
201	258	290	297	337	381	421	450
202	248	269	278	303	339	364	379
203	244	268	282	308	342	367	388
204	258	285	301	336	380	419	437
205	261	285	304	337	374	399	419
206	266	291	306	333	353	369	394
Mean	256	281	295	326	362	390	411
S.D.	8	10	12	16	19	27	29
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

## Appendix 9-4 Body weight in male rats

300 mg/kg group		Unit : g								
Animal No.	Day of administration							Day of recovery		
	-3	1	3	8	15	22	28	1	8	14
301	242	261	260	270	299	318	334	.	.	.
302	251	273	258	278	320	348	369	.	.	.
303	271	303	296	324	366	392	409	.	.	.
304	272	299	297	330	383	426	431	.	.	.
305	264	290	300	330	382	411	439	.	.	.
306	248	276	288	305	355	380	400	.	.	.
307	262	291	272	283	338	384	408	410	451	459
308	246	275	271	298	317	353	373	377	408	419
309	250	278	266	286	322	346	353	351	388	398
310	244	275	245	280	333	377	381	388	415	424
311	263	284	277	293	331	355	373	372	409	413
312	258	286	274	297	335	370	387	382	414	418
Mean	256	283	* 275	* 298	340	372	388	380	414	422
S.D.	10	12	17	21	26	30	31	19	21	20
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

## Appendix 10-1 Body weight in female rats

Control group										Unit : g
Animal No.	Day of administration							Day of recovery		
	-3	1	3	8	15	22	28	1	8	14
401	176	178	188	197	215	223	234	.	.	.
402	169	188	195	208	222	225	247	.	.	.
403	196	205	205	224	239	255	269	.	.	.
404	180	190	197	207	228	243	254	.	.	.
405	188	198	201	207	223	238	245	.	.	.
406	192	200	197	205	218	233	243	.	.	.
407	193	217	209	227	246	263	278	273	281	289
408	189	200	207	222	239	255	271	265	290	301
409	190	192	200	211	223	235	249	246	259	258
410	186	200	200	213	224	246	261	264	270	279
411	191	203	208	218	241	254	274	269	289	291
412	183	192	202	205	233	250	250	254	261	273
Mean	186	197	201	212	229	243	256	262	275	282
S.D.	8	10	6	9	10	13	14	10	14	15
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(6)

## Appendix 10-2 Body weight in female rats

30 mg/kg group

Unit : g

Animal No.	Day of administration						
	-3	1	3	8	15	22	28
501	185	190	199	211	230	240	255
502	193	196	207	224	244	260	273
503	177	181	193	202	222	231	247
504	185	190	199	213	231	235	251
505	204	208	219	228	257	269	281
506	200	212	219	223	242	260	261
Mean	191	196	206	217	238	249	261
S.D.	10	12	11	10	13	16	13
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

## Appendix 10-3 Body weight in female rats

100 mg/kg group

Unit : g

Animal No.	Day of administration						
	-3	1	3	8	15	22	28
601	196	202	208	217	232	238	253
602	181	184	188	186	203	208	214
603	189	190	202	212	231	238	247
604	173	180	182	193	205	210	228
605	196	209	212	210	240	253	265
606	193	203	207	222	244	262	273
Mean	188	195	200	207	226	235	247
S.D.	9	12	12	14	18	22	22
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

## Appendix 10-4 Body weight in female rats

300 mg/kg group

Unit : g

Animal No.	Day of administration							Day of recovery		
	-3	1	3	8	15	22	28	1	8	14
701	190	190	195	184	209	212	221	.	.	.
702	195	209	202	206	216	212	214	.	.	.
703	177	181	188	194	203	204	217	.	.	.
704	185	192	185	199	208	213	227	.	.	.
705	180	183	180	179	200	212	210	.	.	.
706	195	206	208	214	225	238	241	.	.	.
707	198	207	210	217	235	237	252	251	270	272
708	189	205	190	209	231	239	258	258	287	288
709	197	207	192	206	228	240	246	247	274	282
710	190	196	190	205	224	206	231	226	256	261
711	170	188	179	193	190	202	206	209	225	235
712	183	193	196	201	221	229	243	239	247	250
Mean	187	196	193	*	*	**	**	*		
S.D.	9	10	10	11	14	15	17	18	22	20
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)	(6)

\* Significantly different from control (P&lt;0.05)

\*\* Significantly different from control (P&lt;0.01)

## Appendix 11-1 Food consumption in male rats

Control group							Unit : g/day	
Animal No.	Day of administration						Day of recovery	
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>	1~8 <sup>c)</sup>	8~14 <sup>d)</sup>
001	26.4	22.3	23.1	22.6	22.7	21.2	.	.
002	28.6	24.5	26.3	24.9	25.8	25.9	.	.
003	26.1	22.4	22.9	23.6	24.0	22.3	.	.
004	25.8	23.8	24.7	24.8	24.5	22.9	.	.
005	28.0	23.8	24.5	23.7	21.2	18.9	.	.
006	28.4	21.1	22.7	24.3	22.6	22.0	.	.
007	28.4	25.9	25.8	27.4	27.1	26.5	31.0	29.7
008	24.5	20.5	21.5	21.6	22.4	20.4	25.6	27.5
009	26.3	23.9	24.0	23.9	23.8	23.0	28.1	27.5
010	22.6	19.4	20.5	20.5	21.2	20.8	25.6	26.7
011	25.1	20.1	22.5	23.5	23.4	20.7	25.2	27.5
012	28.1	24.0	23.3	22.8	22.4	21.4	26.2	27.0
Mean	26.5	22.6	23.5	23.6	23.4	22.2	27.0	27.7
S.D.	1.9	2.0	1.7	1.7	1.8	2.2	2.2	1.1
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

## Appendix 11-2 Food consumption in male rats

30 mg/kg group Unit : g/day

Animal No.	Day of administration					
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>
101	30.0	22.8	26.2	25.7	25.6	22.6
102	26.0	23.1	23.3	25.0	24.1	20.0
103	24.6	20.2	21.6	21.6	21.3	19.9
104	25.8	21.9	21.2	20.8	21.6	19.1
105	26.9	23.5	25.5	25.0	24.9	23.7
106	24.1	20.9	20.7	20.9	21.3	18.6
Mean	26.2	22.1	23.1	23.2	23.1	20.7
S.D.	2.1	1.3	2.3	2.3	2.0	2.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

## Appendix 11-3 Food consumption in male rats

100 mg/kg group Unit : g/day

Animal No.	Day of administration					
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>
201	26.2	22.0	24.6	23.5	23.6	21.6
202	23.7	21.6	21.4	21.8	22.0	19.9
203	25.2	23.9	23.0	23.1	23.3	19.8
204	24.7	22.6	24.0	24.6	24.3	23.1
205	28.2	25.9	27.0	24.6	22.6	19.2
206	28.6	25.8	25.4	21.7	20.7	21.1
Mean	26.1	23.6	24.2	23.2	22.8	20.8
S.D.	2.0	1.9	1.9	1.3	1.3	1.4
(N)	(6)	(6)	(6)	(6)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

## Appendix 11-4 Food consumption in male rats

300 mg/kg group

Unit : g/day

Animal No.	Day of administration						Day of recovery	
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>	1~8 <sup>c)</sup>	8~14 <sup>d)</sup>
301	26.2	18.5	18.8	19.4	20.6	20.4	.	.
302	25.2	12.2	16.9	23.8	21.4	21.9	.	.
303	27.8	17.1	23.2	25.5	21.0	23.5	.	.
304	27.7	16.5	23.6	26.4	28.3	21.7	.	.
305	27.2	22.6	22.7	25.2	24.1	23.3	.	.
306	24.7	19.5	20.5	24.1	22.3	22.1	.	.
307	26.9	13.8	16.3	24.0	25.8	24.5	29.7	29.3
308	25.1	16.4	19.9	19.9	21.2	21.7	27.8	25.8
309	26.7	14.9	18.8	22.4	20.6	19.7	25.6	25.8
310	25.2	7.3	17.7	23.4	23.0	18.5	26.5	27.1
311	26.8	14.4	18.1	21.7	21.5	22.6	28.0	28.6
312	28.9	15.1	21.5	25.2	27.0	23.5	30.6	29.8
Mean	26.5	15.7	19.8	23.4	23.1	22.0	28.0	27.7
S.D.	1.3	3.8	2.5	2.2	2.6	1.7	1.9	1.8
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

\*\* Significantly different from control (P<0.01)

## Appendix 12-1 Food consumption in female rats

Control group		Unit : g/day						
Animal No.	Day of administration						Day of recovery	
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>	1~8 <sup>c)</sup>	8~14 <sup>d)</sup>
401	16.4	13.6	14.9	15.5	14.6	14.2	.	.
402	19.4	13.9	16.1	15.5	16.2	16.1	.	.
403	17.3	13.4	17.8	17.3	17.7	15.8	.	.
404	19.1	15.2	16.4	17.8	17.3	16.4	.	.
405	15.4	15.4	15.2	16.0	15.5	15.4	.	.
406	17.4	13.6	16.1	16.2	16.0	14.5	.	.
407	19.9	11.8	17.2	17.3	17.6	15.6	18.3	21.3
408	20.7	16.5	18.3	18.2	18.0	17.4	22.1	21.0
409	16.8	15.5	16.5	16.9	15.9	15.4	18.9	19.6
410	17.1	14.0	15.8	16.4	16.5	14.9	19.0	20.8
411	17.6	15.2	15.8	17.7	17.6	16.5	20.7	20.7
412	16.1	17.2	15.9	18.0	15.9	15.5	19.4	19.8
Mean	17.8	14.6	16.3	16.9	16.6	15.6	19.7	20.5
S.D.	1.6	1.5	1.0	1.0	1.1	0.9	1.4	0.7
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

## Appendix 12-2 Food consumption in female rats

30 mg/kg group Unit : g/day

Animal No.	Day of administration					
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>
501	18.7	15.2	16.4	16.9	17.3	16.4
502	19.6	18.3	17.7	18.6	17.6	18.1
503	16.0	14.6	15.7	16.1	15.0	14.4
504	17.5	15.1	15.1	15.9	13.8	13.8
505	19.5	18.7	18.1	20.6	20.0	18.2
506	18.7	17.2	17.0	17.7	19.0	15.3
Mean	18.3	16.5	16.7	17.6	17.1	16.0
S.D.	1.4	1.8	1.2	1.8	2.3	1.9
(N)	(6)	(6)	(6)	(6)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

## Appendix 12-3 Food consumption in female rats

100 mg/kg group Unit : g/day

Animal No.	Day of administration					
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>
601	20.0	16.7	15.7	16.4	15.8	16.2
602	15.7	14.7	16.0	15.6	14.1	13.7
603	17.7	15.4	14.9	15.4	14.4	14.8
604	16.7	12.6	14.4	14.6	14.6	14.7
605	15.5	16.1	14.4	17.1	16.2	15.1
606	18.8	16.2	16.4	17.5	18.0	17.1
Mean	17.4	15.3	15.3	16.1	15.5	15.3
S.D.	1.8	1.5	0.9	1.1	1.5	1.2
(N)	(6)	(6)	(6)	(6)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

## Appendix 12-4 Food consumption in female rats

300 mg/kg group							Unit : g/day	
Animal No.	Day of administration						Day of recovery	
	-3~-1 <sup>a)</sup>	1~3 <sup>a)</sup>	3~8 <sup>b)</sup>	8~15 <sup>c)</sup>	15~22 <sup>c)</sup>	22~28 <sup>d)</sup>	1~8 <sup>c)</sup>	8~14 <sup>d)</sup>
701	18.4	16.1	11.1	17.1	16.5	17.2	.	.
702	18.1	12.4	9.1	16.9	13.2	15.0	.	.
703	17.1	14.8	14.1	16.9	13.1	15.2	.	.
704	15.6	11.4	11.8	16.2	14.8	11.0	.	.
705	13.9	12.8	11.6	15.3	15.3	13.8	.	.
706	15.8	11.7	14.2	14.5	16.4	14.4	.	.
707	16.3	14.7	11.9	17.4	18.2	15.0	21.0	21.2
708	18.6	8.8	13.4	17.3	17.4	17.2	21.1	21.2
709	19.1	10.5	14.2	18.6	20.4	16.9	23.4	21.8
710	16.2	12.4	14.4	17.0	14.6	12.2	23.1	21.6
711	17.4	9.5	11.8	13.1	15.3	11.9	20.4	19.4
712	16.4	12.5	14.1	17.2	16.3	16.1	20.7	19.8
Mean	16.9	12.3	12.6	16.5	16.0	14.7	21.6	20.8
S.D.	1.5	2.2	1.7	1.5	2.1	2.1	1.3	1.0
(N)	(12)	(12)	(12)	(12)	(12)	(12)	(6)	(6)

