

15.5.2.2. 回復期間終了時 (Table 10-2, Appendix 10-2)

雄では、いずれの検査項目においても対照群と 1,000 mg/kg 群との間に有意な差は認められなかつた。

雌では、1,000 mg/kg 群で PT が有意に短縮した。

15.5.2.3. 血液生化学検査

15.5.2.4. 投与期間終了時 (Table 11-1, Appendix 11-1)

雄では、300 および 1,000 mg/kg 群で総蛋白の有意な減少、1,000 mg/kg 群でカリウムの有意な増加が認められた。また、100 mg/kg 群でナトリウム、カリウムおよび塩素が有意に増加したが、用量依存性のない変化であり、被験物質投与の影響とは判断しなかつた。

雌では、1,000 mg/kg 群で中性脂肪が有意に上昇した。

15.5.2.5. 回復期間終了時 (Table 11-2, Appendix 11-2)

雌雄ともにいずれの検査項目においても対照群と 1,000 mg/kg 群との間に有意な差は認められなかつた。

15.5.3. 血清蛋白電気泳動検査

15.5.3.1. 投与期間終了時 (Table 12-1, Appendix 12-1)

雄では、300 および 1,000 mg/kg 群で α_1 グロブリン分画比率および濃度が有意に低下した。

雌では、300 mg/kg 群で α_2 グロブリン分画比率および濃度が有意に増加したが、用量依存性のない変化であり被験物質投与の影響とは判断しなかつた。

15.5.3.2. 回復期間終了時 (Table 12-2, Appendix 12-2)

雄では、いずれの検査項目においても対照群と 1,000 mg/kg 群との間に有意な差は認められなかつた。

雌では、1,000 mg/kg 群で α_2 グロブリン分画濃度が有意に増加したが、軽微な変化であり、毒性学的意義は低いと判断した。

15.5.4. 尿検査

15.5.4.1. 投与期間終了時 (Table 13-1, Appendix 13-1)

雄では、いずれの検査項目においても対照群と被験物質投与各群との間に差は認められなかつた。

雌では、100 mg/kg 群でナトリウム、カリウムおよび塩素総排泄量の有意な減少、300 mg/kg 群でナトリウム総排泄量の有意な減少、1,000 mg/kg 群でカリウムおよび塩素総排泄量の有意な減少が認められた。

15.5.4.2. 回復期間終了時 (Table 13-2, Appendix 13-2)

雄では、1,000 mg/kg 群で浸透圧が有意に低下したが、同群の有意ではない尿量の増加に伴った変化であり、被験物質投与の影響とは判断しなかった。また、ナトリウム、カリウムおよび塩素濃度が有意に減少したが、総排泄量に変化は認められないことから、被験物質投与の影響とは判断しなかった。

雌では、いずれの検査項目においても対照群と 1,000 mg/kg 群との間に差は認められなかった。

15.6. 病理学検査

15.6.1. 器官重量

15.6.1.1. 投与期間終了時 (Table 14-1, 15-1, Appendix 14-1, 15-1)

雄では、いずれの測定器官においても対照群と被験物質投与各群との間に差は認められなかった。

雌では、1,000 mg/kg 群で肝臓の相対重量の有意な増加および絶対重量の増加傾向が認められた。また、100 および 300 mg/kg 群で脾臓の絶対および相対重量の有意な低下が、100 mg/kg 群で卵巣の絶対重量の有意な低下が認められたが、用量依存性のない変化であり、被験物質投与の影響とは判断しなかった。

15.6.1.2. 回復期間終了時 (Table 14-2, 15-2, Appendix 14-2, 15-2)

雄では、いずれの測定器官においても対照群と 1,000 mg/kg 群との間に差は認められなかった。

雌では、1,000 mg/kg 群で心臓および卵巣の相対重量の有意な増加が認められたが、同群での偶発的な低体重に起因した変化と考えられ、被験物質投与の影響とは判断しなかった。

15.6.2. 剖検所見

15.6.2.1. 投与期間終了時 (Table 16-1, Appendix 16)

被験物質投与群において、対照群に比し発生数が明らかに増減した所見は認められなかつた。被験物質投与群で認められた所見は、いずれも単発性あるいは散発性の発生であり、また、ラットにしばしば自然発生する所見であることから、被験物質投与による変化とは考えられなかつた。

15.6.2.2. 回復期間終了時 (Table 16-2, Appendix 16)

対照群および 1,000 mg/kg 群で観察された所見は、いずれも単発性の発生であり、自然発生性の変化と考えられた。

15.6.2.3. 死亡動物 (Appendix 16)

回復期間中に死亡した対照群の 1 例 (動物番号 1010) では、回腸の閉塞、空腸および回腸の内腔拡張、膀胱の赤色斑、脾臓の小型化、胸腺の萎縮、精嚢の萎縮および全身の削瘦が認められた。

15.6.3. 組織所見

15.6.3.1. 投与期間終了時 (Table 17-1, Appendix 17)

被験物質投与の関与が疑われた変化が肝臓に認められた。

肝臓では、小葉中心帯肝細胞肥大 (Photo. 1, 2) が雌雄の 300 および 1,000 mg/kg 群に認められ、雌雄ともに 1,000 mg/kg 群で発生数が有意に増加した。肝細胞肥大は、細胞質の好酸性化を伴っていた。なお、肝細胞巣状壊死が、雄の 1,000 mg/kg 群に 1 例発生した。

その他、散発的に軽度の変化が対照群を含めた各群に観察されたが、用量に関連した発生数の増減も認められず、いずれも自然発生病変と考えられた。

15.6.3.2. 回復期間終了時 (Table 17-2, Appendix 17)

投与期間終了時に、雌雄の 300 および 1,000 mg/kg 群に認められた肝細胞の肥大および巣状壊死は観察されなかった。

その他、散発的に軽度の変化が対照群および 1,000 mg/kg 群に観察されたが、その種類および発生数からいずれも自然発生病変と考えられた。

15.6.3.3. 死亡動物 (Appendix 17)

回復期間中に死亡した対照群の 1 例 (動物番号 1010) では、空腸および回腸の内腔拡張、漿膜のうつ血、水腫および単核細胞浸潤、筋層の肥大、回腸の閉塞、潰瘍、漿膜の線維化および出血がみられ、死亡の主因と考えられた。その他、骨髓のうつ血および重度の造血低下、脾臓および胸腺における重度の萎縮、リンパ節の赤血球食像および洞組織球症、肺の泡沫細胞集簇、肝臓の肝細胞巣状壊死、腎臓の尿細管好塩基化、膀胱の出血、前立腺および精嚢の萎縮、皮膚の浮腫が観察され、二次的な一般状態の悪化と栄養障害が推察された。死因は持続性の腸閉塞であると判断した。

16. 考察および結論

被験物質投与に関連した変化が、毒性試験群の肝臓に認められた。1,000 mg/kg 群の雌で肝臓重量の増加が認められ、対応する所見として、病理組織学的に小葉中心帯の好酸性化を伴った肝細胞の肥大が 300 mg/kg 以上の群の雌雄で認められた。薬物や化学物質の投与により、滑面小胞体の増加やチトクローム P-450 の活性上昇をきたし、組織学的に小葉中心帯の好酸性化を伴った肝細胞の肥大を起こすことが知られていることから^{1), 2), 3)}、小葉中心帯肝細胞肥大は、同様の機序で発生した可能性が考えられた。肝細胞肥大は、被験物質投与群のみに発生がみられるところから、被験物質投与に関連した変化であると考えられた。肝細胞の巣状壊死が、1,000 mg/kg 群の雄 1 例に認められた。巣状壊死は、肝臓の一箇所のみに限局した所見であり、同様の形態学的特徴を持つ肝細胞の巣状壊死は、自然発生病変としてまれに観察されることから、本所見は偶発的な所見で、被験物質投与とは関係のない変化であると考えられた。

血液生化学検査において、毒性試験群の 300 および 1,000 mg/kg 群の雄で総蛋白が低下した。血清蛋白電気泳動検査結果では、同群の雄に α_1 グロブリン分画の低下が認められており、総蛋白の低下は α_1 グロブリン分画の低下に起因した変化であると考えられた。しかし、 α_1 グロブリン分画の低下の機序は不明であった。また、毒性試験群の 1,000 mg/kg 群の雌で中性脂肪が上昇した。中性脂肪の上昇は、総コレステロールの変化を伴わない単独の変化であり、雌の高用量群のみに認められた変化である。したがって、これらの変化の毒性学的意義は不明であるが、被験物質の蛋白・脂質代謝系に対する影響が示唆された。

対照群の雄 1 例が回復期間中に死亡した。この動物は、投与 25 日以降体重および摂餌量が減少し、一般状態および FOB において、全身状態の悪化に関連した症状が観察された。病理組織学検査では、持続性の腸閉塞が認められ、これが死因と考えられた。腸閉塞は、ラットにおいてその発生は珍しいが、対照群に発生したことから、自然発生病変であると考えられた。

一般状態、体重および摂餌量に被験物質投与の影響は認められず、詳細な症状観察、反応性検査、握力および自発運動量にも神経毒性を示唆する変化は認められなかった。

その他、毒性試験群において、血液学検査では、1,000 mg/kg 群の雌 1 例（動物番号 2304）の白血球数が高値を示した。しかし、この動物を含めた同群の病理組織学検査で炎症性の変化は認められず、被験物質投与とは関連のない変化と判断した。また、血液生化学検査では、1,000 mg/kg 群の雄でカリウムが上昇し、尿検査では 100, 300 または 1,000 mg/kg 群の雌で尿中電解質が低下したが、変化の程度が用量に伴っておらず、腎機能に関連する生化学検査項目および他の尿検査項目にも異常はなく、病理学検査においても腎の異常は認められないことから、被験物質投与とは関連のない変化と考え

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られた。回復試験群において、1,000 mg/kg 群の雄で好中球数が減少し、1,000 mg/kg 群の雌で網赤血球率が増加し、PT が短縮した。これらの変化は、投与期間終了時には認められておらず、いずれも軽微な変化であるため、毒性学的意義は低いと考えられた。

以上、当該試験条件下において、2,2',3,3'-テトラクロロ-4,4'-ジアミノジフェニルメタンの反復投与に起因する毒性変化が、雌雄ともに 300 mg/kg/day 以上の投与で認められたことから、無毒性量は、雌雄ともに 100 mg/kg/day と判断された。また、毒性試験群で認められた変化は、いずれも 14 日間の休薬により回復性が認められた。

17. 参考文献

- 1) 伊東信之編著、最新毒性病理学、中山書店：158 (1994).
- 2) 日本毒性病理学会編、毒性病理組織学、アイペック：182 (2000).
- 3) Haschek MW, Rousseaux GC, Fundamentals of toxicologic pathology, Academic press: 139 (1998).

18. 試験関係資料の保存

当該試験の下記資料は、安評センター資料保存施設にて最終報告書作成後 10 年間保存される。その後の保存については、試験委託者と安評センターで協議の上、別途定める。また、病理組織標本作製関係資料については、株式会社 組織科学研究所にて 10 年間保存される。その後の保存については、試験委託者と安評センターならびに株式会社 組織科学研究所で協議の上、別途定める。

- 試験計画書（正本）
- 被験物質（各ロット、2 g）
- 被験物質に関する資料（使用および調製記録、その他）
- 動物および施設に関する記録
- 生データ（一般状態観察記録、体重測定記録、摂餌量測定記録、臨床検査記録、器官重量測定記録、病理学検査所見記録、その他）
- 各種標本類（ブロック標本、病理組織標本、湿臓器、血液塗抹標本、その他）
- 病理組織標本作製関係資料（病理組織標本作製計画書の写し、病理組織標本作製報告書の写し、標本作製過程管理書の写し、その他）
- 最終報告書（正本）、化学物質審査規制法届出様式（写し）

Table 1.

Clinical observation

Exp. No. 9934 (115-213)

Sex: Male

Group No. Dose mg/kg	Finding Part	Day of experiment																	
		1----->			2----->			3----->			4----->			5----->			6----->		
01 control 0	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	Emaciation	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Emaciation	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Emaciation	—	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
04 TCDAM 1000	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	Emaciation	—	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Male

Group No. Dose mg/kg	Finding Part	Day of experiment																	
		7----->			8----->			9----->			10----->			11----->			12----->		
01 control 0	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	Emaciation	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Emaciation	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Emaciation	—	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
04 TCDAM 1000	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	Emaciation	—	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Male

Group No.	Dose mg/kg	Finding Part	Day of experiment																		
			13----->			14----->			15----->			16----->			17----->			18----->			
01 control 0	normal		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
			Total	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	Emaciation		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
03 TCDAM 300	normal		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			Total	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Male

Group No.	Dose mg/kg	Finding Part	Day of experiment																		
			19----->			20----->			21----->			22----->			23----->			24----->			
01 control 0	normal		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			Total	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	Emaciation		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
03 TCDAM 300	normal		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal		-	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
			Total	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Male

Group No.	Dose mg/kg	Finding Part	Day of experiment												
			25-->	26-->	27-->	28-->	29	1	2	3	1	2	3	1	
01 control 0		normal	-	10	10	10	10	10	10	10	10	10	10	9	9
			Total	10	10	10	10	10	10	10	10	10	9	9	5
		Emaciation	-	10	10	10	10	10	10	10	10	10	9	9	5
			+	0	0	0	0	0	0	0	0	0	1	1	0
			Total	10	10	10	10	10	10	10	10	10	10	10	5
02 TCDAM 100		normal	-	5	5	5	5	5	5	5	5	5	5	5	5
			Total	5	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300		normal	-	5	5	5	5	5	5	5	5	5	5	5	5
			Total	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000		normal	-	10	10	10	10	10	10	10	10	10	10	10	5
			Total	10	10	10	10	10	10	10	10	10	10	10	5

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Female

Group No.	Dose mg/kg	Finding Part	Day of experiment												
			1-->	2-->	3-->	1-->	2-->	3-->	1-->	2-->	3-->	1-->	2-->	3-->	
01 control 0		normal	-	10	10	10	10	10	10	10	10	10	10	10	10
			Total	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100		normal	-	5	5	5	5	5	5	5	5	5	5	5	5
			Total	5	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300		normal	-	5	5	5	5	5	5	5	5	5	5	5	5
			Total	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000		normal	-	10	10	10	10	10	10	10	10	10	10	10	10
			Total	10	10	10	10	10	10	10	10	10	10	10	10

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Finding Part	Day of experiment																	
		7--> 1	2	3	8--> 1	2	3	9--> 1	2	3	10--> 1	2	3	11--> 1	2	3	12--> 1	2	3
01 control 0	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Finding Part	Day of experiment																	
		13--> 1	2	3	14--> 1	2	3	15--> 1	2	3	16--> 1	2	3	17--> 1	2	3	18--> 1	2	3
01 control 0	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300	normal	—	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal	—	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Finding Part	Day of experiment											
		19	20	21	22	23	24	1	2	3	1	2	3
01 control 0	normal	-	10	10	10	10	10	10	10	10	10	10	10
		Total	10	10	10	10	10	10	10	10	10	10	10
02 TCDAM 100	normal	-	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300	normal	-	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal	-	10	10	10	10	10	10	10	10	10	10	10
		Total	10	10	10	10	10	10	10	10	10	10	10

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

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Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Finding Part	Day of experiment											
		25	26	27	28	29	1	2	3	1	2	3	1
01 control 0	normal	-	10	10	10	10	10	10	10	10	10	10	5
		Total	10	10	10	10	10	10	10	10	10	10	5
02 TCDAM 100	normal	-	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5
03 TCDAM 300	normal	-	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal	-	10	10	10	10	10	10	10	10	10	10	5
		Total	10	10	10	10	10	10	10	10	10	10	5

1: Before dosing 2: 30 to 60 minutes after dosing 3: 3 to 4 hours after dosing
 TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

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Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Male

Group No. Dose mg/kg	Finding Part	Day of experiment														
		29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
01 control 0	normal	-	4	4	4	4	4	4	4	4	4	4	4	4	4	4
		Total	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	Emaciation	-	4	4	4	4	4	4	4	4	4	4	4	4	4	4
		+	1	1	1	1	1	1	1	1	1	1	1	0	0	0
		Total	5	5	5	5	5	5	5	5	5	5	5	5	4	4
	Abdominal distention	-	5	5	5	5	5	5	5	4	4	4	4	4	4	4
		+	0	0	0	0	0	0	1	1	1	1	1	0	0	0
		Total	5	5	5	5	5	5	5	5	5	5	5	4	4	4
04 TCDAM 1000	normal	-	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 1.

-continued Clinical observation

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Finding Part	Day of experiment														
		29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
01 control 0	normal	-	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5
04 TCDAM 1000	normal	-	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 2.

Body weight

Exp. No. 9934 (115-213)

Sex: Male

Group No. Dose mg/kg	Day of experiment									Gain 1-28 Unit:g
		1	4	8	11	15	18	22	25	
01 control 0	N	10	10	10	10	10	10	10	9	9
	Mean	151	173	200	220	243	263	285	304	168
	S.D.	6	10	14	18	23	26	30	31	29
02 TCDAM 100	N	5	5	5	5	5	5	5	5	5
	Mean	150	172	199	219	246	264	283	300	168
	S.D.	6	10	13	15	21	24	29	33	40
03 TCDAM 300	N	5	5	5	5	5	5	5	5	5
	Mean	149	171	198	223	248	272	296	313	183
	S.D.	6	8	14	16	17	18	20	22	18
04 TCDAM 1000	N	10	10	10	10	10	10	10	10	10
	Mean	151	172	197	219	240	257	277	292	158
	S.D.	6	9	13	17	20	22	24	27	23

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 2.

-continued Body weight

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Day of experiment									Gain 1-28 Unit:g
		1	4	8	11	15	18	22	25	
01 control 0	N	10	10	10	10	10	10	10	10	10
	Mean	117	131	146	160	169	179	191	197	90
	S.D.	5	6	6	9	10	9	11	10	10
02 TCDAM 100	N	5	5	5	5	5	5	5	5	5
	Mean	117	132	144	157	164	172	181	187	82
	S.D.	5	7	9	11	12	12	12	15	11
03 TCDAM 300	N	5	5	5	5	5	5	5	5	5
	Mean	117	129	141	154	162	169	178	187	77
	S.D.	5	7	10	13	16	21	23	25	24
04 TCDAM 1000	N	10	10	10	10	10	10	10	10	10
	Mean	117	131	143	155	163	173	185	190	80
	S.D.	5	6	7	7	7	9	9	8	10

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 2. -continued Body weight

Exp. No. 9934 (115-213)

Sex: Male

Group No. Dose mg/kg	Day of experiment					Gain 29-42	Unit:g
	29	32	36	39	42		
01 control 0	N	4	4	4	4	4	4
	Mean	339	355	375	390	404	65
	S.D.	25	24	27	27	29	5
04 TCDAM 1000	N	5	5	5	5	5	5
	Mean	318	332	346	363	372	54
	S.D.	25	26	23	20	19	10

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

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Table 2. -continued Body weight

Exp. No. 9934 (115-213)

Sex: Female

Group No. Dose mg/kg	Day of experiment					Gain 29-42	Unit:g
	29	32	36	39	42		
01 control 0	N	5	5	5	5	5	5
	Mean	210	219	227	234	240	30
	S.D.	9	12	12	11	9	4
04 TCDAM 1000	N	5	5	5	5	5	5
	Mean	196	202	209	218	222*	26
	S.D.	13	16	19	16	15	5

Significantly different from 01 group * $P \leq 0.05$ (Dunnett)
TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

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Table 3. Food consumption

Exp. No. 9934 (115-213)

Sex: Male

Group No.	Dose mg/kg	Day of experiment						Unit:g/animal/day
		=> 8	=> 15	=> 22	=> 28	=> 36	=> 42	
01 control 0	N	10	10	10	9	4	4	
	Mean	23	24	25	25	28	29	
	S.D.	2	3	3	2	1	2	
02 TCDAM 100	N	5	5	5	5			
	Mean	23	25	25	25			
	S.D.	2	3	4	5			
03 TCDAM 300	N	5	5	5	5			
	Mean	23	25	27	27			
	S.D.	1	2	2	2			
04 TCDAM 1000	N	10	10	10	10	5	5	
	Mean	22	24	24	24	26	26	
	S.D.	2	3	3	3	2	2	