Mean daily food consumption was calculated as follows :

- a) 2-day cumulative food consumption / 2
- b) 5-day cumulative food consumption / 5
- c) 7-day cumulative food consumption / 7
- d) 6-day cumulative food consumption / 6

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 13-1-1 Urinary findings in male rats  
- The 4th week of administration -

Control group											
Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
001	25.2	10.7	Y	1.043	8.5	+-	-	+	-	-	0.1
002	45.0	28.2	Y	1.027	8.0	-	-	-	-	-	0.1
003	35.9	17.4	Y	1.035	8.0	+	-	-	-	-	0.1
004	25.7	11.6	Y	1.044	8.0	+-	-	+-	-	-	0.1
005	29.3	13.6	Y	1.038	8.0	-	-	+-	-	-	0.1
006	36.3	15.1	Y	1.038	8.0	-	-	-	-	-	0.1
007	22.9	9.0	Y	1.050	8.5	+	-	+	-	-	0.1
008	37.4	26.3	Y	1.027	7.5	-	-	-	-	-	0.1
009	28.1	16.2	Y	1.036	8.5	-	-	+	-	-	0.1
010	44.4	26.0	Y	1.027	8.5	-	-	-	-	-	0.1
011	14.4	8.6	Y	1.045	8.5	+-	-	+	-	-	0.1
012	28.0	11.2	Y	1.045	8.5	+-	-	+	-	-	0.1
Mean	31.1	16.2		1.038							
S.D.	9.0	7.0		0.008							
(N)	(12)	(12)		(12)							

Appendix 13-1-2 Urinary findings in male rats  
- The 4th week of administration -

## 30 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
101	29.2	19.2	Y	1.034	8.0	-	-	+	-	-	0.1
102	25.1	8.9	Y	1.047	8.0	-	-	+	-	-	0.1
103	20.5	8.6	Y	1.052	8.5	+-	-	+	-	-	0.1
104	20.5	8.7	Y	1.046	8.5	+	-	+	-	-	0.1
105	34.1	16.2	Y	1.036	8.5	-	-	+	-	-	0.1
106	27.1	14.3	Y	1.035	8.0	+	-	+	-	+	0.1
Mean	26.1	12.7		1.042							
S.D.	5.3	4.6		0.008							
(N)	(6)	(6)		(6)							

2000TT278

Appendix 13-1-3 Urinary findings in male rats  
- The 4th week of administration -

100 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
201	18.2	6.0	Y	1.054	8.5	+-	-	-	-	-	0.1
202	24.3	11.0	Y	1.043	8.0	-	-	-	-	-	0.1
203	24.6	12.0	Y	1.036	8.5	+-	-	+-	-	-	0.1
204	30.0	14.4	Y	1.037	8.5	+-	-	+-	-	-	0.1
205	35.8	14.8	Y	1.037	8.5	+	-	+	-	-	0.1
206	22.7	10.2	Y	1.046	8.5	+-	-	+-	-	-	0.1
Mean	25.9	11.4		1.042							
S.D.	6.1	3.2		0.007							
(N)	(6)	(6)		(6)							

Appendix 13-1-4 Urinary findings in male rats  
 - The 4th week of administration -

## 300 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
301	23.6	7.9	Y	1.050	8.5	+	-	-	-	-	0.1
302	28.2	12.4	Y	1.041	8.0	-	-	-	-	-	0.1
303	28.5	10.6	Y	1.047	8.0	-	-	+	-	-	0.1
304	32.6	14.8	Y	1.037	8.0	+	-	+	-	-	0.1
305	34.1	16.0	Y	1.037	8.0	-	-	-	-	-	0.1
306	40.2	14.0	Y	1.041	8.0	-	-	-	-	-	0.1
307	35.7	11.0	Y	1.046	8.0	-	-	-	-	-	0.1
308	32.5	18.3	Y	1.033	8.0	-	-	-	-	-	0.1
309	23.0	8.0	Y	1.052	8.5	-	-	-	-	-	0.1
310	43.6	23.6	Y	1.031	7.5	-	-	-	-	-	0.1
311	33.8	18.8	Y	1.035	8.5	-	-	-	-	-	0.1
312	33.1	10.4	Y	1.048	8.5	-	-	-	-	-	0.1
Mean	32.4	13.8		1.042							
S.D.	6.0	4.7		0.007							
(N)	(12)	(12)		(12)							

2000TT278

Appendix 13-2-1 Urinary findings in male rats  
- The 2nd week of recovery -

## Control group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
007	36.3	12.8	Y	1.045	8.5	+-	-	-	-	-	0.1
008	52.4	33.4	Y	1.025	8.0	-	-	-	-	-	0.1
009	31.5	15.0	Y	1.036	8.5	+-	-	+	-	-	0.1
010	42.2	27.0	Y	1.030	8.0	-	-	-	-	-	0.1
011	21.8	8.2	Y	1.050	8.5	-	-	-	-	-	0.1
012	29.7	17.6	Y	1.039	8.5	-	-	-	-	-	0.1
Mean	35.7	19.0		1.038							
S.D.	10.7	9.4		0.009							
(N)	(6)	(6)		(6)							

2000TT278

Appendix 13-2-2 Urinary findings in male rats  
- The 2nd week of recovery -

## 300 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
307	34.0	11.8	Y	1.049	8.0	-	-	-	-	-	0.1
308	20.4	11.6	Y	1.041	8.5	-	-	+	-	-	0.1
309	21.7	10.6	Y	1.048	8.5	-	-	+	-	-	0.1
310	31.2	15.8	Y	1.041	8.5	+	-	-	-	-	0.1
311	41.9	24.0	Y	1.034	8.0	-	-	-	-	-	0.1
312	27.5	11.0	Y	1.053	8.5	+	-	+	-	+	0.1
Mean	29.5	14.1		1.044							
S.D.	8.1	5.2		0.007							
(N)	(6)	(6)		(6)							

Appendix 14-1-1 Urinary findings in female rats  
- The 4th week of administration -

## Control group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
401	16.7	6.0	Y	1.045	8.5	-	-	-	-	-	0.1
402	17.4	6.4	Y	1.049	8.0	-	-	-	-	-	0.1
403	19.5	5.1	Y	1.048	8.0	-	-	-	-	-	0.1
404	18.3	12.3	Y	1.036	8.0	-	-	-	-	-	0.1
405	18.6	10.4	Y	1.037	8.0	-	-	-	-	-	0.1
406	10.1	4.0	Y	1.056	8.5	-	-	-	-	-	0.1
407	8.6	3.0	Y	1.067	8.5	+	-	-	-	-	0.1
408	22.4	13.1	Y	1.035	8.0	+	-	-	-	-	0.1
409	24.2	12.9	Y	1.034	8.5	-	-	-	-	-	0.1
410	12.3	6.0	Y	1.050	8.5	+	-	-	-	-	0.1
411	15.4	9.3	Y	1.041	7.0	+	-	-	-	-	0.1
412	29.7	17.2	Y	1.030	8.0	-	-	-	-	-	0.1
Mean	17.8	8.8		1.044							
S.D.	5.9	4.4		0.011							
(N)	(12)	(12)		(12)							

2000TT278

Appendix 14-1-2 Urinary findings in female rats  
- The 4th week of administration -

## 30 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
501	16.6	5.4	Y	1.054	8.5	+-	-	-	-	-	0.1
502	20.9	13.5	Y	1.035	8.0	-	-	-	-	-	0.1
503	29.0	17.6	Y	1.028	8.0	-	-	-	-	-	0.1
504	24.6	14.2	Y	1.030	8.0	-	-	-	-	-	0.1
505	19.6	8.2	Y	1.046	8.5	+	-	-	-	-	0.1
506	14.9	8.1	Y	1.045	7.0	+	-	-	-	+++	0.1
Mean	20.9	11.2		1.040							
S.D.	5.2	4.6		0.010							
(N)	(6)	(6)		(6)							

2000TT278

Appendix 14-1-3 Urinary findings in female rats  
- The 4th week of administration -

100 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
601	29.8	15.6	Y	1.035	8.5	-	-	-	-	-	0.1
602	19.4	11.4	Y	1.036	8.0	+	-	-	-	-	0.1
603	19.4	13.0	Y	1.035	8.0	-	-	-	-	-	0.1
604	18.7	9.4	Y	1.038	8.5	-	-	-	-	-	0.1
605	27.2	11.6	Y	1.035	8.5	+	-	-	-	+	0.1
606	16.2	6.0	Y	1.050	8.5	-	-	-	-	-	0.1
Mean	21.8	11.2		1.038							
S.D.	5.4	3.3		0.006							
(N)	(6)	(6)		(6)							

Appendix 14-1-4 Urinary findings in female rats  
- The 4th week of administration -

## 300 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
701	15.3	8.9	Y	1.043	8.0	-	-	-	-	-	0.1
702	47.0	38.4	LY	1.018	7.0	-	-	-	-	-	0.1
703	26.9	10.8	Y	1.038	8.5	-	-	-	-	-	0.1
704	35.6	9.3	Y	1.038	6.5	-	-	-	-	-	0.1
705	23.1	17.4	Y	1.027	8.0	-	-	-	-	-	0.1
706	46.2	32.9	Y	1.020	7.5	-	-	-	-	-	0.1
707	29.9	9.2	Y	1.043	8.5	-	-	-	-	-	0.1
708	31.1	22.2	Y	1.028	8.5	-	-	-	-	-	0.1
709	0.8	9.2	Y	1.039	8.0	-	-	-	-	-	0.1
710	34.7	20.6	Y	1.030	8.5	-	-	-	-	-	0.1
711	24.9	13.0	Y	1.035	8.5	-	-	-	-	-	0.1
712	27.2	11.8	Y	1.040	7.5	-	-	-	-	-	0.1
	**	*		*							
Mean	28.6	17.0		1.033							
S.D.	12.6	9.9		0.009							
(N)	(12)	(12)		(12)							

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Appendix 14-2-1 Urinary findings in female rats  
- The 2nd week of recovery -

## Control group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
407	24.1	9.8	Y	1.047	8.0	-	-	-	-	+	0.1
408	11.2	8.0	Y	1.049	8.0	-	-	-	-	-	0.1
409	34.4	24.8	Y	1.026	8.0	-	-	-	-	-	0.1
410	17.4	9.4	Y	1.046	8.0	-	-	-	-	-	0.1
411	27.2	18.8	Y	1.031	7.5	-	-	-	-	-	0.1
412	30.3	13.6	Y	1.038	8.0	-	-	-	-	-	0.1
Mean	24.1	14.1		1.040							
S.D.	8.5	6.6		0.009							
(N)	(6)	(6)		(6)							

2000TT278

Appendix 14-2-2 Urinary findings in female rats  
- The 2nd week of recovery -

300 mg/kg group

Animal No.	Water intake (mL/16hr)	Vol. (mL/16hr)	Col.	S.G.	pH	Pro.	Glu.	Ket.	Bil.	Occ.	Uro. (Ehrlich unit/dL)
707	19.7	8.0	Y	1.049	8.0	-	-	-	-	-	0.1
708	16.6	8.6	Y	1.046	8.0	-	-	-	-	-	0.1
709	14.2	6.8	Y	1.053	8.0	-	-	-	-	-	0.1
710	28.1	15.4	Y	1.038	8.0	-	-	-	-	-	0.1
711	17.4	6.6	Y	1.052	8.0	-	-	-	-	-	0.1
712	20.7	8.6	Y	1.050	8.0	-	-	-	-	-	0.1
Mean	19.5	9.0		1.048							
S.D.	4.8	3.3		0.005							
(N)	(6)	(6)		(6)							