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 3. -continued Food consumption

Exp. No. 9934 (115-213)

Sex: Female

Group No.	Dose mg/kg	Day of experiment						Unit:g/animal/day
		=> 8	=> 15	=> 22	=> 28	=> 36	=> 42	
01 control 0	N	10	10	10	10	5	5	
	Mean	17	18	18	18	20	19	
	S.D.	1	1	1	1	2	1	
02 TCDAM 100	N	5	5	5	5			
	Mean	18	18	18	17			
	S.D.	1	2	2	2			
03 TCDAM 300	N	5	5	5	5			
	Mean	17	18	18	18			
	S.D.	1	2	3	3			
04 TCDAM 1000	N	10	10	10	10	5	5	
	Mean	17	18	19	18	20	19	
	S.D.	2	2	2	2	2	2	

TCDAM: 2,2',3,3'-Tetrachloro-4,4'-diamino diphenylmethane

Table 4. Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Male	Signs	Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)	
			B. G.	1	2	3	4	1
REMoval FROM CAGE	No. of animals	0	10	10	10	10	10	5
Ease of removal	Very easy	100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5
	Easy	0	10	10	10	10	10	5
		100	0	0	0	0	0	0
		300	0	1	0	0	3	1
Vocalization	None	1000	0	3	0	1	1	0
		0	10	10	10	10	10	5
		100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5

B. G. : Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types
Exp. No. 9934 (115-213)

Sex: Male	Signs	Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)	
			B. G.	1	2	3	4	1
HANDLING OBSERVATIONS								
Muscle tone	Normal	0	10	10	10	10	9	4
		100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5
Decrease or limp		0	0	0	0	0	1	1
	Absent	100	0	0	0	0	0	0
		300	0	0	0	0	0	0
		1000	0	0	0	0	0	0
Subnormal temperature	Absent	0	10	10	10	10	10	5
		100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5
Piloerection	Absent	0	10	10	10	10	10	5
		100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5
Staining hair	Absent	0	10	10	10	10	10	5
		100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5
Unkempt hair	Absent	0	10	10	10	10	10	5
		100	5	5	5	5	5	4
		300	5	5	5	5	5	5
		1000	10	10	10	10	10	5
Rough fur	Absent	0	0	0	0	0	0	0
		100	0	0	0	0	0	0
		300	0	0	0	0	0	0
		1000	0	0	0	0	0	0

B. G. : Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Male

Signs		Dose level (mg/kg)	B. G.	Administration period (Week)				Recovery period (Week)	
				1	2	3	4	1	2
Skin color	Normal	0		10	10	10	10	5	4
		100		5	5	5	5	-	-
		300		5	5	5	5	-	-
		1000		10	10	10	10	5	5
Lacration	Absent	0		10	10	10	10	5	4
		100		5	5	5	5	-	-
		300		5	5	5	5	-	-
		1000		10	10	10	10	5	5
Exophthalmos	Absent	0		10	10	10	10	5	4
		100		5	5	5	5	-	-
		300		5	5	5	5	-	-
		1000		10	10	10	10	5	5
Pupillary size	Normal	0		10	10	10	10	5	4
		100		5	5	5	5	-	-
		300		5	5	5	5	-	-
		1000		10	10	10	10	5	5
Salivation	Absent	0		10	10	10	10	5	4
		100		5	5	5	5	-	-
		300		5	5	5	5	-	-
		1000		10	10	10	10	5	5

B. G.: Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Male

Signs		Dose level (mg/kg)	B. G.	Administration period (Week)				Recovery period (Week)		
				1	2	3	4	1	2	
OBSERVATIONS IN ARENA										
Posture	Normal	0		10	10	10	10	5	4	
		100		5	5	5	5	-	-	
		300		5	5	5	5	-	-	
		1000		10	10	10	10	5	5	
Motor activity	Normal	0		10	10	10	10	5	4	
		100		5	5	5	5	-	-	
		300		5	5	5	5	-	-	
		1000		10	10	10	10	5	5	
Respiration	Normal	0		10	10	10	10	5	4	
		100		5	5	5	5	-	-	
		300		5	5	5	5	-	-	
		1000		10	10	10	10	5	5	
Lid closure	Wide open	0		10	10	10	10	5	4	
		100		5	5	5	5	-	-	
		300		5	5	5	5	-	-	
		1000		10	10	10	10	5	5	
Gait	Normal	0		10	10	10	10	5	4	
		100		5	5	5	5	-	-	
		300		5	5	5	5	-	-	
		1000		10	10	10	10	5	5	
Tremor	None	0		10	10	10	10	5	4	
		100		5	5	5	5	-	-	
		300		5	5	5	5	-	-	
		1000		10	10	10	10	5	5	

B. G.: Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Male

Signs	Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)		
		B. G.	1	2	3	4	1	2
Twitch	None	0	10	10	10	10	5	4
		100	5	5	5	5	-	-
		300	5	5	5	5	5	5
		1000	10	10	10	10	5	5
Convulsion	None	0	10	10	10	10	5	4
		100	5	5	5	5	-	-
		300	5	5	5	5	5	5
		1000	10	10	10	10	5	5
Stereotypic behavior	None	0	10	10	10	10	5	4
		100	5	5	5	5	-	-
		300	5	5	5	5	5	5
		1000	10	10	10	10	5	5
Abnormal behavior	None	0	10	10	10	10	5	4
		100	5	5	5	5	-	-
		300	5	5	5	5	5	5
		1000	10	10	10	10	5	5

B. G. : Before grouping

Signs	Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)		
		B. G.	1	2	3	4	1	2
SEX: Male								
SENSOR/MOTOR FUNCTION								
Approach contact	Normal a)	0	9	-	4	-		
		100	5	-	-			
		300	5	-	-			
		1000	10	-	-			
Freezing	0	1	0	0	0	0		
	100	0	-	-	-	-		
	300	0	-	-	-	-		
	1000	0	-	-	-	-		
Touch response	Moderate reaction	0	9	4	4	-		
	100	4	5	-	-			
	300	5	10	-	-			
	1000	10	5	-	-			
Vocalization, energetically reaction	0	0	0	0	0	0		
	100	1	1	1	1	1		
	300	0	0	0	0	0		
	1000	0	0	0	0	0		
Freezing	0	1	0	0	0	0		
	100	0	-	-	-	-		
	300	0	-	-	-	-		
	1000	0	-	-	-	-		
Pinna response	Normal	0	10	4	4	-		
	100	5	5	-	-			
	300	5	10	-	-			
	1000	10	5	-	-			

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

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B. G. : Before grouping

a) Rat slowly approaches and sniffs at object or turns away

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Male

Signs		Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)		
			B. G.	1	2	3	4	1	2
Pain response(Tail pinch)	Slowly turns	0				1		0	
		100				0		-	
		300				0		-	
		1000				0		0	
	Walk away from stimulus	0			2			0	
		100			0			-	
		300			1			-	
		1000			0			0	
	Freezing	0			0			0	
		100			0			-	
		300			0			-	
		1000			0			1	
53	Normal	0				7		4	
		100				5		-	
		300				4		-	
		1000				10		4	
	Pupillary reflex	0				10		4	
		100				5		-	
		300				5		-	
		1000				10		5	
Air righting reflex	Normal	0				10		4	
		100				5		-	
		300				5		-	
		1000				10		5	

B. G.: Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Female

Signs		Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)		
			B. G.	1	2	3	4	1	2
No. of animals		0		10	10	10	10	10	5
		100		5	5	5	5	5	-
		300		5	5	5	5	5	-
		1000		10	10	10	10	10	5
54	REMOVAL FROM CAGE	Ease of removal	Very easy	0	6	7	9	7	5
				100	3	5	5	3	-
				300	3	5	5	5	-
				1000	6	10	10	9	4
		Easy	Easy	0	4	3	1	3	0
				100	2	0	0	2	-
				300	2	0	0	0	-
				1000	4	0	0	1	1
		Vocalization	None	0	10	10	10	10	5
				100	5	5	5	5	-
				300	5	5	5	5	-
				1000	10	10	10	10	5

B. G.: Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Female

Signs	Handling observations	Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)		
			B. G.	1	2	3	4	1	2
Muscle tone	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
Subnormal temperature	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
Piloperection	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
Staining hair	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
Unkempt hair	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
Skin color	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
		1000	10	10	10	10	10	5	5
		3000	10	10	10	10	10	5	5
		10000	10	10	10	10	10	5	5
		30000	10	10	10	10	10	5	5
		100000	10	10	10	10	10	5	5

B. G. : Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Female

Signs	Sex: Female	Dose level (mg/kg)	Administration period (Week)				Recovery period (Week)		
			B. G.	1	2	3	4	1	2
Lacrimation	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
		1000	10	10	10	10	10	5	5
Exophthalmos	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
		1000	10	10	10	10	10	5	5
Pupillary size	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
		1000	10	10	10	10	10	5	5
Salivation	Absent	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	5	5
		1000	10	10	10	10	10	5	5

B. G. : Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Female

Signs		Dose level (mg/kg)	Administration period (Week)					Recovery period (Week)	
			B.G.	1	2	3	4	1	2
OBSERVATIONS IN ARENA									
Posture	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Motor activity	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Respiration	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Lid closure	Wide open	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Gait	Normal	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Tremor	None	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5

B. G. : Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Female

Signs		Dose level (mg/kg)	Administration period (Week)					Recovery period (Week)	
			B.G.	1	2	3	4	1	2
Twitch									
	None	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Convulsion									
	None	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Stereotypic behavior									
	None	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5
Abnormal behavior									
	None	0	10	10	10	10	10	5	5
		100	5	5	5	5	5	-	-
		300	5	5	5	5	5	-	-
		1000	10	10	10	10	10	5	5

B. G. : Before grouping

Table 4. -continued Detailed clinical observation and sensory reactivity to stimuli of different types

Exp. No. 9934 (115-213)

Sex: Female

Signs	Dose level (mg/kg)	B. G. Administration period (Week)				Recovery period (Week)	
		1	2	3	4	1	2
SENSOR/MOTOR FUNCTION Approach contact	Normal a)	0	100	500	1000	10	5
		100	300	1000	1000	5	-
Touch response	Moderate reaction	0	100	300	1000	10	5
		100	300	1000	1000	5	-
Pinna response	Normal	0	100	300	1000	10	5
		100	300	1000	1000	5	-
Pain response(Tail pinch)	Normal	0	100	300	1000	10	5
		100	300	1000	1000	5	-
Pupillary reflex	Normal	0	100	300	1000	10	5
		100	300	1000	1000	5	-
Air righting reflex	Normal	0	100	300	1000	10	5
		100	300	1000	1000	5	-

B. G. : Before grouping
a) Mean \pm S.D.
Values in parentheses are expressed no. of animals examined

Table 5. Summary of number of defecation

Exp. No. 9934(115-213)

Sex	Dose level (mg/kg)	No. of animals	B. G.	Administration period (week)		Recovery period (week)	
				1	2	3	4
Female	0	10	0.0 \pm 0.0 a)	0.3 \pm 0.9	0.0 \pm 0.0	0.2 \pm 0.6	0.3 \pm 1.0 (9)
						0.0 \pm 0.0 (4)	0.0 \pm 0.0 (4)
Male	100	5	0.4 \pm 0.9	1.0 \pm 1.4	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0
	300	5	0.4 \pm 0.9	0.4 \pm 0.9	0.0 \pm 0.0	0.2 \pm 0.4	0.6 \pm 1.3
	1,000	10	0.6 \pm 1.1	0.8 \pm 1.1	0.2 \pm 0.6	0.3 \pm 0.9	0.1 \pm 0.3
						0.4 \pm 0.9 (5)	0.0 \pm 0.0 (5)
	0	10	0.2 \pm 0.6	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0 (5)
Female	100	5	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0
	300	5	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0
	1,000	10	0.1 \pm 0.3	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0 (5)

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B. G. : Before grouping

a) Mean \pm S.D.

Values in parentheses are expressed no. of animals examined

Table 6. Summary of number of pools of urine

Exp. No. 9934(115-213)

Sex	Dose level (mg/kg)	No. of animals	B. G.	Administration period (week)				Recovery period (week)		
				1	2	3	4	1	2	
	0	10	0.6 ± 0.8 a)	0.3 ± 0.5	0.2 ± 0.6	0.4 ± 0.8	0.2 ± 0.4 (9)	0.0 ± 0.0 (4)	0.5 ± 0.6 (4)	
Male	100	5	0.6 ± 0.9	0.2 ± 0.4	0.0 ± 0.0	0.2 ± 0.4	0.0 ± 0.0			
	300	5	0.2 ± 0.4	0.8 ± 1.3	0.4 ± 0.5	0.2 ± 0.4	0.0 ± 0.0			
	1,000	10	1.0 ± 1.1	0.7 ± 0.8	0.2 ± 0.4	0.8 ± 0.9	0.3 ± 0.5	0.2 ± 0.4 (5)	0.2 ± 0.4 (5)	
Female	0	10	0.3 ± 0.7	0.2 ± 0.4	0.1 ± 0.3	0.1 ± 0.3	0.2 ± 0.4	0.0 ± 0.0 (5)	0.0 ± 0.0 (5)	
	100	5	0.2 ± 0.4	0.0 ± 0.0	0.2 ± 0.4	0.0 ± 0.0	0.4 ± 0.5			
	300	5	0.4 ± 0.9	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0			
	1,000	10	0.2 ± 0.6	0.5 ± 1.0	0.1 ± 0.3	0.0 ± 0.0	0.2 ± 0.4	0.0 ± 0.0 (5)	0.0 ± 0.0 (5)	

B. G. : Before grouping

a) Mean ± S.D.

Values in parentheses are expressed no. of animals examined

Table 7. Summary of grip strength

Exp. No. 9934(115-213)

4 week of administration				Unit : g
Sex	Dose level (mg/kg)	No. of animals	Forelimb	Hindlimb
	0	9	1338 ± 147 a)	703 ± 139
Male	100	5	1457 ± 206	822 ± 228
	300	5	1370 ± 211	721 ± 129
	1,000	10	1281 ± 170	739 ± 205
	0	10	620 ± 171	321 ± 77
Female	100	5	741 ± 99	289 ± 42
	300	5	551 ± 99	307 ± 34
	1,000	10	605 ± 126	301 ± 74

a) Mean ± S.D.

Table 7. -continued Summary of grip strength

Exp. No. 9934(115-213)

2 week of recovery				Unit : g	
Sex	Dose level (mg/kg)	No. of animals		Fore limb	Hind limb
Male	0	4		1381 ± 408 a)	707 ± 284
	1,000	5		1604 ± 241	574 ± 190
Female	0	5		1080 ± 291	
	1,000	5		889 ± 249	510 ± 269

a) Mean ± S.D.

Table 8. Summary of motor activity

Exp. No. 9934 (115-213)

4 week of administration		Motor activity (counts)							
Sex	Dose level (mg/kg)	No. of animals	0-10 a)	10-20	20-30	30-40	40-50	50-60	Total (0-60)
Male	0	9	194 ± 27 b)	169 ± 25	151 ± 40	129 ± 33	102 ± 40	102 ± 59	847 ± 139
	100	5	195 ± 35	178 ± 15	147 ± 30	127 ± 29	111 ± 57	132 ± 21	890 ± 132
	300	5	216 ± 22	159 ± 27	145 ± 25	111 ± 30	96 ± 58	102 ± 52	829 ± 153
Female	1,000	10	204 ± 17	169 ± 26	157 ± 25	130 ± 35	105 ± 64	74 ± 57	838 ± 146
	0	10	127 ± 28	68 ± 28	72 ± 20	77 ± 33	44 ± 25	58 ± 20	445 ± 114
	100	5	133 ± 22	113 ± 31**	91 ± 35	69 ± 37	87 ± 27*	62 ± 32	554 ± 117
Female	300	5	105 ± 23	102 ± 21*	69 ± 41	74 ± 25	51 ± 15	53 ± 30	455 ± 125
	1,000	10	126 ± 30	101 ± 17*	72 ± 23	74 ± 33	59 ± 32	46 ± 22	478 ± 103

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a) interval time (minutes)

b) Mean ± S.D.

Significantly different from control group * p ≤ 0.05 ** p ≤ 0.01 (Dunnett)

Table 8. -continued Summary of motor activity

Exp. No. 9934 (115-213)

2 week of recovery

Sex	Dose level (mg/kg)	No. of animals	Motor activity (counts)						Total (0-60)
			0-10 a)	10-20	20-30	30-40	40-50	50-60	
Male	0	4	181 ± 38 b)	150 ± 34	128 ± 7	52 ± 45	24 ± 29	11 ± 18	546 ± 89
	1,000	5	183 ± 32	132 ± 68	110 ± 57	115 ± 52	68 ± 49	46 ± 52	653 ± 262
Female	0	5	137 ± 11	126 ± 35	94 ± 27	105 ± 58	108 ± 113	65 ± 68	636 ± 247
	1,000	5	161 ± 58	128 ± 55	106 ± 65	99 ± 70	104 ± 72	55 ± 57	652 ± 355

a) interval time (minutes)

b) Mean ± S.D.

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Table 9-1. Hematology
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	HCT (%)	HGB (g/dL)	RBC ($\times 10^6/\text{mm}^3$)	MCV (μm^3)	MCH (μg)	MCHC (%)
Male	0	5	41.8 ± 1.3	15.5 ± 0.4	7.72 ± 0.13	54.2 ± 1.0	20.1 ± 0.2	37.1 ± 0.6
	100	5	42.0 ± 1.5	15.5 ± 0.6	7.71 ± 0.27	54.5 ± 1.2	20.1 ± 0.5	36.9 ± 0.2
	300	5	40.5 ± 1.6	14.9 ± 0.5	7.31 ± 0.32	55.4 ± 2.4	20.4 ± 0.7	36.7 ± 0.4
	1,000	5	41.3 ± 2.0	15.2 ± 0.8	7.52 ± 0.29	54.9 ± 0.9	20.3 ± 0.4	36.9 ± 0.2
Female	0	5	39.5 ± 1.2	14.8 ± 0.4	7.22 ± 0.24	54.8 ± 0.4	20.5 ± 0.4	37.4 ± 0.5
	100	5	40.7 ± 1.8	15.3 ± 0.7	7.66 ± 0.38	53.2 ± 0.6#	20.0 ± 0.2	37.6 ± 0.4
	300	5	39.5 ± 1.4	14.9 ± 0.3	7.38 ± 0.38	53.6 ± 1.6	20.3 ± 0.8	37.7 ± 0.6
	1,000	5	39.4 ± 1.3	14.5 ± 0.5	7.24 ± 0.28	54.4 ± 1.9	20.0 ± 0.6	36.8 ± 0.3

Mean ± S.D.