2000TT278

Appendix 15-1-1 Hematological findings in male rats  
- End of administration -

## Control group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
001	805	16.3	46.3	11.5	20.9	93.0	110	0.0	11.0	0.0	0.0	88.5	0.5
002	792	16.5	47.2	11.9	19.8	165.7	133	0.0	7.5	1.0	0.0	91.0	0.5
003	836	16.7	48.2	12.1	20.4	102.3	73	0.0	13.5	0.5	0.0	85.0	1.0
004	737	14.8	42.3	11.8	23.8	101.9	75	0.0	8.0	0.0	0.0	91.5	0.5
005	821	16.1	46.4	11.9	23.7	98.2	117	0.5	1.5	0.0	0.0	97.5	0.5
006	824	17.3	48.4	12.9	22.1	79.0	74	0.0	2.5	0.0	0.0	97.0	0.5
Mean	803	16.3	46.5	12.0	21.8	106.7	97	0.1	7.3	0.3	0.0	91.8	0.6
S.D.	36	0.8	2.2	0.5	1.7	30.2	26	0.2	4.7	0.4	0.0	4.8	0.2
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 15-1-2 Hematological findings in male rats  
- End of administration -

## 30 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
101	850	17.8	50.2	15.9	28.0	104.1	130	0.0	8.5	0.5	0.0	90.5	0.5
102	779	15.6	44.7	12.8	19.4	92.3	66	0.0	2.5	1.0	0.5	96.0	0.0
103	806	15.7	44.8	11.6	27.3	105.9	88	0.0	3.5	0.0	0.0	96.5	0.0
104	772	15.4	43.8	13.2	27.1	89.6	66	0.5	11.5	0.0	0.0	87.5	0.5
105	813	16.7	47.6	14.4	19.1	74.7	59	0.0	8.0	0.0	0.0	91.5	0.5
106	843	17.2	48.7	20.0	31.6	84.0	92	0.0	3.5	0.5	0.0	95.5	0.5
Mean	811	16.4	46.6	14.7	25.4	91.8	84	0.1	6.3	0.3	0.1	92.9	0.3
S.D.	32	1.0	2.6	3.0	5.0	11.9	26	0.2	3.6	0.4	0.2	3.6	0.3
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 15-1-3 Hematological findings in male rats  
- End of administration -

## 100 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
201	791	16.0	45.6	18.9	31.0	90.7	87	0.0	5.0	0.0	0.0	95.0	0.0
202	821	15.8	44.9	16.8	25.9	100.9	62	0.0	4.5	0.5	0.0	94.0	1.0
203	813	16.2	46.2	15.6	27.1	90.7	67	0.0	7.5	0.0	0.0	91.5	1.0
204	761	16.0	44.9	13.7	31.2	100.5	77	0.0	6.5	0.0	0.0	93.5	0.0
205	748	15.6	44.0	18.0	33.0	103.0	98	0.0	4.0	0.0	0.0	95.5	0.5
206	843	17.0	47.7	17.8	27.0	92.7	103	0.0	6.0	0.0	0.0	94.0	0.0
					**								
Mean	796	16.1	45.6	16.8	29.2	96.4	82	0.0	5.6	0.1	0.0	93.9	0.4
S.D.	37	0.5	1.3	1.9	2.9	5.6	17	0.0	1.3	0.2	0.0	1.4	0.5
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\*\* Significantly different from control (P<0.01)

Appendix 15-1-4 Hematological findings in male rats  
- End of administration -

## 300 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
301	819	17.4	49.1	21.9	32.6	94.0	77	0.0	6.0	0.0	0.0	94.0	0.0
302	801	15.6	43.6	23.9	32.5	98.7	117	0.0	4.0	0.5	0.0	95.0	0.5
303	776	16.5	46.5	23.3	31.5	85.4	67	0.0	9.0	0.5	0.0	90.5	0.0
304	803	16.6	46.7	23.0	37.5	108.6	113	0.0	7.0	0.0	0.0	93.0	0.0
305	787	16.4	47.1	19.2	31.4	100.0	113	0.0	3.0	0.0	0.0	96.5	0.5
306	821	16.0	45.4	23.1	30.1	99.5	136	0.0	4.5	0.0	0.0	95.0	0.5
Mean	801	16.4	46.4	** 22.4	** 32.6	97.7	104	0.0	5.6	0.2	0.0	94.0	0.3
S.D.	18	0.6	1.8	1.7	2.6	7.7	26	0.0	2.2	0.3	0.0	2.1	0.3
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\*\* Significantly different from control (P<0.01)

Appendix 15-2-1 Hematological findings in male rats  
- End of recovery -

Control group													
Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
007	801	15.6	44.4	10.8	17.9	106.3	116	0.5	5.0	0.0	0.0	94.0	0.5
008	811	16.4	46.5	10.8	18.2	115.1	121	0.0	3.5	0.5	0.0	96.0	0.0
009	831	16.1	46.4	12.0	22.4	107.2	82	0.0	7.5	0.5	0.0	91.5	0.5
010	833	16.9	48.4	13.8	23.7	93.5	85	0.0	19.0	0.5	0.0	80.0	0.5
011	820	16.1	45.4	10.2	13.3	114.8	101	0.0	9.0	0.5	0.0	90.5	0.0
012	851	16.6	47.9	12.7	25.4	92.3	88	0.5	11.5	0.5	0.0	87.5	0.0
Mean	825	16.3	46.5	11.7	20.2	104.9	99	0.2	9.3	0.4	0.0	89.9	0.3
S.D.	18	0.5	1.5	1.4	4.5	10.0	17	0.3	5.6	0.2	0.0	5.7	0.3
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 15-2-2 Hematological findings in male rats  
- End of recovery -

## 300 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
307	782	15.9	46.4	11.6	22.2	111.2	120	0.0	6.5	1.0	0.0	92.0	0.5
308	810	15.3	44.6	12.1	23.1	89.3	104	0.0	12.0	0.5	0.5	86.5	0.5
309	831	15.8	46.5	13.2	16.1	111.0	100	0.0	12.0	0.5	0.0	87.5	0.0
310	789	15.5	44.1	11.1	17.9	100.3	78	0.0	19.5	0.0	0.0	80.0	0.5
311	834	16.3	48.3	12.9	23.2	101.4	77	0.0	12.5	0.5	0.0	87.0	0.0
312	762	15.5	44.8	12.3	22.0	105.7	95	0.0	14.0	1.0	0.0	84.5	0.5
		*											
Mean	801	15.7	45.8	12.2	20.8	103.2	96	0.0	12.8	0.6	0.1	86.3	0.3
S.D.	29	0.4	1.6	0.8	3.0	8.2	16	0.0	4.2	0.4	0.2	3.9	0.3
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

Appendix 16-1-1 Hematological findings in female rats  
- End of administration -

## Control group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
401	686	14.1	38.4	9.1	12.1	125.1	78	0.0	9.0	0.0	0.0	90.0	1.0
402	766	14.9	42.1	10.3	18.4	96.1	67	0.0	5.5	0.0	0.0	94.5	0.0
403	745	15.7	43.4	9.4	11.7	85.5	41	0.0	5.0	1.0	0.0	94.0	0.0
404	687	15.0	39.9	9.3	13.4	115.7	70	0.0	8.0	0.5	0.0	91.0	0.5
405	751	15.4	42.9	9.3	12.7	98.7	91	0.0	4.0	0.0	0.0	95.5	0.5
406	836	16.2	46.1	9.6	15.2	118.7	94	0.0	4.0	0.5	0.0	95.5	0.0
Mean	745	15.2	42.1	9.5	13.9	106.6	74	0.0	5.9	0.3	0.0	93.4	0.3
S.D.	56	0.7	2.7	0.4	2.5	15.4	19	0.0	2.1	0.4	0.0	2.4	0.4
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 16-1-2 Hematological findings in female rats  
- End of administration -

## 30 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
501	660	14.3	37.7	9.3	13.1	100.9	111	0.0	2.5	0.0	0.0	97.5	0.0
502	716	14.1	39.0	9.7	15.0	106.5	72	0.0	3.0	0.5	0.0	96.5	0.0
503	723	14.9	41.6	9.4	12.5	111.6	38	0.0	2.0	0.5	0.0	96.5	1.0
504	808	15.5	42.8	9.6	18.3	122.6	101	0.0	5.5	0.5	0.0	94.0	0.0
505	789	15.9	45.4	9.0	11.2	111.6	55	0.0	3.5	0.0	0.0	96.0	0.5
506	737	16.0	42.1	9.1	14.2	116.9	115	0.0	3.5	0.0	0.0	96.5	0.0
Mean	739	15.1	41.4	9.4	14.1	111.7	82	0.0	3.3	0.3	0.0	96.2	0.3
S.D.	53	0.8	2.8	0.3	2.5	7.6	32	0.0	1.2	0.3	0.0	1.2	0.4
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 16-1-3 Hematological findings in female rats  
- End of administration -

100 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
601	713	14.9	41.9	9.2	13.3	98.1	54	0.0	2.0	0.5	0.0	97.5	0.0
602	785	15.8	45.1	9.7	18.9	81.4	74	0.0	4.0	1.0	0.0	95.0	0.0
603	708	14.7	39.5	9.7	18.8	93.4	51	0.0	1.5	0.0	0.0	98.5	0.0
604	797	16.4	45.7	9.8	15.8	110.4	73	0.0	4.0	0.5	0.0	95.5	0.0
605	742	15.0	42.3	9.5	11.3	101.4	72	0.0	1.5	0.0	0.0	98.5	0.0
606	752	16.6	44.6	9.5	13.7	97.2	85	0.0	7.0	0.0	0.0	93.0	0.0
Mean	750	15.6	43.2	9.6	15.3	97.0	68	0.0	3.3	0.3	0.0	96.3	0.0
S.D.	36	0.8	2.4	0.2	3.1	9.6	13	0.0	2.1	0.4	0.0	2.2	0.0
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

Appendix 16-1-4 Hematological findings in female rats  
- End of administration -

## 300 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
701	758	15.4	41.8	9.1	12.3	113.3	56	0.0	1.5	0.5	0.0	98.0	0.0
702	826	17.0	45.6	12.9	27.0	123.0	70	0.0	1.0	0.5	0.0	98.5	0.0
703	750	15.3	42.6	10.4	19.3	105.9	41	0.0	4.0	0.0	0.0	95.5	0.5
704	627	13.4	35.7	9.8	17.6	98.6	90	0.0	5.0	0.0	0.0	94.5	0.5
705	767	16.2	42.3	9.9	22.0	98.6	84	0.0	4.0	0.0	0.0	96.0	0.0
706	791	16.4	44.2	9.0	9.6	106.0	101	0.0	0.0	0.5	0.0	99.0	0.5
Mean	753	15.6	42.0	10.2	18.0	107.6	74	0.0	*	0.3	0.0	96.9	0.3
S.D.	68	1.3	3.4	1.4	6.4	9.3	22	0.0	2.0	0.3	0.0	1.8	0.3
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

2000TT278

Appendix 16-2-1 Hematological findings in female rats  
- End of recovery -

## Control group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
407	728	14.8	40.4	9.7	11.8	105.4	93	0.0	5.0	0.5	0.0	94.5	0.0
408	759	15.6	43.1	8.6	11.1	113.7	66	0.0	23.5	0.5	0.0	73.5	2.5
409	720	15.5	41.3	9.7	15.6	111.6	62	0.0	16.0	0.0	0.0	83.5	0.5
410	695	14.4	40.0	9.5	13.6	100.4	49	0.0	9.5	0.0	0.0	90.5	0.0
411	806	16.0	45.2	9.8	14.6	83.8	76	0.0	11.0	1.5	0.0	86.5	1.0
412	742	15.1	43.5	8.5	10.0	98.9	66	0.0	4.5	1.0	0.0	94.0	0.5
Mean	742	15.2	42.3	9.3	12.8	102.3	69	0.0	11.6	0.6	0.0	87.1	0.8
S.D.	38	0.6	2.0	0.6	2.2	10.8	15	0.0	7.2	0.6	0.0	7.9	0.9
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 16-2-2 Hematological findings in female rats  
- End of recovery -