Significantly different from control group; #: P ≤ 0.05 (Steel)

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Table 9-1. -continued Hematology
--Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	WBC ($\times 10^3/\text{mm}^3$)	Differential leukocyte counts (%)					EOSN	BASO	LUC
				NEUT	LYMPH	MONO					
Male	0	5	9.26 ± 2.60	15.3 ± 1.8	81.5 ± 1.6	1.8 ± 0.5	0.7 ± 0.3	0.1 ± 0.1	0.6 ± 0.1		
	100	5	8.46 ± 2.65	14.4 ± 3.4	82.4 ± 3.8	1.5 ± 0.4	0.8 ± 0.4	0.1 ± 0.0	0.7 ± 0.3		
	300	5	8.11 ± 1.02	18.3 ± 2.5	79.0 ± 2.9	1.5 ± 0.3	0.7 ± 0.3	0.1 ± 0.0	0.6 ± 0.3		
	1,000	5	9.62 ± 2.25	18.2 ± 3.5	78.5 ± 3.5	1.7 ± 0.2	0.7 ± 0.3	0.1 ± 0.0	0.8 ± 0.4		
Female	0	5	5.21 ± 2.63	14.0 ± 4.2	83.1 ± 4.5	1.1 ± 0.3	0.9 ± 0.4	0.2 ± 0.2	0.7 ± 0.2		
	100	5	5.12 ± 0.82	14.3 ± 2.9	82.6 ± 3.4	1.2 ± 0.3	1.2 ± 0.6	0.1 ± 0.0	0.6 ± 0.1		
	300	5	4.94 ± 1.19	16.9 ± 8.1	80.3 ± 7.9	1.3 ± 0.4	0.8 ± 0.3	0.1 ± 0.0	0.6 ± 0.3		
	1,000	5	8.71 ± 2.92*	14.4 ± 4.3	82.1 ± 4.9	1.3 ± 0.7	1.1 ± 0.4	0.1 ± 0.1	1.0 ± 0.4		

NEUT: Neutrophil LYMPH: Lymphocyte MONO: Monocyte EOSN: Eosinophil BASO: Basophil LUC: Large unstained cells
Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

Table 9-1. -continued Hematology
--Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	NEUT ($\times 10^3/\text{mm}^3$)	LYMPH ($\times 10^3/\text{mm}^3$)	MONO ($\times 10^3/\text{mm}^3$)	EOSN ($\times 10^3/\text{mm}^3$)	BASO ($\times 10^3/\text{mm}^3$)	LUC ($\times 10^3/\text{mm}^3$)
Male	0	5	1.41 ± 0.40	7.56 ± 2.14	0.17 ± 0.09	0.06 ± 0.03	0.01 ± 0.01	0.06 ± 0.02
	100	5	1.21 ± 0.41	6.98 ± 2.25	0.13 ± 0.03	0.07 ± 0.05	0.01 ± 0.01	0.06 ± 0.03
	300	5	1.48 ± 0.28	6.40 ± 0.82	0.12 ± 0.03	0.05 ± 0.03	0.01 ± 0.01	0.05 ± 0.02
	1,000	5	1.75 ± 0.57	7.55 ± 1.79	0.16 ± 0.04	0.07 ± 0.04	0.01 ± 0.01	0.08 ± 0.05
Female	0	5	0.68 ± 0.20	4.38 ± 2.41	0.06 ± 0.02	0.04 ± 0.01	0.01 ± 0.01	0.04 ± 0.03
	100	5	0.72 ± 0.12	4.24 ± 0.80	0.06 ± 0.02	0.06 ± 0.03	0.00 ± 0.00	0.03 ± 0.00
	300	5	0.82 ± 0.38	3.98 ± 1.18	0.06 ± 0.01	0.04 ± 0.01	0.00 ± 0.01	0.03 ± 0.01
	1,000	5	1.29 ± 0.70	7.10 ± 2.11	0.13 ± 0.12	0.09 ± 0.04	0.01 ± 0.01	0.09 ± 0.07

NEUT: Neutrophil LYMPH: Lymphocyte MONO: Monocyte EOSN: Eosinophil BASO: Basophil LUC: Large unstained cells
Mean ± S.D.

Table 9-1. -continued Hematology
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	PLT ($\times 10^3/\text{mm}^3$)	Reticulocyte (%)
Male	0	5	1153 ± 164	2.7 ± 0.5
	100	5	1135 ± 178	2.7 ± 0.5
	300	5	1218 ± 58	3.0 ± 0.1
	1,000	5	1169 ± 178	3.0 ± 0.4
Female	0	5	1382 ± 185	2.6 ± 0.8
	100	5	1284 ± 136	2.2 ± 0.3
	300	5	1226 ± 152	2.4 ± 0.3
	1,000	5	1264 ± 190	3.2 ± 0.7

Mean ± S.D.

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Table 9-2. Hematology
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	HCT (%)	HGB (g/dL)	RBC ($\times 10^6/\text{mm}^3$)	MCV (μm^3)	MCH (pg)	MCHC (%)
Male	0	4	42.7 ± 2.0	15.6 ± 0.6	8.06 ± 0.19	52.9 ± 1.5	19.4 ± 0.4	36.5 ± 0.3
	1,000	5	42.2 ± 1.6	15.3 ± 0.7	8.03 ± 0.54	52.6 ± 2.2	19.1 ± 0.7	36.3 ± 0.5
Female	0	5	41.9 ± 2.6	15.7 ± 1.0	7.91 ± 0.42	53.0 ± 1.4	19.9 ± 0.3	37.5 ± 0.8
	1,000	5	40.3 ± 2.4	15.0 ± 0.8	7.62 ± 0.58	52.9 ± 1.7	19.7 ± 0.7	37.3 ± 0.4

Mean ± S.D.

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Table 9-2. -continued Hematology
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	WBC ($\times 10^3/\text{mm}^3$)	Differential leukocyte counts (%)					EOSN	BASO	LUC
				NEUT	LYMPH	MONO					
Male	0	4	10.00 ± 2.46	16.7 ± 3.6	79.8 ± 3.7	1.8 ± 0.2	1.0 ± 0.5	0.1 ± 0.0	0.6 ± 0.1		
	1,000	5	10.20 ± 2.74	11.9 ± 4.7	84.4 ± 5.2	1.9 ± 0.6	1.0 ± 0.4	0.2 ± 0.1	0.6 ± 0.1		
Female	0	5	6.69 ± 2.02	19.4 ± 7.4	77.4 ± 6.9	1.7 ± 0.4	1.0 ± 0.3	0.1 ± 0.0	0.6 ± 0.2		
	1,000	5	5.81 ± 2.87	16.3 ± 5.8	79.7 ± 6.2	1.8 ± 0.4	1.6 ± 0.7	0.0 ± 0.1	0.6 ± 0.2		

NEUT: Neutrophil LYMPH: Lymphocyte MONO: Monocyte EOSN: Eosinophil BASO: Basophil LUC: Large unstained cells
Mean ± S.D.

Table 9-2. -continued Hematology
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	NEUT	LYMPH	MONO	EOSN	BASO	LUC
			($\times 10^3/\text{mm}^3$)					
Male	0	4	1.62 ± 0.28	8.03 ± 2.17	0.18 ± 0.06	0.10 ± 0.06	0.01 ± 0.00	0.06 ± 0.02
	1,000	5	1.15 ± 0.25*	8.69 ± 2.66	0.18 ± 0.03	0.10 ± 0.06	0.02 ± 0.01	0.06 ± 0.02
Female	0	5	1.33 ± 0.83	5.14 ± 1.38	0.11 ± 0.04	0.06 ± 0.03	0.00 ± 0.01	0.04 ± 0.02
	1,000	5	0.92 ± 0.45	4.66 ± 2.53	0.10 ± 0.03	0.08 ± 0.03	0.00 ± 0.00	0.04 ± 0.04

NEUT: Neutrophil LYMPH: Lymphocyte MONO: Monocyte EOSN: Eosinophil BASO: Basophil LUC: Large unstained cells
Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

Table 9-2. -continued Hematology
---Recovery Period---

Sex	Dose level (mg/kg)	No. of animals	PLT ($\times 10^3/\mu\text{m}^3$)	Reticulocyte (%)
Male	0	4	1169 ± 192	2.4 ± 0.2
	1,000	5	1047 ± 74	2.6 ± 0.5
Female	0	5	1276 ± 142	2.0 ± 0.5
	1,000	5	1173 ± 112	2.9 ± 0.5*

Mean ± S.D.

*Significantly different from control group; *: $P \leq 0.05$ (Dunnett)

Exp. No. 9934 (115-213)

Table 10-1. Coagulation
---Administration period---

Sex	Dose level (mg/kg)	No. of animals	PT (sec.)	APTT (sec.)
Male	0	5	19.1 ± 0.6	23.9 ± 1.7
	100	5	20.7 ± 3.5	24.9 ± 2.0
	300	5	19.9 ± 1.5	24.0 ± 2.1
	1,000	5	20.4 ± 1.0	25.2 ± 3.7
Female	0	5	17.3 ± 0.9	17.8 ± 2.6
	100	5	17.3 ± 0.8	18.4 ± 0.6
	300	5	17.6 ± 0.9	19.1 ± 1.8
	1,000	5	16.6 ± 0.4	18.7 ± 1.3

Mean ± S.D.

Table 10-2. Coagulation
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	PT (sec.)	APTT (sec.)
Male	0	4	19.4 ± 1.5	24.1 ± 1.7
	1,000	5	21.5 ± 1.4	25.1 ± 2.4
Female	0	5	17.9 ± 0.5	17.9 ± 1.0
	1,000	5	16.9 ± 0.4**	18.6 ± 0.7

Mean ± S.D.
Significantly different from control group; **: P ≤ 0.01 (Dunnett)

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Table 11-1. Blood chemistry
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	T.protein (g/dL)	Glucose (mg/dL)	Triglyceride (mg/dL)	T.cholesterol (mg/dL)
Male	0	5	5.77 ± 0.16	145 ± 16	28.5 ± 16.7	61 ± 10
	100	5	5.62 ± 0.13	163 ± 19	51.0 ± 29.9	61 ± 12
	300	5	5.46 ± 0.15*	148 ± 24	43.5 ± 13.6	57 ± 6
	1,000	5	5.50 ± 0.21*	161 ± 26	51.4 ± 20.7	59 ± 8
Female	0	5	5.93 ± 0.31	115 ± 21	8.5 ± 5.1	63 ± 14
	100	5	5.84 ± 0.20	125 ± 19	17.2 ± 5.5	75 ± 7
	300	5	5.96 ± 0.13	118 ± 13	13.0 ± 6.5	66 ± 6
	1,000	5	5.89 ± 0.26	141 ± 25	20.1 ± 7.3*	71 ± 11

Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

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Table 11-1. -continued Blood chemistry
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	BUN (mg/dL)	Creatinine (mg/dL)	T.bilirubin (mg/dL)	Total bile acid (μ mol/L)
Male	0	5	12.5 ± 0.7	0.21 ± 0.02	0.04 ± 0.01	42.3 ± 23.9
	100	5	12.1 ± 1.2	0.22 ± 0.03	0.03 ± 0.01	13.4 ± 5.0
	300	5	11.6 ± 1.2	0.22 ± 0.00	0.03 ± 0.01	10.8 ± 4.6
	1,000	5	13.2 ± 2.4	0.21 ± 0.02	0.03 ± 0.01	19.4 ± 15.8
Female	0	5	15.5 ± 1.7	0.27 ± 0.03	0.03 ± 0.01	16.8 ± 4.1
	100	5	13.3 ± 1.1	0.23 ± 0.03	0.03 ± 0.01	11.8 ± 7.8
	300	5	15.7 ± 2.0	0.25 ± 0.01	0.04 ± 0.01	13.2 ± 5.8
	1,000	5	14.5 ± 1.6	0.24 ± 0.02	0.04 ± 0.01	8.8 ± 1.6

Mean ± S.D.

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Table 11-1. -continued Blood chemistry
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	AST (U/L)	ALT (U/L)	ALP (U/L)	Gamma-GTP (U/L)
Male	0	5	82 ± 3	29 ± 6	860 ± 126	0.4 ± 0.1
	100	5	83 ± 7	31 ± 5	818 ± 84	0.3 ± 0.1
	300	5	78 ± 9	29 ± 3	762 ± 131	0.3 ± 0.1
	1,000	5	85 ± 10	31 ± 5	804 ± 172	0.4 ± 0.1
Female	0	5	84 ± 13	24 ± 7	409 ± 75	0.7 ± 0.1
	100	5	95 ± 15	22 ± 3	384 ± 40	0.8 ± 0.4
	300	5	88 ± 12	23 ± 6	397 ± 50	0.8 ± 0.1
	1,000	5	71 ± 10	21 ± 3	427 ± 108	0.8 ± 0.2

Mean ± S.D.

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Table 11-1. -continued Blood chemistry
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Calcium (mg/dL)	T.phosphorus (mg/dL)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)
Male	0	5	9.84 ± 0.14	8.27 ± 0.60	143.4 ± 0.5	4.48 ± 0.17	106.6 ± 0.7
	100	5	9.92 ± 0.21	8.75 ± 0.38	144.2 ± 0.3#	4.89 ± 0.17*	108.5 ± 0.2†
	300	5	9.78 ± 0.40	8.69 ± 0.43	143.9 ± 1.5	4.46 ± 0.17	107.2 ± 1.3
	1,000	5	9.65 ± 0.33	9.03 ± 0.68	142.5 ± 0.8	5.04 ± 0.28**	107.2 ± 1.4
Female	0	5	9.78 ± 0.36	7.84 ± 0.64	144.0 ± 1.3	4.46 ± 0.12	109.3 ± 1.3
	100	5	9.66 ± 0.20	7.86 ± 0.48	142.7 ± 1.0	4.36 ± 0.27	108.4 ± 1.8
	300	5	9.75 ± 0.34	7.95 ± 0.61	143.6 ± 0.3	4.26 ± 0.22	108.9 ± 1.8
	1,000	5	9.95 ± 0.12	8.34 ± 0.87	143.7 ± 1.1	4.28 ± 0.29	107.9 ± 1.5

Mean ± S.D.

Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)
Significantly different from control group; #: P ≤ 0.05 (Steel)Table 11-2. Blood chemistry
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	T.protein (g/dL)	Glucose (mg/dL)	Triglyceride (mg/dL)	T.cholesterol (mg/dL)
Male	0	4	5.55 ± 0.28	149 ± 19	39.3 ± 7.6	55 ± 16
	1,000	5	5.53 ± 0.11	156 ± 18	50.3 ± 21.8	58 ± 11
Female	0	5	5.85 ± 0.15	115 ± 10	11.4 ± 3.0	61 ± 14
	1,000	5	5.95 ± 0.26	129 ± 22	12.4 ± 4.7	65 ± 9

Mean ± S.D.

Table 11-2. -continued Blood chemistry
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	BUN (mg/dL)	Creatinine (mg/dL)	T.bilirubin (mg/dL)	Total bile acid (μ mol/L)
Male	0	4	11.5 ± 1.1	0.27 ± 0.02	0.04 ± 0.02	23.2 ± 21.4
	1,000	5	11.6 ± 1.4	0.26 ± 0.04	0.03 ± 0.01	20.9 ± 14.3
Female	0	5	15.6 ± 1.2	0.30 ± 0.03	0.05 ± 0.01	18.7 ± 20.2
	1,000	5	15.6 ± 2.6	0.27 ± 0.04	0.05 ± 0.01	16.4 ± 6.3

Mean ± S.D.

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Table 11-2. -continued Blood chemistry
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	AST (U/L)	ALT (U/L)	ALP (U/L)	Gamma-GTP (U/L)
Male	0	4	96 ± 15	31 ± 3	486 ± 70	0.4 ± 0.1
	1,000	5	84 ± 6	30 ± 4	565 ± 76	0.4 ± 0.1
Female	0	5	86 ± 20	25 ± 3	358 ± 79	0.9 ± 0.4
	1,000	5	78 ± 10	25 ± 2	375 ± 31	0.9 ± 0.2

Mean ± S.D.

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Table 11-2. -continued Blood chemistry
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Calcium (mg/dL)	Inorganic phosphorus (mg/dL)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)
Male	0	4	9.67 ± 0.32	7.58 ± 0.26	142.6 ± 1.3	4.73 ± 0.22	106.2 ± 1.0
	1,000	5	9.86 ± 0.25	7.71 ± 0.45	143.3 ± 0.6	4.60 ± 0.52	106.1 ± 0.9
Female	0	5	9.74 ± 0.24	7.52 ± 1.02	142.1 ± 1.2	4.55 ± 0.30	107.4 ± 1.6
	1,000	5	9.80 ± 0.30	6.84 ± 0.78	142.8 ± 1.9	4.33 ± 0.25	107.8 ± 1.5

Mean ± S.D.

Table 12-1. Electrophoresis
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Albumin (%)	Alpha-1 (%)	Alpha-2 (%)	Beta (%)	Gamma (%)	A/G
Male	0	5	50.6 ± 1.7	22.7 ± 1.4	7.9 ± 0.6	14.8 ± 0.7	4.1 ± 0.5	1.02 ± 0.07
	100	5	51.4 ± 3.2	21.0 ± 0.8	8.4 ± 0.9	15.5 ± 1.4	3.7 ± 0.7	1.07 ± 0.15
	300	5	52.6 ± 2.3	19.4 ± 2.5*	7.9 ± 0.6	15.5 ± 0.5	4.6 ± 0.2	1.12 ± 0.10
	1,000	5	52.9 ± 1.4	18.4 ± 2.0**	8.4 ± 0.6	15.5 ± 1.6	4.8 ± 0.7	1.12 ± 0.07
Female	0	5	52.7 ± 1.6	19.6 ± 2.2	7.5 ± 0.7	15.1 ± 0.5	5.2 ± 1.0	1.12 ± 0.07
	100	5	54.7 ± 3.4	18.4 ± 1.5	7.9 ± 0.3	14.9 ± 1.3	4.0 ± 1.1	1.22 ± 0.18
	300	5	54.1 ± 0.8	17.0 ± 0.8	8.8 ± 0.7**	15.3 ± 1.1	4.8 ± 0.9	1.18 ± 0.04
	1,000	5	55.0 ± 2.3	17.3 ± 1.6	8.1 ± 0.6	15.1 ± 1.3	4.5 ± 1.4	1.23 ± 0.12

Mean ± S.D.

Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)

Table 12-1. -continued Electrophoresis
--Administration Period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Albumin (g/dL)	Alpha-1 (g/dL)	Alpha-2 (g/dL)	Beta (g/dL)	Gamma (g/dL)
Male	0	5	2.92 ± 0.17	1.31 ± 0.06	0.46 ± 0.04	0.85 ± 0.04	0.23 ± 0.03
	100	5	2.89 ± 0.18	1.18 ± 0.06	0.47 ± 0.05	0.87 ± 0.09	0.21 ± 0.03
	300	5	2.87 ± 0.08	1.06 ± 0.16*	0.43 ± 0.03	0.84 ± 0.03	0.25 ± 0.02
	1,000	5	2.91 ± 0.08	1.02 ± 0.15**	0.46 ± 0.04	0.85 ± 0.06	0.26 ± 0.04
Female	0	5	3.12 ± 0.12	1.17 ± 0.20	0.44 ± 0.04	0.89 ± 0.02	0.30 ± 0.06
	100	5	3.20 ± 0.26	1.07 ± 0.09	0.46 ± 0.01	0.87 ± 0.07	0.23 ± 0.07
	300	5	3.22 ± 0.10	1.01 ± 0.03	0.52 ± 0.03**	0.91 ± 0.08	0.29 ± 0.06
	1,000	5	3.24 ± 0.23	1.02 ± 0.13	0.48 ± 0.04	0.89 ± 0.05	0.26 ± 0.07

Mean ± S.D. Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)

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Table 12-2. --Electrophoresis
--Recovery Period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Albumin (%)	Alpha-1 (%)	Alpha-2 (%)	Beta (%)	Gamma (%)	A/G
Male	0	4	48.7 ± 2.9	22.7 ± 3.6	8.0 ± 0.9	16.3 ± 0.9	4.3 ± 0.7	0.95 ± 0.11
	1,000	5	49.7 ± 2.7	21.9 ± 2.1	8.4 ± 1.0	15.9 ± 0.9	4.2 ± 1.3	0.99 ± 0.11
Female	0	5	51.3 ± 1.7	19.8 ± 1.0	7.6 ± 0.3	15.0 ± 0.6	6.3 ± 1.1	1.06 ± 0.07
	1,000	5	51.3 ± 2.4	19.0 ± 1.4	8.3 ± 0.7	15.9 ± 1.0	5.6 ± 1.3	1.05 ± 0.10

Mean ± S.D.