## 300 mg/kg group

Animal No.	RBC ( $10^4/\mu\text{L}$ )	Hb (g/dL)	Ht (%)	PT (sec.)	APTT (sec.)	Plate. ( $10^4/\mu\text{L}$ )	WBC ( $10^2/\mu\text{L}$ )	WBC differential count (%)					
								St.	Seg.	Eo.	Ba.	Ly.	Mo.
707	743	15.1	42.0	9.1	12.9	105.4	51	0.0	10.5	0.5	0.0	88.0	1.0
708	780	16.0	45.5	9.1	12.7	123.1	91	0.0	12.0	0.0	0.5	87.5	0.0
709	764	15.7	44.7	9.9	13.8	111.8	64	0.0	7.5	1.5	0.5	90.5	0.0
710	708	14.8	41.6	9.3	12.3	116.1	80	0.0	6.0	1.5	0.0	92.5	0.0
711	790	15.3	43.7	10.1	15.3	108.7	46	0.0	16.5	0.5	0.0	82.5	0.5
712	768	16.0	45.3	8.8	10.8	129.6	71	0.0	5.0	1.5	0.0	93.0	0.5
						*							
Mean	759	15.5	43.8	9.4	13.0	115.8	67	0.0	9.6	0.9	0.2	89.0	0.3
S.D.	30	0.5	1.7	0.5	1.5	9.1	17	0.0	4.3	0.7	0.3	3.9	0.4
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

2000TT278

Appendix 17-1-1 Blood chemistry findings in male rats  
- End of administration -

Control group										
Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
001	69.5	23.6	164	0.04	12.9	0.46	45	37.4	6.11	2.59
002	77.0	28.4	137	0.05	12.2	0.39	51	31.0	5.88	2.37
003	66.0	24.2	127	0.05	11.7	0.34	47	33.7	6.09	2.56
004	57.1	19.5	116	0.04	14.7	0.37	56	13.9	5.60	2.31
005	78.9	27.2	112	0.06	13.5	0.38	50	12.2	5.87	2.51
006	58.7	16.1	118	0.05	12.3	0.30	48	9.9	5.80	2.34
Mean	67.9	23.2	129	0.05	12.9	0.37	50	23.0	5.89	2.45
S.D.	9.1	4.7	19	0.01	1.1	0.05	4	12.3	0.19	0.12
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 17-1-2 Blood chemistry findings in male rats  
- End of administration -

## 30 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
101	67.2	26.7	138	0.04	9.9	0.29	53	57.6	6.08	2.46
102	67.0	21.6	125	0.04	12.7	0.39	52	20.4	5.57	2.22
103	66.7	24.4	128	0.05	13.4	0.36	55	31.0	5.73	2.33
104	68.3	26.4	120	0.05	13.5	0.32	72	12.9	6.05	2.49
105	61.2	20.7	115	0.05	12.7	0.32	64	34.5	6.18	2.54
106	75.1	24.4	134	0.05	12.4	0.39	59	17.8	5.58	2.48
Mean	67.6	24.0	127	0.05	12.4	0.35	59	29.0	5.87	2.42
S.D.	4.5	2.5	9	0.01	1.3	0.04	8	16.2	0.27	0.12
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 17-1-3 Blood chemistry findings in male rats  
- End of administration -

## 100 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
201	63.4	26.4	135	0.04	12.7	0.44	62	80.6	5.33	2.39
202	70.3	41.2	133	0.03	14.1	0.34	53	20.1	5.96	2.74
203	59.9	27.6	126	0.03	11.6	0.32	42	24.0	5.83	2.65
204	62.9	29.3	119	0.04	13.7	0.28	61	26.7	5.43	2.37
205	64.5	22.4	116	0.05	13.5	0.32	68	36.8	5.92	2.28
206	71.8	33.4	121	0.04	11.6	0.30	67	26.0	5.80	2.48
Mean	65.5	30.1	125	0.04	12.9	0.33	59	35.7	5.71	2.49
S.D.	4.6	6.5	8	0.01	1.1	0.06	10	22.7	0.27	0.18
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

2000TT278

Appendix 17-1-4 Blood chemistry findings in male rats  
- End of administration -

300 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
301	70.5	26.5	135	0.06	17.2	0.37	62	17.7	5.54	2.36
302	66.2	27.7	99	0.05	15.8	0.29	57	21.8	5.26	2.21
303	70.6	29.4	107	0.06	13.6	0.37	70	13.6	6.33	2.61
304	88.3	33.7	112	0.05	10.9	0.37	52	15.4	6.22	2.60
305	76.6	38.4	136	0.06	13.5	0.38	78	28.0	5.96	2.60
306	72.8	37.3	141	0.05	14.8	0.44	99	19.0	5.82	2.55
		*					**			
Mean	74.2	32.2	122	0.06	14.3	0.37	70	19.3	5.86	2.49
S.D.	7.7	5.0	18	0.01	2.2	0.05	17	5.1	0.41	0.17
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Appendix 17-2-1 Blood chemistry findings in male rats  
- End of recovery -

Control group										
Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
007	82.0	34.2	143	0.08	21.7	0.44	53	30.7	5.65	2.45
008	86.7	24.8	140	0.07	17.5	0.49	66	24.6	5.74	2.32
009	79.7	28.9	137	0.06	15.4	0.48	50	21.0	6.00	2.24
010	82.8	24.8	143	0.07	14.8	0.43	67	47.6	5.94	2.44
011	68.9	24.7	137	0.08	15.0	0.42	84	41.7	6.32	2.45
012	88.7	37.7	160	0.07	20.1	0.48	41	31.7	5.98	2.34
Mean	81.5	29.2	143	0.07	17.4	0.46	60	32.9	5.94	2.37
S.D.	7.0	5.6	9	0.01	2.9	0.03	15	10.1	0.23	0.09
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 17-2-2 Blood chemistry findings in male rats  
- End of recovery -

300 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
307	71.7	39.7	148	0.05	18.9	0.54	74	38.8	5.51	2.33
308	68.7	27.3	126	0.06	17.8	0.39	76	34.5	6.22	2.49
309	70.5	25.0	143	0.05	15.4	0.44	57	29.5	5.48	2.25
310	76.5	21.8	131	0.05	20.6	0.37	71	22.3	5.99	2.34
311	77.4	32.0	136	0.06	17.6	0.39	48	25.8	6.17	2.57
312	76.3	27.1	120	0.07	18.7	0.38	73	18.6	5.84	2.43
	*			**						
Mean	73.5	28.8	134	0.06	18.2	0.42	67	28.3	5.87	2.40
S.D.	3.7	6.3	10	0.01	1.7	0.06	11	7.6	0.32	0.12
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Appendix 18-1-1 Blood chemistry findings in female rats  
- End of administration -

Control group										
Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
401	67.5	16.2	140	0.04	13.7	0.42	44	5.1	5.91	2.53
402	76.9	23.4	124	0.05	13.4	0.35	58	3.4	5.69	2.62
403	65.6	20.1	119	0.05	15.3	0.39	56	6.6	6.15	2.67
404	62.1	21.6	126	0.04	13.1	0.38	61	9.6	5.69	2.69
405	61.1	17.6	106	0.08	16.8	0.40	32	3.5	5.44	2.28
406	73.9	20.7	114	0.07	16.9	0.31	53	3.3	5.67	2.57
Mean	67.9	19.9	122	0.06	14.9	0.38	51	5.3	5.76	2.56
S.D.	6.4	2.6	12	0.02	1.7	0.04	11	2.5	0.24	0.15
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 18-1-2 Blood chemistry findings in female rats  
- End of administration -

30 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
501	59.9	15.3	135	0.04	15.3	0.41	48	5.6	5.50	2.31
502	61.9	21.2	133	0.05	15.8	0.45	44	5.2	5.53	2.44
503	65.3	22.6	145	0.05	11.3	0.40	77	6.5	6.06	2.73
504	56.0	17.3	123	0.06	12.5	0.42	75	16.8	5.67	2.57
505	53.7	24.3	138	0.05	13.2	0.36	61	11.4	6.26	2.68
506	73.9	27.9	111	0.07	16.3	0.44	86	5.9	6.47	2.73
Mean	61.8	21.4	131	0.05	14.1	0.41	65	8.6	5.92	2.58
S.D.	7.2	4.6	12	0.01	2.0	0.03	17	4.6	0.41	0.17
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 18-1-3 Blood chemistry findings in female rats  
- End of administration -

100 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
601	60.7	22.6	137	0.04	13.1	0.48	82	9.3	6.13	2.64
602	64.1	23.4	121	0.05	16.1	0.41	62	10.5	6.13	2.92
603	65.3	20.1	110	0.05	16.8	0.39	61	5.0	5.86	2.42
604	56.0	17.1	109	0.05	17.1	0.33	67	15.1	5.72	2.64
605	63.6	21.9	108	0.05	14.2	0.41	74	10.8	6.23	2.64
606	52.5	16.8	139	0.06	16.0	0.42	90	9.5	6.34	2.57
Mean	60.4	20.3	121	0.05	15.6	0.41	73	10.0	6.07	2.64
S.D.	5.1	2.8	14	0.01	1.6	0.05	12	3.2	0.23	0.16
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 18-1-4 Blood chemistry findings in female rats  
- End of administration -

300 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
701	63.3	23.2	113	0.08	15.4	0.35	80	23.1	5.77	2.35
702	57.0	23.2	83	0.05	10.5	0.27	65	11.6	5.36	2.19
703	65.3	22.4	101	0.06	12.0	0.36	86	9.7	6.16	2.48
704	57.9	22.0	117	0.05	14.1	0.37	66	15.8	5.96	2.68
705	57.0	21.0	76	0.05	14.2	0.31	97	21.4	5.25	2.35
706	58.8	21.7	103	0.06	16.0	0.37	140	18.0	6.18	2.47
Mean	59.9	22.3	99	0.06	13.7	0.34	89	16.6	5.78	2.42
S.D.	3.5	0.9	16	0.01	2.1	0.04	28	5.3	0.40	0.17
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

2000TT278

Appendix 18-2-1 Blood chemistry findings in female rats  
- End of recovery -

Control group										
Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
407	98.7	37.2	144	0.09	19.9	0.56	91	42.5	6.15	2.61
408	83.3	32.5	151	0.06	19.3	0.52	70	19.5	6.36	2.83
409	68.9	24.6	119	0.08	18.8	0.44	50	9.5	5.89	2.45
410	73.1	25.5	128	0.06	19.4	0.48	75	15.5	6.20	2.77
411	67.7	24.9	110	0.07	19.0	0.63	86	10.0	6.21	2.84
412	70.4	18.4	127	0.11	19.0	0.45	77	20.7	6.52	2.77
Mean	77.0	27.2	130	0.08	19.2	0.51	75	19.6	6.22	2.71
S.D.	12.0	6.6	15	0.02	0.4	0.07	14	12.1	0.21	0.15
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 18-2-2 Blood chemistry findings in female rats  
- End of recovery -

300 mg/kg group

Animal No.	GOT (IU/L)	GPT (IU/L)	GLU (mg/dL)	BIL (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TP (g/dL)	ALB (g/dL)
707	83.3	21.4	116	0.08	17.8	0.54	112	27.1	6.48	2.68
708	51.7	17.5	127	0.05	19.0	0.46	94	41.5	6.13	2.65
709	63.5	25.7	133	0.07	16.3	0.40	98	26.1	6.07	2.77
710	70.7	27.1	102	0.07	21.9	0.51	69	6.7	6.48	2.73
711	71.7	21.9	130	0.05	17.8	0.48	77	5.6	6.24	2.74
712	65.9	21.6	138	0.06	19.8	0.47	76	20.0	6.05	2.76
Mean	67.8	22.5	124	0.06	18.8	0.48	88	21.2	6.24	2.72
S.D.	10.4	3.4	13	0.01	1.9	0.05	16	13.6	0.20	0.05
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

2000TT278

Appendix 19-1-1 Gross pathological findings in male rats  
- End of administration -

Control group

Animal	Findings
No.	Findings
001	No abnormalities
002	No abnormalities
003	No abnormalities
004	No abnormalities
005	No abnormalities
006	No abnormalities

2000TT278

Appendix 19-1-2 Gross pathological findings in male rats  
- End of administration -

30 mg/kg group

Animal	Findings
No.	Findings
101	Spleen : Elevated area, from surface, Local, Indistinct boundary, Increase in number of the follicles from cut-surface
102	No abnormalities
103	No abnormalities
104	No abnormalities
105	No abnormalities
106	No abnormalities

2000TT278

Appendix 19-1-3 Gross pathological findings in male rats  
- End of administration -

100 mg/kg group

Animal	Findings
No.	
201	No abnormalities
202	No abnormalities
203	No abnormalities
204	No abnormalities
205	No abnormalities
206	No abnormalities

2000TT278

Appendix 19-1-4 Gross pathological findings in male rats  
- End of administration -

300 mg/kg group

Animal	
No.	Findings
301	No abnormalities
302	No abnormalities
303	No abnormalities
304	No abnormalities
305	No abnormalities
306	No abnormalities

2000TT278

Appendix 19-2-1 Gross pathological findings in male rats  
- End of recovery -

Control group

Animal No.	Findings
007	No abnormalities
008	No abnormalities
009	No abnormalities
010	No abnormalities
011	No abnormalities
012	No abnormalities

2000TT278

Appendix 19-2-2 Gross pathological findings in male rats  
- End of recovery -

300 mg/kg group

Animal	
No.	Findings
307	No abnormalities
308	No abnormalities
309	No abnormalities
310	No abnormalities
311	No abnormalities
312	No abnormalities

2000TT278

Appendix 20-1-1 Gross pathological findings in female rats  
- End of administration -

Control group

Animal No.	Findings
401	No abnormalities
402	No abnormalities
403	No abnormalities
404	No abnormalities
405	No abnormalities
406	No abnormalities

2000TT278

Appendix 20-1-2 Gross pathological findings in female rats  
- End of administration -

30 mg/kg group

Animal	
No.	Findings
501	No abnormalities
502	No abnormalities
503	No abnormalities
504	No abnormalities
505	No abnormalities
506	No abnormalities

2000TT278

Appendix 20-1-3 Gross pathological findings in female rats  
- End of administration -

100 mg/kg group

Animal	
No.	Findings
601	No abnormalities
602	No abnormalities
603	No abnormalities
604	No abnormalities
605	No abnormalities
606	No abnormalities

2000TT278

Appendix 20-1-4 Gross pathological findings in female rats  
- End of administration -

300 mg/kg group

Animal	
No.	Findings
701	No abnormalities
702	No abnormalities
703	No abnormalities
704	No abnormalities
705	No abnormalities
706	No abnormalities

2000TT278

Appendix 20-2-1 Gross pathological findings in female rats  
- End of recovery -

Control group

Animal	
No.	Findings
407	No abnormalities
408	No abnormalities
409	No abnormalities
410	No abnormalities
411	No abnormalities
412	No abnormalities

2000TT278

Appendix 20-2-2 Gross pathological findings in female rats  
- End of recovery -

300 mg/kg group

Animal	Findings
No.	
707	No abnormalities
708	No abnormalities
709	No abnormalities
710	No abnormalities
711	No abnormalities
712	No abnormalities

Appendix 21-1-1-1 Absolute organ weights in male rats  
- End of administration -

## Control group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Testis		Epididymis	
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (g)	Right (g)	Left (g)	Right (g)
001	378	2.07	520	1.24	1.224	11.5	0.767	26	24	1.24	1.20	1.56	1.58	0.49	0.52
002	412	2.11	560	1.31	1.242	11.1	0.649	30	25	1.30	1.29	1.56	1.59	0.47	0.51
003	411	2.01	594	1.43	1.225	12.5	0.676	38	40	1.33	1.40	1.53	1.52	0.52	0.54
004	403	2.06	325	1.36	1.294	12.3	0.738	34	33	1.40	1.40	1.67	1.59	0.53	0.54
005	356	2.03	358	1.28	1.184	9.4	0.590	35	28	1.09	1.18	1.58	1.59	0.50	0.53
006	355	1.94	502	1.37	1.207	10.5	0.657	33	38	1.34	1.38	1.53	1.53	0.53	0.54
Mean	386	2.04	477	1.33	1.229	11.2	0.680	32.7	31.3	1.28	1.31	1.57	1.57	0.51	0.53
S.D.	27	0.06	110	0.07	0.037	1.2	0.064	4.2	6.7	0.11	0.10	0.05	0.03	0.02	0.01
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 21-1-1-2 Absolute organ weights in male rats  
- End of administration -

30 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Testis		Epididymis	
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (g)	Right (g)	Left (g)	Right (g)
101	408	2.05	621	1.48	1.243	13.7	0.978	30	28	1.49	1.58	1.72	1.73	0.54	0.60
102	386	2.07	491	1.22	1.154	12.1	0.651	30	25	1.25	1.31	1.63	1.62	0.57	0.61
103	378	2.10	363	1.09	1.184	11.4	0.516	36	30	1.35	1.34	1.47	1.47	0.46	0.44
104	361	1.99	430	1.24	1.184	10.9	0.549	30	29	1.39	1.47	1.71	1.74	0.54	0.55
105	397	2.06	440	1.48	1.347	13.7	0.512	26	25	1.41	1.55	1.64	1.59	0.60	0.61
106	357	2.03	519	1.25	1.139	10.2	0.488	29	31	1.37	1.41	1.49	1.62	0.53	0.54
Mean	381	2.05	477	1.29	1.209	12.0	0.616	30.2	28.0	1.38	1.44	1.61	1.63	0.54	0.56
S.D.	20	0.04	89	0.16	0.077	1.5	0.187	3.3	2.5	0.08	0.11	0.11	0.10	0.05	0.07
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 21-1-1-3 Absolute organ weights in male rats  
- End of administration -

100 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Testis		Epididymis	
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (g)	Right (g)	Left (g)	Right (g)
201	416	2.11	520	1.29	1.301	15.2	0.693	28	24	1.31	1.35	1.57	1.56	0.50	0.58
202	355	2.01	461	1.19	1.086	13.1	0.518	28	26	1.36	1.41	1.42	1.50	0.56	0.52
203	369	1.99	439	1.33	1.087	14.2	0.683	27	27	1.32	1.42	1.69	1.67	0.48	0.49
204	415	2.11	417	1.45	1.202	14.9	0.624	27	25	1.63	1.65	1.61	1.59	0.53	0.53
205	390	1.91	505	1.29	1.312	15.2	0.509	26	23	1.38	1.44	1.54	1.50	0.53	0.55
206	371	2.08	423	1.38	1.286	13.4	0.609	32	31	1.33	1.32	1.48	1.46	0.49	0.60
						**									
Mean	386	2.04	461	1.32	1.212	14.3	0.606	28.0	26.0	1.39	1.43	1.55	1.55	0.52	0.55
S.D.	25	0.08	43	0.09	0.105	0.9	0.079	2.1	2.8	0.12	0.12	0.10	0.08	0.03	0.04
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\*\* Significantly different from control (P<0.01)

Appendix 21-1-1-4 Absolute organ weights in male rats  
- End of administration -

## 300 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Testis		Epididymis	
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (g)	Right (g)	Left (g)	Right (g)
301	296	1.84	447	1.01	0.868	13.3	0.428	21	20	1.07	1.08	1.46	1.50	0.43	0.47
302	323	2.03	359	1.12	1.014	13.2	0.566	27	26	1.21	1.27	1.62	1.62	0.50	0.52
303	374	2.05	328	1.28	1.146	15.5	0.426	24	25	1.46	1.46	1.80	1.78	0.55	0.55
304	394	1.95	373	1.26	1.220	17.2	0.630	32	34	1.55	1.59	1.46	1.57	0.50	0.44
305	391	1.96	398	1.27	1.135	16.8	0.542	28	28	1.31	1.32	1.47	1.46	0.47	0.47
306	352	1.92	336	1.17	1.061	14.5	0.563	30	32	1.31	1.25	1.45	1.49	0.50	0.55
Mean	355	1.96	374	1.19	1.074	15.1	0.526	27.0	27.5	1.32	1.33	1.54	1.57	0.49	0.50
S.D.	39	0.08	44	0.11	0.124	1.7	0.082	4.0	5.0	0.17	0.18	0.14	0.12	0.04	0.05
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 21-1-2-1 Relative organ weights in male rats  
- End of administration -

## Control group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Testis		Epididymis	
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)
001	0.548	138	0.328	0.324	3.04	0.203	6.88	6.35	0.328	0.317	0.413	0.418	0.130	0.138
002	0.512	136	0.318	0.301	2.69	0.158	7.28	6.07	0.316	0.313	0.379	0.386	0.114	0.124
003	0.489	145	0.348	0.298	3.04	0.164	9.25	9.73	0.324	0.341	0.372	0.370	0.127	0.131
004	0.511	81	0.337	0.321	3.05	0.183	8.44	8.19	0.347	0.347	0.414	0.395	0.132	0.134
005	0.570	101	0.360	0.333	2.64	0.166	9.83	7.87	0.306	0.331	0.444	0.447	0.140	0.149
006	0.546	141	0.386	0.340	2.96	0.185	9.30	10.70	0.377	0.389	0.431	0.431	0.149	0.152
Mean	0.529	124	0.346	0.320	2.90	0.177	8.50	8.15	0.333	0.340	0.409	0.408	0.132	0.138
S.D.	0.030	26	0.024	0.017	0.19	0.017	1.19	1.82	0.026	0.028	0.028	0.029	0.012	0.011
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 21-1-2-2 Relative organ weights in male rats  
- End of administration -

## 30 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Testis		Epididymis	
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)
101	0.502	152	0.363	0.305	3.36	0.240	7.35	6.86	0.365	0.387	0.422	0.424	0.132	0.147
102	0.536	127	0.316	0.299	3.13	0.169	7.77	6.48	0.324	0.339	0.422	0.420	0.148	0.158
103	0.556	96	0.288	0.313	3.02	0.137	9.52	7.94	0.357	0.354	0.389	0.389	0.122	0.116
104	0.551	119	0.343	0.328	3.02	0.152	8.31	8.03	0.385	0.407	0.474	0.482	0.150	0.152
105	0.519	111	0.373	0.339	3.45	0.129	6.55	6.30	0.355	0.390	0.413	0.401	0.151	0.154
106	0.569	145	0.350	0.319	2.86	0.137	8.12	8.68	0.384	0.395	0.417	0.454	0.148	0.151
Mean	0.539	125	0.339	0.317	3.14	0.161	7.94	7.38	0.362	0.379	0.423	0.428	0.142	0.146
S.D.	0.025	21	0.032	0.015	0.22	0.041	1.00	0.97	0.023	0.026	0.028	0.034	0.012	0.015
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 21-1-2-3 Relative organ weights in male rats  
- End of administration -

100 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Testis		Epididymis	
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)
201	0.507	125	0.310	0.313	3.65	0.167	6.73	5.77	0.315	0.325	0.377	0.375	0.120	0.139
202	0.566	130	0.335	0.306	3.69	0.146	7.89	7.32	0.383	0.397	0.400	0.423	0.158	0.146
203	0.539	119	0.360	0.295	3.85	0.185	7.32	7.32	0.358	0.385	0.458	0.453	0.130	0.133
204	0.508	100	0.349	0.290	3.59	0.150	6.51	6.02	0.393	0.398	0.388	0.383	0.128	0.128
205	0.490	129	0.331	0.336	3.90	0.131	6.67	5.90	0.354	0.369	0.395	0.385	0.136	0.141
206	0.561	114	0.372	0.347	3.61	0.164	8.63	8.36	0.358	0.356	0.399	0.394	0.132	0.162
					**									
Mean	0.529	120	0.343	0.315	3.72	0.157	7.29	6.78	0.360	0.372	0.403	0.402	0.134	0.142
S.D.	0.031	11	0.022	0.023	0.13	0.019	0.83	1.04	0.027	0.028	0.028	0.030	0.013	0.012
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\*\* Significantly different from control (P<0.01)

Appendix 21-1-2-4 Relative organ weights in male rats  
- End of administration -