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Table 12-2. -continued Electrophoresis
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Albumin (g/dL)	Alpha-1 (g/dL)	Alpha-2 (g/dL)	Beta (g/dL)	Gamma (g/dL)
Male	0	4	2.70 ± 0.14	1.27 ± 0.24	0.45 ± 0.03	0.91 ± 0.04	0.24 ± 0.05
	1,000	5	2.75 ± 0.12	1.21 ± 0.12	0.46 ± 0.06	0.88 ± 0.07	0.23 ± 0.08
Female	0	5	3.00 ± 0.06	1.16 ± 0.09	0.45 ± 0.02	0.88 ± 0.04	0.37 ± 0.07
	1,000	5	3.05 ± 0.18	1.13 ± 0.13	0.49 ± 0.02**	0.95 ± 0.06	0.33 ± 0.08

Mean ± S.D.
Significantly different from control group; **: P ≤ 0.01 (Dunnett)

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Table 13-1. Urinalysis
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Volume (mL)	Osmotic pressure (mOsm/kg)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)
Male	0	10	12.1 ± 4.1	1550 ± 532	122 ± 49	254.8 ± 94.5	170.0 ± 68.7
	100	5	16.8 ± 13.1	1469 ± 477	120 ± 40	233.2 ± 75.5	161.5 ± 57.2
	300	5	17.1 ± 7.5	1321 ± 425	116 ± 40	216.1 ± 70.1	142.1 ± 50.8
	1,000	10	11.1 ± 2.1	1571 ± 355	128 ± 26	252.2 ± 58.0	170.6 ± 41.4
Female	0	10	15.8 ± 7.1	1205 ± 385	99 ± 33	187.5 ± 61.5	127.7 ± 43.3
	100	5	10.9 ± 4.2	1378 ± 515	109 ± 47	214.2 ± 78.4	145.0 ± 59.3
	300	5	10.3 ± 3.9	1692 ± 516	119 ± 41	251.8 ± 67.6	168.6 ± 57.7
	1,000	10	11.2 ± 3.3	1388 ± 347	115 ± 26	212.3 ± 59.0	145.6 ± 35.8

Mean ± S.D.

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Table 13-1. -continued Urinalysis
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Sodium (mmol/day)	Potassium (mmol/day)	Chloride (mmol/day)
Male	0	10	1.34 ± 0.37	2.76 ± 0.40	1.84 ± 0.35
	100	5	1.61 ± 0.42	3.16 ± 0.89	2.15 ± 0.55
	300	5	1.78 ± 0.33	3.31 ± 0.39	2.18 ± 0.41
	1,000	10	1.39 ± 0.12	2.72 ± 0.29	1.83 ± 0.15
Female	0	10	1.39 ± 0.16	2.63 ± 0.34	1.79 ± 0.23
	100	5	1.04 ± 0.14**	2.09 ± 0.26*	1.39 ± 0.12**
	300	5	1.10 ± 0.16**	2.38 ± 0.39	1.56 ± 0.21
	1,000	10	1.23 ± 0.16	2.24 ± 0.35*	1.54 ± 0.20*

Mean ± S.D.

Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)

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Table 13-1. -continued Urinalysis
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Color	pH											Occult blood													
				1	2	3	4	5	6	7	8	9	10	11	5	5.5	6	6.5	7	7.5	8	8.5	≥ 9	-	+/-	1+	2+	3+
Male	0	10	9 1												1	2	7							9	1			
	100	5	5												2	1	2							5				
	300	5	5												1	1	3							4	1			
	1,000	10	10												1	1	2	6						9	1			
Female	0	10	10												1	2	1	5	1					8	2			
	100	5	5												1	2	2							4	1			
	300	5	4 1												1	1	3							3	2			
	1,000	10	10												1	3	6							10				

Color : 1= Colorless, 2= Slight yellow, 3= Yellow-brown, 4= Red, 5= Red-brown, 6= Dark red, 7= Dark brown,
8= Brown-black, 9= Milky white, 10= Fluorescent green, 11= Blue

Occult blood : -(negative), +/- (trace), 1+ (slight), 2+ (moderate), 3+ (marked)

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Table 13-1. -continued Urinalysis
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Ketone bodies					Glucose (g/dL)					Protein (mg/dL)				
			-	+-	1+	2+	3+	-	0.1	0.25	0.5	≥ 1.0	-	+-	30	100	≥ 300
Male	0	10	7	2	1			9	1				2	4	3	1	
	100	5	4		1			5					4		1		
	300	5	4	1				5					1	2	2		
	1,000	10	8	1	1			10					1	8		1	
Female	0	10	10					10					8	2			
	100	5	5					5					3	2			
	300	5	3	2				4	1				1	2	1	1	
	1,000	10	10					10					6	3	1		

Ketone bodies : -(negative), +/-(5 mg/dL), 1+(15 mg/dL), 2+(40 mg/dL), 3+(≥ 80 mg/dL)

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Table 13-1. -continued Urinalysis
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Bilirubin			Urobilinogen (E.U./dL)						
			-	1+	2+	3+	0.1	1.0	2.0	4.0	8.0	≥ 12
Male	0	10	9	1			9	1				
	100	5	5				5					
	300	5	5				5					
	1,000	10	10				10					
Female	0	10	10				10					
	100	5	5				5					
	300	5	4	1			4	1				
	1,000	10	10				10					

Bilirubin : -(negative), 1+(slight), 2+(moderate), 3+(marked)

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Table 13-1. -continued Urinalysis : Microscopic examination of sediment
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Erythrocytes - 1+ 2+ 3+	Leukocytes - 1+ 2+ 3+	Epithelial cells - 1+ 2+ 3+	Casts - +	Fat globules - +	Mucous threads - +	Crystals - +
Male	0	10	10	10	10	10	10	10	10
	100	5	5	5	5	5	5	5	5
	300	5	5	5	5	5	5	4 1	5
	1,000	10	10	10	10	10	10	10	4 6
Female	0	10	10	10	10	10	10	10	2 8
	100	5	5	5	4 1	5	5	5	5
	300	5	5	5	5	5	5	5	5
	1,000	10	10	10	10	10	10	10	10

Erythrocytes, Leukocytes and Epithelial cells (cells/ μ L) : ~ (0-4), 1+ (5-14), 2+ (15-29), 3+ (30 or more)
Casts, Fat globules, Mucous threads and Crystals : - (not observed), + (observed)

Table 13-2. Urinalysis
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Volume (mL)	Osmotic pressure (mOsm/kg)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)
Male	0	4	10.1 ± 1.7	2102 ± 146	179 ± 5	316.1 ± 25.0	232.4 ± 17.4
	1,000	5	13.3 ± 3.6	1611 ± 374*	128 ± 24#	243.1 ± 48.9*	164.1 ± 31.0**
Female	0	5	13.8 ± 5.0	1552 ± 480	122 ± 46	221.6 ± 66.1	151.4 ± 52.2
	1,000	5	14.2 ± 6.9	1536 ± 611	119 ± 51	223.6 ± 88.5	155.6 ± 66.3

Mean ± S.D.

Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)

Significantly different from control group; #: P ≤ 0.05 (Steel)

Table 13-2. -continued Urinalysis
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Sodium (mmol/day)	Potassium (mmol/day)	Chloride (mmol/day)
Male	0	4	1.81 ± 0.29	3.18 ± 0.43	2.34 ± 0.29
	1,000	5	1.63 ± 0.20	3.11 ± 0.43	2.10 ± 0.29
Female	0	5	1.51 ± 0.05	2.81 ± 0.25	1.89 ± 0.13
	1,000	5	1.43 ± 0.19	2.73 ± 0.43	1.87 ± 0.22

Mean ± S.D.

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Table 13-2. -continued Urinalysis
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Color	pH									Occult blood															
				1	2	3	4	5	6	7	8	9	10	11	5	5.5	6	6.5	7	7.5	8	8.5	≥ 9	-	+/-	1+	2+	3+
Male	0	4	4													1	3							4				
	1,000	5	5														5							5				
Female	0	5	5														2	3						5				
	1,000	5	5														1	4						4	1			

Color : 1= Colorless, 2= Slight yellow, 3= Yellow-brown, 4= Red, 5= Red-brown, 6= Dark red, 7= Dark brown,
8= Brown-black, 9= Milky white, 10= Fluorescent green, 11= Blue

Occult blood : -(negative), +/-(trace), 1+(slight), 2+(moderate), 3+(marked)

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Table 13-2. -continued Urinalysis
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Ketone bodies				Glucose (g/dL)				Protein (mg/dL)						
			-	+/-	1+	2+	3+	-	0.1	0.25	0.5	≥ 1.0	-	+/-	30	100	≥ 300
Male	0	4		1	3			3	1				1	1	2		
	1,000	5		1	2	2		5					1	2	2		
Female	0	5		1	4			4	1				1	2	2		
	1,000	5		1	4			5					1	2	2		

Ketone bodies : -(negative), +/-(5 mg/dL), 1+(15 mg/dL), 2+(40 mg/dL), 3+(≥ 80 mg/dL)

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Table 13-2. -continued Urinalysis
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Bilirubin				Urobilinogen (E.U./dL)					
			-	1+	2+	3+	0.1	1.0	2.0	4.0	8.0	≥ 12
Male	0	4		4			3	1				
	1,000	5		4	1		3	2				
Female	0	5		5			2	3				
	1,000	5		5			1	4				

Bilirubin : -(negative), 1+(slight), 2+(moderate), 3+(marked)

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Table 13-2. -continued Urinalysis : Microscopic examination of sediment
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Erythrocytes - 1+ 2+ 3+	Leukocytes - 1+ 2+ 3+	Epithelial cells - 1+ 2+ 3+	Casts - +	Fat globules - +	Mucous threads - +	Crystals - +
Male	0	4	4	4	4	4	4	4	4
	1,000	5	5	5	5	5	5	5	5
Female	0	5	5	5	5	5	5	5	5
	1,000	5	5	5	5	5	5	5	5

Erythrocytes, Leukocytes and Epithelial cells (cells/ μ L) : -(0-4), 1+(5-14), 2+(15-29), 3+(30 or more)
Casts, Fat globules, Mucous threads and Crystals : -(not observed), +(observed)

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Table 14-1. Organ weight
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (g)	Heart (g)	Liver (g)	Kidneys (g)
Male	0	5	283 ± 30	2.12 ± 0.03	1.03 ± 0.10	8.56 ± 1.05	2.34 ± 0.15
	100	5	293 ± 35	2.08 ± 0.08	1.07 ± 0.11	9.48 ± 1.97	2.40 ± 0.23
	300	5	306 ± 23	2.12 ± 0.08	1.10 ± 0.07	9.76 ± 0.80	2.59 ± 0.11
	1,000	5	272 ± 22	2.00 ± 0.09	1.00 ± 0.11	8.64 ± 1.30	2.35 ± 0.32
Female	0	5	189 ± 8	1.96 ± 0.06	0.72 ± 0.04	5.85 ± 0.29	1.62 ± 0.15
	100	5	182 ± 14	1.88 ± 0.08	0.69 ± 0.06	5.63 ± 0.64	1.46 ± 0.17
	300	5	181 ± 24	1.90 ± 0.05	0.70 ± 0.07	5.75 ± 0.52	1.58 ± 0.16
	1,000	5	186 ± 6	1.88 ± 0.10	0.73 ± 0.07	6.42 ± 0.63	1.57 ± 0.06

Mean ± S.D.