## 300 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Testis		Epididymis	
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)
301	0.622	151	0.341	0.293	4.49	0.145	7.09	6.76	0.361	0.365	0.493	0.507	0.145	0.159
302	0.628	111	0.347	0.314	4.09	0.175	8.36	8.05	0.375	0.393	0.502	0.502	0.155	0.161
303	0.548	88	0.342	0.306	4.14	0.114	6.42	6.68	0.390	0.390	0.481	0.476	0.147	0.147
304	0.495	95	0.320	0.310	4.37	0.160	8.12	8.63	0.393	0.404	0.371	0.398	0.127	0.112
305	0.501	102	0.325	0.290	4.30	0.139	7.16	7.16	0.335	0.338	0.376	0.373	0.120	0.120
306	0.545	95	0.332	0.301	4.12	0.160	8.52	9.09	0.372	0.355	0.412	0.423	0.142	0.156
Mean	0.557	107	0.335	0.302	4.25	0.149	7.61	7.73	0.371	0.374	0.439	0.447	0.139	0.143
S.D.	0.057	23	0.011	0.009	0.16	0.021	0.84	1.01	0.021	0.026	0.060	0.056	0.013	0.021
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 21-2-1-1 Absolute organ weights in male rats  
- End of recovery -

## Control group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Testis		Epididymis	
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (g)	Right (g)	Left (g)	Right (g)
007	482	1.98	592	1.39	1.401	12.4	0.874	32	31	1.36	1.36	1.75	1.75	0.63	0.64
008	397	1.93	467	1.37	1.398	12.5	0.815	28	29	1.20	1.19	1.58	1.63	0.55	0.56
009	437	2.19	530	1.49	1.294	10.5	0.766	38	33	1.31	1.37	1.58	1.60	0.57	0.57
010	381	2.02	387	1.31	1.101	10.0	0.660	25	26	1.18	1.23	1.69	1.74	0.66	0.58
011	443	2.09	534	1.43	1.179	11.8	0.629	35	30	1.45	1.38	1.56	1.62	0.62	0.63
012	400	2.08	381	1.30	1.245	10.7	0.764	35	30	1.30	1.30	1.82	1.83	0.65	0.69
Mean	423	2.05	482	1.38	1.270	11.3	0.751	32.2	29.8	1.30	1.31	1.66	1.70	0.61	0.61
S.D.	38	0.09	86	0.07	0.120	1.1	0.093	4.9	2.3	0.10	0.08	0.11	0.09	0.04	0.05
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 21-2-1-2 Absolute organ weights in male rats  
- End of recovery -

## 300 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Testis		Epididymis	
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (g)	Right (g)	Left (g)	Right (g)
307	430	1.98	586	1.28	1.334	11.8	0.664	35	30	1.33	1.29	1.57	1.59	0.59	0.62
308	393	1.98	343	1.13	1.139	10.9	0.676	25	27	1.48	1.39	1.50	1.55	0.51	0.53
309	368	1.98	517	1.16	1.235	9.5	0.661	32	31	1.25	1.30	1.60	1.63	0.50	0.55
310	395	1.96	397	1.55	1.373	11.3	0.788	43	41	1.78	1.72	1.43	1.52	0.56	0.60
311	383	2.10	321	1.24	1.319	10.4	0.619	26	25	1.32	1.40	1.57	1.53	0.55	0.48
312	392	1.89	425	1.22	1.268	11.5	0.719	33	32	1.45	1.43	1.56	1.56	0.50	0.56
Mean	394	1.98	432	1.26	1.278	10.9	0.688	32.3	31.0	1.44	1.42	*	**	**	
S.D.	20	0.07	102	0.15	0.084	0.8	0.059	6.6	5.5	0.19	0.16	0.06	0.04	0.04	0.05
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 21-2-2-1 Relative organ weights in male rats  
- End of recovery -

## Control group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Testis		Epididymis	
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)
007	0.411	123	0.288	0.291	2.57	0.181	6.64	6.43	0.282	0.282	0.363	0.363	0.131	0.133
008	0.486	118	0.345	0.352	3.15	0.205	7.05	7.30	0.302	0.300	0.398	0.411	0.139	0.141
009	0.501	121	0.341	0.296	2.40	0.175	8.70	7.55	0.300	0.314	0.362	0.366	0.130	0.130
010	0.530	102	0.344	0.289	2.62	0.173	6.56	6.82	0.310	0.323	0.444	0.457	0.173	0.152
011	0.472	121	0.323	0.266	2.66	0.142	7.90	6.77	0.327	0.312	0.352	0.366	0.140	0.142
012	0.520	95	0.325	0.311	2.68	0.191	8.75	7.50	0.325	0.325	0.455	0.458	0.163	0.173
Mean	0.487	113	0.328	0.301	2.68	0.178	7.60	7.06	0.308	0.309	0.396	0.404	0.146	0.145
S.D.	0.043	12	0.022	0.029	0.25	0.021	0.99	0.45	0.017	0.016	0.045	0.045	0.018	0.016
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 21-2-2-2 Relative organ weights in male rats  
- End of recovery -

## 300 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Testis		Epididymis	
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)	Left (g%)	Right (g%)
307	0.460	136	0.298	0.310	2.74	0.154	8.14	6.98	0.309	0.300	0.365	0.370	0.137	0.144
308	0.504	87	0.288	0.290	2.77	0.172	6.36	6.87	0.377	0.354	0.382	0.394	0.130	0.135
309	0.538	140	0.315	0.336	2.58	0.180	8.70	8.42	0.340	0.353	0.435	0.443	0.136	0.149
310	0.496	101	0.392	0.348	2.86	0.199	10.89	10.38	0.451	0.435	0.362	0.385	0.142	0.152
311	0.548	84	0.324	0.344	2.72	0.162	6.79	6.53	0.345	0.366	0.410	0.399	0.144	0.125
312	0.482	108	0.311	0.323	2.93	0.183	8.42	8.16	0.370	0.365	0.398	0.398	0.128	0.143
Mean	0.505	109	0.321	0.325	2.77	0.175	8.22	7.89	0.365	0.362	0.392	0.398	0.136	0.141
S.D.	0.033	24	0.037	0.022	0.12	0.016	1.61	1.43	0.048	0.043	0.028	0.024	0.006	0.010
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

Appendix 22-1-1-1 Absolute organ weights in female rats  
- End of administration -

## Control group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Ovary		Uterus (g)
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (mg)	Right (mg)	
401	215	1.92	389	0.98	0.783	6.5	0.566	31	32	0.79	0.77	55	59	0.61
402	233	1.90	522	1.02	0.787	6.7	0.479	33	31	0.84	0.81	45	40	1.14
403	253	1.94	357	1.12	0.829	7.6	0.399	30	33	0.85	0.93	47	37	0.58
404	238	1.83	450	0.94	0.781	7.1	0.532	42	39	0.80	0.80	54	44	0.42
405	235	1.91	366	1.12	0.775	6.3	0.519	33	53	0.82	0.87	57	63	0.45
406	224	2.01	425	1.03	0.682	6.2	0.422	33	34	0.80	0.81	45	43	0.43
Mean	233	1.92	418	1.04	0.773	6.7	0.486	33.7	37.0	0.82	0.83	50.5	47.7	0.61
S.D.	13	0.06	62	0.07	0.049	0.5	0.065	4.3	8.3	0.02	0.06	5.4	10.7	0.27
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 22-1-1-2 Absolute organ weights in female rats  
- End of administration -

## 30 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Ovary		Uterus (g)
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (mg)	Right (mg)	
501	238	2.00	504	1.06	0.792	7.3	0.688	36	35	0.90	0.83	48	51	0.53
502	256	1.79	420	1.01	0.856	8.2	0.553	30	26	0.76	0.82	56	62	0.51
503	224	1.76	394	1.00	0.769	7.3	0.504	37	35	0.80	0.82	43	37	0.74
504	232	1.93	341	0.93	0.778	7.5	0.489	34	30	0.78	0.76	40	46	0.54
505	265	1.96	623	1.13	1.015	8.4	0.459	30	31	0.88	0.92	55	51	0.71
506	246	1.87	631	1.13	0.817	7.9	0.517	45	38	0.88	0.86	57	58	0.38
							*							
Mean	244	1.89	486	1.04	0.838	7.8	0.535	35.3	32.5	0.83	0.84	49.8	50.8	0.57
S.D.	15	0.10	122	0.08	0.092	0.5	0.081	5.6	4.3	0.06	0.05	7.3	8.8	0.13
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

Appendix 22-1-1-3 Absolute organ weights in female rats  
- End of administration -

## 100 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Ovary		Uterus (g)
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (mg)	Right (mg)	
601	231	1.87	415	1.05	0.786	8.4	0.392	38	34	0.80	0.84	36	47	1.15
602	199	1.91	423	0.97	0.726	7.0	0.371	36	31	0.76	0.79	37	39	0.39
603	234	1.93	369	0.99	0.712	7.6	0.378	33	33	0.82	0.78	41	49	0.51
604	211	1.81	347	0.97	0.759	7.3	0.451	34	34	0.79	0.78	32	39	0.79
605	240	2.07	453	1.01	0.835	8.8	0.608	35	32	0.83	0.84	54	48	0.44
606	255	1.98	537	1.11	0.791	9.1	0.416	49	45	0.94	0.98	76	64	0.60
						**								
Mean	228	1.93	424	1.02	0.768	8.0	0.436	37.5	34.8	0.82	0.84	46.0	47.7	0.65
S.D.	20	0.09	67	0.05	0.045	0.9	0.089	5.9	5.1	0.06	0.08	16.5	9.2	0.28
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\*\* Significantly different from control (P<0.01)

Appendix 22-1-1-4 Absolute organ weights in female rats  
- End of administration -

## 300 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Ovary		Uterus (g)
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (mg)	Right (mg)	
701	207	1.81	369	0.85	0.764	8.8	0.327	31	34	0.82	0.87	44	38	0.40
702	198	1.80	415	0.90	0.682	9.6	0.402	39	34	0.83	0.83	32	42	0.54
703	199	1.82	315	0.97	0.623	8.4	0.465	31	33	0.72	0.76	37	27	0.86
704	203	1.81	324	0.90	0.777	10.3	0.478	37	32	0.88	0.88	47	52	0.62
705	194	1.79	271	0.98	0.680	8.8	0.354	42	41	0.84	0.83	32	45	0.47
706	220	1.96	571	0.94	0.681	9.4	0.419	29	36	0.76	0.84	40	49	0.42
Mean	** 204	1.83	378	* 0.92	0.701	9.2	0.408	34.8	35.0	0.81	0.84	38.7	42.2	0.55
S.D.	9	0.06	107	0.05	0.058	0.7	0.060	5.2	3.2	0.06	0.04	6.2	8.9	0.17
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 22-1-2-1 Relative organ weights in female rats  
- End of administration -

Control group													
Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Ovary		Uterus (g%)
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (mg%)	Right (mg%)	
401	0.893	181	0.456	0.364	3.02	0.263	14.42	14.88	0.367	0.358	25.6	27.4	0.284
402	0.815	224	0.438	0.338	2.88	0.206	14.16	13.30	0.361	0.348	19.3	17.2	0.489
403	0.767	141	0.443	0.328	3.00	0.158	11.86	13.04	0.336	0.368	18.6	14.6	0.229
404	0.769	189	0.395	0.328	2.98	0.224	17.65	16.39	0.336	0.336	22.7	18.5	0.176
405	0.813	156	0.477	0.330	2.68	0.221	14.04	22.55	0.349	0.370	24.3	26.8	0.191
406	0.897	190	0.460	0.304	2.77	0.188	14.73	15.18	0.357	0.362	20.1	19.2	0.192
Mean	0.826	180	0.445	0.332	2.89	0.210	14.48	15.89	0.351	0.357	21.8	20.6	0.260
S.D.	0.058	29	0.028	0.019	0.14	0.036	1.86	3.49	0.013	0.013	2.9	5.3	0.119
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 22-1-2-2 Relative organ weights in female rats  
- End of administration -

## 30 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Ovary		Uterus (g%)
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (mg%)	Right (mg%)	
501	0.840	212	0.445	0.333	3.07	0.289	15.13	14.71	0.378	0.349	20.2	21.4	0.223
502	0.699	164	0.395	0.334	3.20	0.216	11.72	10.16	0.297	0.320	21.9	24.2	0.199
503	0.786	176	0.446	0.343	3.26	0.225	16.52	15.63	0.357	0.366	19.2	16.5	0.330
504	0.832	147	0.401	0.335	3.23	0.211	14.66	12.93	0.336	0.328	17.2	19.8	0.233
505	0.740	235	0.426	0.383	3.17	0.173	11.32	11.70	0.332	0.347	20.8	19.2	0.268
506	0.760	257	0.459	0.332	3.21	0.210	18.29	15.45	0.358	0.350	23.2	23.6	0.154
Mean	0.776	199	0.429	0.343	3.19	0.221	14.61	13.43	0.343	0.343	20.4	20.8	0.235
S.D.	0.054	43	0.026	0.020	0.07	0.038	2.71	2.21	0.028	0.017	2.1	2.9	0.060
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 22-1-2-3 Relative organ weights in female rats  
- End of administration -

100 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Ovary		Uterus (g%)
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (mg%)	Right (mg%)	
601	0.810	180	0.455	0.340	3.64	0.170	16.45	14.72	0.346	0.364	15.6	20.3	0.498
602	0.960	213	0.487	0.365	3.52	0.186	18.09	15.58	0.382	0.397	18.6	19.6	0.196
603	0.825	158	0.423	0.304	3.25	0.162	14.10	14.10	0.350	0.333	17.5	20.9	0.218
604	0.858	164	0.460	0.360	3.46	0.214	16.11	16.11	0.374	0.370	15.2	18.5	0.374
605	0.863	189	0.421	0.348	3.67	0.253	14.58	13.33	0.346	0.350	22.5	20.0	0.183
606	0.776	211	0.435	0.310	3.57	0.163	19.22	17.65	0.369	0.384	29.8	25.1	0.235
					*								
Mean	0.849	186	0.447	0.338	3.52	0.191	16.43	15.25	0.361	0.366	19.9	20.7	0.284
S.D.	0.063	23	0.025	0.026	0.15	0.036	1.97	1.54	0.016	0.023	5.5	2.3	0.125
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

Appendix 22-1-2-4 Relative organ weights in female rats  
- End of administration -

## 300 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Ovary		Uterus (g%)
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (mg%)	Right (mg%)	
701	0.874	178	0.411	0.369	4.25	0.158	14.98	16.43	0.396	0.420	21.3	18.4	0.193
702	0.909	210	0.455	0.344	4.85	0.203	19.70	17.17	0.419	0.419	16.2	21.2	0.273
703	0.915	158	0.487	0.313	4.22	0.234	15.58	16.58	0.362	0.382	18.6	13.6	0.432
704	0.892	160	0.443	0.383	5.07	0.235	18.23	15.76	0.433	0.433	23.2	25.6	0.305
705	0.923	140	0.505	0.351	4.54	0.182	21.65	21.13	0.433	0.428	16.5	23.2	0.242
706	0.891	260	0.427	0.310	4.27	0.190	13.18	16.36	0.345	0.382	18.2	22.3	0.191
Mean	0.901	184	0.455	0.345	4.53	0.200	17.22	17.24	0.398	0.411	19.0	20.7	0.273
S.D.	0.018	44	0.036	0.029	0.36	0.030	3.19	1.96	0.037	0.023	2.8	4.2	0.090
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 22-2-1-1 Absolute organ weights in female rats  
- End of recovery -

## Control group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Ovary		Uterus (g)
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (mg)	Right (mg)	
407	270	1.99	430	1.06	0.865	7.5	0.475	37	33	0.92	0.94	39	34	0.54
408	277	1.97	337	1.06	0.899	8.1	0.559	43	40	0.84	0.90	51	63	0.43
409	243	2.03	330	1.20	0.910	6.3	0.559	37	46	0.87	0.93	46	59	0.46
410	264	1.99	279	1.08	0.876	7.9	0.486	43	45	0.93	0.98	36	47	0.62
411	281	1.72	420	1.03	0.887	7.7	0.554	36	30	0.75	0.81	57	51	0.41
412	256	1.84	329	1.14	0.787	7.1	0.440	38	36	0.82	0.85	46	55	0.70
Mean	265	1.92	354	1.10	0.871	7.4	0.512	39.0	38.3	0.86	0.90	45.8	51.5	0.53
S.D.	14	0.12	59	0.06	0.044	0.7	0.052	3.2	6.5	0.07	0.06	7.7	10.3	0.12
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 22-2-1-2 Absolute organ weights in female rats  
- End of recovery -

## 300 mg/kg group

Animal No.	Body weight (g)	Brain (g)	Thymus (mg)	Lungs (g)	Heart (g)	Liver (g)	Spleen (g)	Adrenal		Kidney		Ovary		Uterus (g)
								Left (mg)	Right (mg)	Left (g)	Right (g)	Left (mg)	Right (mg)	
707	255	2.05	427	1.11	0.899	8.1	0.581	40	40	0.92	0.91	42	50	0.47
708	269	1.88	402	1.10	0.920	7.9	0.567	38	36	0.92	0.94	48	49	0.48
709	260	1.93	471	1.22	0.912	7.6	0.601	34	32	0.95	0.97	43	43	0.50
710	243	1.92	465	1.10	0.800	7.2	0.500	40	39	0.79	0.83	38	48	0.42
711	216	1.84	419	1.14	0.802	6.4	0.457	34	32	0.72	0.74	41	51	0.92
712	229	1.93	427	0.94	0.802	7.1	0.500	44	43	0.75	0.73	39	49	0.73
			*											
Mean	245	1.93	435	1.10	0.856	7.4	0.534	38.3	37.0	0.84	0.85	41.8	48.3	0.59
S.D.	20	0.07	27	0.09	0.060	0.6	0.057	3.9	4.5	0.10	0.10	3.5	2.8	0.20
(N)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

Appendix 22-2-2-1 Relative organ weights in female rats  
- End of recovery -

Control group													
Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Ovary		Uterus (g%)
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (mg%)	Right (mg%)	
407	0.737	159	0.393	0.320	2.78	0.176	13.70	12.22	0.341	0.348	14.4	12.6	0.200
408	0.711	122	0.383	0.325	2.92	0.202	15.52	14.44	0.303	0.325	18.4	22.7	0.155
409	0.835	136	0.494	0.374	2.59	0.230	15.23	18.93	0.358	0.383	18.9	24.3	0.189
410	0.754	106	0.409	0.332	2.99	0.184	16.29	17.05	0.352	0.371	13.6	17.8	0.235
411	0.612	149	0.367	0.316	2.74	0.197	12.81	10.68	0.267	0.288	20.3	18.1	0.146
412	0.719	129	0.445	0.307	2.77	0.172	14.84	14.06	0.320	0.332	18.0	21.5	0.273
Mean	0.728	134	0.415	0.329	2.80	0.194	14.73	14.56	0.324	0.341	17.3	19.5	0.200
S.D.	0.072	19	0.047	0.024	0.14	0.021	1.27	3.04	0.034	0.034	2.7	4.2	0.048
(N)	(6)	(6)	(6)	(6)	(6)	(6)	6.00	(6)	(6)	(6)	(6)	(6)	(6)

Appendix 22-2-2-2 Relative organ weights in female rats  
- End of recovery -

## 300 mg/kg group

Animal No.	Brain (g%)	Thymus (mg%)	Lungs (g%)	Heart (g%)	Liver (g%)	Spleen (g%)	Adrenal		Kidney		Ovary		Uterus (g%)
							Left (mg%)	Right (mg%)	Left (g%)	Right (g%)	Left (mg%)	Right (mg%)	
707	0.804	167	0.435	0.353	3.18	0.228	15.69	15.69	0.361	0.357	16.5	19.6	0.184
708	0.699	149	0.409	0.342	2.94	0.211	14.13	13.38	0.342	0.349	17.8	18.2	0.178
709	0.742	181	0.469	0.351	2.92	0.231	13.08	12.31	0.365	0.373	16.5	16.5	0.192
710	0.790	191	0.453	0.329	2.96	0.206	16.46	16.05	0.325	0.342	15.6	19.8	0.173
711	0.852	194	0.528	0.371	2.96	0.212	15.74	14.81	0.333	0.343	19.0	23.6	0.426
712	0.843	186	0.410	0.350	3.10	0.218	19.21	18.78	0.328	0.319	17.0	21.4	0.319
Mean	0.788	178	0.451	0.349	3.01	0.218	15.72	15.17	0.342	0.347	17.1	19.9	0.245
S.D.	0.059	17	0.045	0.014	0.10	0.010	2.11	2.26	0.017	0.018	1.2	2.5	0.104
(N)	(6)	(6)	(6)	(6)	(6)	(6)	6.00	(6)	(6)	(6)	(6)	(6)	(6)

\* Significantly different from control (P<0.05)

\*\* Significantly different from control (P<0.01)

Appendix 23-1-1 Histopathological findings in male rats  
- End of administration -

Control group								
Organ and tissue	Findings	Animal No.	001	002	003	004	005	006
Liver	Hypertrophy of centrilobular hepatocyte		-	-	-	-	-	-
	Microgranuloma		+	+	+	+	-	+
	Apoptotic necrosis of hepatocyte		-	+	+	+	-	+
	Brown pigmentation		-	-	-	-	-	-
Kidney	Basophilic tubule		-	-	-	-	-	-
	Vacuolation of tubular epithelium, proximal		-	-	-	-	-	-
	Protein cast		-	-	-	-	-	-
	Mononuclear cell infiltration, cortex		-	+	+	-	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		-	-	-	-	-	-
	Ectopic thymus		-	-	-	-	-	-
Lungs(Bronchi)	Foam cell accumulation, alveolar space		+	-	+	+	+	-
	Mononuclear cell infiltration, perivascular		+	+	+	-	-	-
	Microgranuloma		-	-	-	-	-	-
	Osseous metaplasia of alveolar wall		-	-	-	-	-	-
	Calcification in artery		-	-	+	+	+	-
	Hemorrhage		-	-	+	-	-	-
	Bronchiolar/alveolar hyperplasia		-	-	-	-	-	-
Trachea	Mononuclear cell infiltration, submucosa		-	+	-	-	-	-
Heart	Fibrosis of myocardium, septum		-	-	-	-	-	-
	Mononuclear cell infiltration		-	+ <sup>a)</sup>	-	-	-	-
Stomach	Mononuclear cell infiltration, glandular submucosa		-	-	-	-	-	-
Epididymis	Mononuclear cell infiltration, interstitium		-	-	-	-	-	+
Prostate	Mononuclear cell infiltration, interstitium		-	-	-	-	+	+
Laryngopharynx, Urinary bladder, Thymus, Spleen, Mandibular lymph node, Mesenteric lymph node, Submaxillary gland, Sublingual gland, Tongue, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Testis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities					

- : No change      + : Slight change

<sup>a)</sup> right ventricular wall

2000TT278

Appendix 23-1-2 Histopathological findings in male rats  
- End of administration -

## 30 mg/kg group

Organ and tissue	Findings	Animal No.	101	102	103	104	105	106
Liver	Hypertrophy of centrilobular hepatocyte		+	+	+	+	+	+
	Microgranuloma		+	+	+	+	-	+
	Apoptotic necrosis of hepatocyte		+	+	+	+	-	+
Kidney	Basophilic tubule		-	-	-	-	-	-
	Vacuolation of tubular epithelium, proximal		-	-	-	-	-	-
	Mononuclear cell infiltration, cortex		-	+	-	+	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		+	-	+	+	++	-
Spleen	Follicular hyperplasia of lymphocyte		++	.	.	.	.	.

- : No change

+ : Slight change

++ : Moderate change

. : Not examined

2000TT278

Appendix 23-1-3 Histopathological findings in male rats  
- End of administration -

100 mg/kg group

Organ and tissue	Findings	Animal No.	201	202	203	204	205	206
Liver	Hypertrophy of centrilobular hepatocyte		+	++	+	+	+	+
	Microgranuloma		+	+	+	+	-	+
	Apoptotic necrosis of hepatocyte		+	+	+	+	-	+
Kidney	Basophilic tubule		-	-	-	+	-	-
	Vacuolation of tubular epithelium, proximal		-	-	-	+	-	-
	Mononuclear cell infiltration, cortex		-	+	-	-	+	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		+	-	+	-	+	+
Spleen	Follicular hyperplasia of lymphocyte		•	•	•	•	•	•

- : No change

+ : Slight change

++ : Moderate change

• : Not examined

Appendix 23-1-4 Histopathological findings in male rats  
- End of administration -

## 300 mg/kg group

Organ and tissue	Findings	Animal No.	301	302	303	304	305	306
Liver	Hypertrophy of centrilobular hepatocyte		++	+	++	++	++	++
	Microgranuloma		-	+	+	+	-	-
	Apoptotic necrosis of hepatocyte		-	+	+	+	-	-
	Brown pigmentation		-	-	-	+	-	-
Kidney	Basophilic tubule		-	++	+	+	+	+
	Vacuolation of tubular epithelium, proximal		+	-	+	-	-	-
	Protein cast		+	-	-	+	-	+
	Mononuclear cell infiltration, cortex		-	+	-	-	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		++	++	++	+	++	++
	Ectopic thymus		-	-	-	+	-	-
Lungs(Bronchi)	Foam cell accumulation, alveolar space		+	+	-	+	+	+
	Mononuclear cell infiltration, perivascular		+	-	+	+	-	-
	Microgranuloma		-	-	-	+	-	-
	Osseous metaplasia of alveolar wall		-	-	-	+	-	-
	Calcification in artery		-	+	-	+	+	+
	Hemorrhage		-	-	-	-	+	-
	Bronchiolar/alveolar hyperplasia		-	-	-	-	+	-
Trachea	Mononuclear cell infiltration, submucosa		-	-	-	-	-	+
Heart	Fibrosis of myocardium, septum		-	+	-	-	-	-
	Mononuclear cell infiltration		-	+ <sup>a)</sup>	+ <sup>b)</sup>	-	-	-
Stomach	Mononuclear cell infiltration, glandular submucosa		+	-	-	-	-	-
Epididymis	Mononuclear cell infiltration, interstitium		-	-	-	-	-	-
Prostate	Mononuclear cell infiltration, interstitium		+	-	-	+	-	-
Laryngopharynx, Urinary bladder, Thymus, Spleen, Mandibular lymph node, Mesenteric lymph node, Submaxillary gland, Sublingual gland, Tongue, Esophagus, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Testis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities					

- : No change      + : Slight change      ++ : Moderate change

<sup>a)</sup> right ventricular wall, septum

<sup>b)</sup> papillary muscle

Appendix 23-2 Histopathological findings in male rats  
- End of recovery -

Organ and tissue	Findings	Group	Control						300 mg/kg					
		Animal No.	007	008	009	010	011	012	307	308	309	310	311	312
Kidney	Basophilic tubule		-	-	-	-	-	-	+	+	+	++	+	+
	Protein cast		-	-	-	-	-	-	-	-	-	+	-	-
	Mononuclear cell infiltration, cortex		-	+	+	+	-	-	+	-	+	+	+	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		-	-	-	-	-	-	+	+	+	-	+	-
	Remnant of ultimobranchial body		-	-	-	-	-	-	-	-	+	-	-	-
Lungs(Bronchi)	Foam cell accumulation, alveolar space		-	+	+	-	+	-	+	+	+	+	+	-
	Mononuclear cell infiltration, perivascular		-	-	-	+	+	-	-	-	+	+	-	+
	Osseous metaplasia of alveolar wall		-	-	-	-	-	-	-	+	-	-	-	-
	Calcification in artery		-	-	+	+	-	-	-	+	-	-	-	-
	Hemorrhage		-	-	+	-	-	-	-	-	-	-	-	-
Heart	Fibrosis of myocardium, septum		+	-	-	-	-	-	-	-	+	-	-	-
	Mononuclear cell infiltration		-	-	-	-	-	-	-	-	-	+ <sup>a)</sup>	-	-
Sublingual gland	Mononuclear cell infiltration, interstitium		-	-	-	-	-	-	-	-	-	-	+	-
Cecum	Mononuclear cell infiltration, mucosa		-	-	-	-	+	-	-	-	-	-	-	-
Epididymis	Mononuclear cell infiltration, interstitium		-	-	-	-	-	-	-	-	-	-	-	+
Prostate	Mononuclear cell infiltration, interstitium		+	-	-	-	+	-	-	-	-	-	-	-
Skin	Significant lesion		.	.	.	.	.	.	.	.	.	-	.	.
Laryngopharynx, Trachea, Urinary bladder, Thymus, Spleen, Mandibular lymph node, Mesenteric lymph node, Liver, Submaxillary gland, Tongue, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Rectum, Testis, Seminal vesicle, Coagulating gland, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities											

- : No change      + : Slight change      ++ : Moderate change      . : Not examined

<sup>a)</sup> septum

Appendix 24-1-1 Histopathological findings in female rats  
- End of administration -

## Control group

Organ and tissue	Findings	Animal No.	401	402	403	404	405	406
Liver	Hypertrophy of centrilobular hepatocyte		-	-	-	-	-	-
	Microgranuloma		+	-	-	+	+	+
	Apoptotic necrosis of hepatocyte		-	-	-	-	+	+
Kidney	Basophilic tubule		-	-	-	-	-	-
	Vacuolation of tubular epithelium, proximal		-	-	-	-	-	-
	Mononuclear cell infiltration, cortex		-	+	+	-	-	+
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		-	-	-	-	-	-
	Remnant of ultimobranchial body		-	+	-	-	+	-
Lungs(Bronchi)	Foam cell accumulation, alveolar space		+	-	-	-	-	-
	Mononuclear cell infiltration, perivascular		-	+	+	+	+	+
	Osseous metaplasia of alveolar wall		-	-	-	-	-	-
Laryngopharynx	Neutrophil infiltration, submucosa		-	+	-	-	-	-
Heart	Mononuclear cell infiltration		-	-	+ <sup>a)</sup>	-	-	-
Thymus	Epithelial tubule		+	-	-	-	-	-
Mandibular lymph node	Lymphocytic hyperplasia		-	-	-	-	-	-
Esophagus	Degeneration of muscle fiber		-	-	+	-	-	-
	Mononuclear cell infiltration, muscular		-	-	+	-	-	-
Ovary	Luteal cyst		-	-	-	-	-	+
Sciatic nerve	Inflammatory cell infiltration, paraneurium		-	+	-	-	-	-
Skin	Significant lesion		.	.	.	.	.	.
Trachea, Urinary bladder, Spleen, Mesenteric lymph node, Submaxillary gland, Sublingual gland, Tongue, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Uterus, Vagina, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities					

- : No change      + : Slight change      . : Not examined

<sup>a)</sup> right ventricular wall, aortic

2000TT278

Appendix 24-1-2 Histopathological findings in female rats  
- End of administration -

## 30 mg/kg group

Organ and tissue	Findings	Animal No.	501	502	503	504	505	506
Liver	Hypertrophy of centrilobular hepatocyte		+	+	+	+	+	+
	Microgranuloma		+	+	+	-	+	+
	Apoptotic necrosis of hepatocyte		+	+	+	-	+	+
Kidney	Vacuolation of tubular epithelium, proximal		-	+	+	-	-	+
	Mononuclear cell infiltration, cortex		-	+	-	+	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		+	+	-	-	+	-
	Ectopic thymus		-	-	-	-	-	-
	Remnant of ultimobranchial body		-	-	-	-	-	-
	Mononuclear cell infiltration		-	-	-	-	-	-

- : No change

+ : Slight change

2000TT278

Appendix 24-1-3 Histopathological findings in female rats  
- End of administration -

100 mg/kg group

Organ and tissue	Findings	Animal No.	601	602	603	604	605	606
Liver	Hypertrophy of centrilobular hepatocyte		+	+	+	+	+	+
	Microgranuloma		-	+	-	+	-	+
	Apoptotic necrosis of hepatocyte		-	+	-	+	-	+
Kidney	Vacuolation of tubular epithelium, proximal		-	+	+	-	-	-
	Mononuclear cell infiltration, cortex		-	+	-	+	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		+	-	-	-	+	++
	Ectopic thymus		+	-	-	-	-	-
	Remnant of ultimobranchial body		-	+	-	-	-	-
	Mononuclear cell infiltration		+	-	-	-	-	-

- : No change

+ : Slight change

++ : Moderate change

Appendix 24-1-4 Histopathological findings in female rats  
- End of administration -

## 300 mg/kg group

Organ and tissue	Findings	Animal No.	701	702	703	704	705	706
Liver	Hypertrophy of centrilobular hepatocyte		++	++	+	++	+	+
	Microgranuloma		-	-	+	+	+	+
	Apoptotic necrosis of hepatocyte		-	-	+	+	+	+
Kidney	Basophilic tubule		-	-	-	+	+	-
	Vacuolation of tubular epithelium, proximal		+	+	+	+	+	+
	Mononuclear cell infiltration, cortex		-	-	-	-	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		+	++	+	+	+	++
	Remnant of ultimobranchial body		-	-	-	-	-	-
Lungs(Bronchi)	Foam cell accumulation, alveolar space		-	+	+	+	+	-
	Mononuclear cell infiltration, perivascular		-	+	-	-	-	-
	Osseous metaplasia of alveolar wall		-	-	-	-	+	+
Laryngopharynx	Neutrophil infiltration, submucosa		-	-	-	-	-	-
Heart	Mononuclear cell infiltration		-	-	-	-	-	-
Thymus	Epithelial tubule		-	+	-	-	-	-
Mandibular lymph node	Lymphocytic hyperplasia		-	-	-	-	-	+
Esophagus	Degeneration of muscle fiber		-	+	-	+	-	-
	Mononuclear cell infiltration, muscular		-	+	-	+	-	-
Ovary	Luteal cyst		-	-	-	-	-	+
Sciatic nerve	Inflammatory cell infiltration, paraneurium		-	-	-	-	-	-
Skin	Significant lesion		-	-	•	-	•	•
Trachea, Urinary bladder, Spleen, Mesenteric lymph node, Submaxillary gland, Sublingual gland, Tongue, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Uterus, Vagina, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities					

- : No change      + : Slight change      ++ : Moderate change      • : Not examined

Appendix 24-2 Histopathological findings in female rats  
- End of recovery -

Organ and tissue	Findings	Group Animal No.	Control						300 mg/kg					
			407	408	409	410	411	412	707	708	709	710	711	712
Liver	Hypertrophy of centrilobular hepatocyte		-	-	-	-	-	-	-	-	+	-	-	-
Kidney	Mononuclear cell infiltration, cortex		-	-	-	-	-	-	-	+	+	-	-	-
Thyroid	Hyperplasia/hypertrophy of follicular epithelium		-	-	-	-	-	-	-	+	-	-	-	+
Lungs(Bronchi)	Foam cell accumulation, alveolar space		-	-	-	+	+	+	+	+	+	-	-	-
	Mononuclear cell infiltration, perivascular		+	+	+	+	+	+	+	-	+	+	+	-
	Calcification in artery		-	-	+	-	-	-	-	-	-	-	-	-
Thymus	Epithelial tubule		-	-	-	-	-	-	-	-	-	-	-	+
Mesenteric lymph node	Lymphocytic hyperplasia		-	-	-	-	-	+	-	-	-	-	-	-
Sublingual gland	Ductal hyperplasia		-	-	-	-	+	-	-	-	-	-	-	-
Tongue	Mononuclear cell infiltration, submucosa		-	+	-	-	-	-	-	-	-	-	-	-
Ovary	Luteal cyst		-	-	+	-	-	-	-	-	-	+	-	-
	Follicular cyst		-	-	-	-	-	-	-	+	-	-	-	-
	Corpus albicans		-	-	-	+	-	-	-	-	-	-	-	-
Skin	Significant lesion		•	•	•	•	•	•	•	-	•	-	-	-
Laryngopharynx, Trachea, Heart, Urinary bladder, Spleen, Mandibular lymph node, Submaxillary gland, Esophagus, Stomach, Duodenum, Jejunum, Ileum, Cecum, Colon, Rectum, Uterus, Vagina, Cerebrum, Cerebellum, Medulla oblongata, Spinal cord, Sciatic nerve, Pituitary, Parathyroid, Adrenal, Sternum, Femur, Bone marrow			No abnormalities											

- : No change      + : Slight change      • : Not examined