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Table 14-1. -continued Organ weight
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Spleen (g)	Adrenals (mg)	Testes (g)	Ovaries (mg)	Thyroid (mg)
Male	0	5	0.53 ± 0.09	47 ± 6	2.79 ± 0.26		20 ± 3
	100	5	0.55 ± 0.10	45 ± 6	3.03 ± 0.19		17 ± 2
	300	5	0.60 ± 0.12	54 ± 7	2.98 ± 0.15		22 ± 5
	1,000	5	0.53 ± 0.09	48 ± 5	2.82 ± 0.20		20 ± 6
Female	0	5	0.46 ± 0.07	60 ± 8		80 ± 4	15 ± 4
	100	5	0.35 ± 0.04*	62 ± 8		64 ± 10**	15 ± 2
	300	5	0.36 ± 0.05*	64 ± 7		79 ± 5	14 ± 2
	1,000	5	0.43 ± 0.06	64 ± 10		73 ± 7	15 ± 4

Mean ± S.D.

Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)

Table 14-1. -continued Organ weight
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Pituitary (mg)	Thymus (mg)	Epididymides (mg)	Mandibular gland (mg)
Male	0	5	8 ± 2	513 ± 101	625 ± 80	516 ± 68
	100	5	8 ± 1	484 ± 69	658 ± 39	532 ± 107
	300	5	10 ± 1	540 ± 81	654 ± 35	525 ± 34
	1,000	5	8 ± 3	483 ± 122	603 ± 62	500 ± 29
Female	0	5	12 ± 2	452 ± 85		369 ± 27
	100	5	10 ± 1	463 ± 35		353 ± 39
	300	5	9 ± 2	432 ± 101		370 ± 18
	1,000	5	10 ± 4	406 ± 63		377 ± 43

Mean ± S.D.

Table 14-2. Organ weight
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (g)	Heart (g)	Liver (g)	Kidneys (g)
Male	0	4	379 ± 30	2.16 ± 0.09	1.28 ± 0.07	11.09 ± 0.86	2.79 ± 0.15
	1,000	5	346 ± 20	2.11 ± 0.08	1.21 ± 0.11	10.02 ± 0.97	2.64 ± 0.18
Female	0	5	225 ± 9	1.99 ± 0.08	0.81 ± 0.04	6.31 ± 0.47	1.71 ± 0.04
	1,000	5	206 ± 14*	1.97 ± 0.10	0.81 ± 0.07	6.26 ± 0.96	1.70 ± 0.27

Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

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Table 14-2. -continued Organ weight
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Spleen (g)	Adrenals (mg)	Testes (g)	Ovaries (mg)	Thyroid (mg)
Male	0	4	0.66 ± 0.11	56 ± 2	3.37 ± 0.42		19 ± 4
	1,000	5	0.65 ± 0.15	51 ± 8	3.17 ± 0.11		20 ± 4
Female	0	5	0.50 ± 0.07	65 ± 4		75 ± 12	14 ± 1
	1,000	5	0.47 ± 0.14	66 ± 9		86 ± 13	14 ± 1

Mean ± S.D.

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Table 14-2. -continued Organ weight
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Pituitary (mg)	Thymus (mg)	Epididymides (mg)	Mandibular gland (mg)
Male	0	4	11 ± 2	397 ± 11	964 ± 54	619 ± 38
	1,000	5	9 ± 2	484 ± 134	944 ± 35	589 ± 37
Female	0	5	13 ± 2	436 ± 66		448 ± 50
	1,000	5	13 ± 4	447 ± 90		409 ± 46

Mean ± S.D.

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Table 15-1. Organ weight per body weight
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (%)	Heart (%)	Liver (%)	Kidneys (%)
Male	0	5	283 ± 30	0.754 ± 0.073	0.366 ± 0.010	3.025 ± 0.108	0.831 ± 0.048
	100	5	293 ± 35	0.721 ± 0.112	0.366 ± 0.025	3.215 ± 0.323	0.824 ± 0.071
	300	5	306 ± 23	0.695 ± 0.053	0.360 ± 0.011	3.186 ± 0.079	0.849 ± 0.039
	1,000	5	272 ± 22	0.737 ± 0.040	0.365 ± 0.017	3.161 ± 0.244	0.861 ± 0.073
Female	0	5	189 ± 8	1.037 ± 0.059	0.381 ± 0.018	3.097 ± 0.093	0.855 ± 0.058
	100	5	182 ± 14	1.037 ± 0.087	0.378 ± 0.011	3.081 ± 0.139	0.798 ± 0.054
	300	5	181 ± 24	1.061 ± 0.149	0.389 ± 0.023	3.194 ± 0.265	0.878 ± 0.102
	1,000	5	186 ± 6	1.010 ± 0.064	0.395 ± 0.032	3.446 ± 0.252*	0.843 ± 0.022

Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

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Table 15-1. -continued Organ weight per body weight
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Spleen (%)	Adrenals (%)	Testes (%)	Ovaries (%)	Thyroid (%)
Male	0	5	0.188 ± 0.024	0.017 ± 0.001	0.998 ± 0.155		0.007 ± 0.001
	100	5	0.187 ± 0.015	0.016 ± 0.002	1.046 ± 0.118		0.006 ± 0.000
	300	5	0.195 ± 0.029	0.018 ± 0.001	0.977 ± 0.065		0.007 ± 0.002
	1,000	5	0.194 ± 0.027	0.018 ± 0.002	1.038 ± 0.073		0.007 ± 0.002
Female	0	5	0.240 ± 0.029	0.032 ± 0.004		0.042 ± 0.002	0.008 ± 0.002
	100	5	0.192 ± 0.007**	0.034 ± 0.004		0.035 ± 0.007	0.008 ± 0.001
	300	5	0.202 ± 0.024*	0.036 ± 0.006		0.044 ± 0.009	0.008 ± 0.002
	1,000	5	0.229 ± 0.023	0.034 ± 0.005		0.039 ± 0.003	0.008 ± 0.002

Mean ± S.D.

Significantly different from control group; *: P ≤ 0.05 **: P ≤ 0.01 (Dunnett)

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Table 15-1. -continued Organ weight per body weight
---Administration period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Pituitary (%)	Thymus (%)	Epididymides (%)	Mandibular gland (%)
Male	0	5	0.003 ± 0.001	0.180 ± 0.021	0.224 ± 0.040	0.182 ± 0.011
	100	5	0.003 ± 0.000	0.165 ± 0.014	0.227 ± 0.024	0.181 ± 0.020
	300	5	0.003 ± 0.000	0.177 ± 0.026	0.214 ± 0.014	0.172 ± 0.009
	1,000	5	0.003 ± 0.001	0.177 ± 0.038	0.222 ± 0.021	0.184 ± 0.014
Female	0	5	0.006 ± 0.001	0.239 ± 0.041		0.195 ± 0.011
	100	5	0.006 ± 0.001	0.255 ± 0.030		0.193 ± 0.009
	300	5	0.005 ± 0.001	0.237 ± 0.038		0.206 ± 0.023
	1,000	5	0.006 ± 0.002	0.219 ± 0.039		0.202 ± 0.019

Mean ± S.D.

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Table 15-2. Organ weight per body weight
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (%)	Heart (%)	Liver (%)	Kidneys (%)
Male	0	4	379 ± 30	0.571 ± 0.035	0.338 ± 0.013	2.930 ± 0.111	0.739 ± 0.052
	1,000	5	346 ± 20	0.611 ± 0.029	0.352 ± 0.041	2.898 ± 0.193	0.766 ± 0.073
Female	0	5	225 ± 9	0.889 ± 0.074	0.359 ± 0.018	2.809 ± 0.167	0.761 ± 0.045
	1,000	5	206 ± 14*	0.958 ± 0.057	0.393 ± 0.024*	3.018 ± 0.280	0.823 ± 0.101

Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

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Table 15-2. -continued Organ weight per body weight
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Spleen (%)	Adrenals (%)	Testes (%)	Ovaries (%)	Thyroid (%)
Male	0	4	0.174 ± 0.026	0.015 ± 0.001	0.888 ± 0.063		0.005 ± 0.001
	1,000	5	0.189 ± 0.038	0.015 ± 0.002	0.921 ± 0.078		0.006 ± 0.001
Female	0	5	0.225 ± 0.036	0.029 ± 0.001		0.034 ± 0.004	0.006 ± 0.000
	1,000	5	0.225 ± 0.054	0.032 ± 0.004		0.042 ± 0.005*	0.007 ± 0.000

Mean ± S.D.
Significantly different from control group; *: P ≤ 0.05 (Dunnett)

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Table 15-2. -continued Organ weight per body weight
---Recovery period---

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	Pituitary (%)	Thymus (%)	Epididymides (%)	Mandibular gland (%)
Male	0	4	0.003 ± 0.001	0.105 ± 0.008	0.255 ± 0.012	0.164 ± 0.009
	1,000	5	0.003 ± 0.000	0.140 ± 0.041	0.274 ± 0.024	0.171 ± 0.015
Female	0	5	0.006 ± 0.001	0.194 ± 0.030		0.200 ± 0.023
	1,000	5	0.006 ± 0.002	0.215 ± 0.031		0.198 ± 0.014

Mean ± S.D.

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Table 16-1.

Summary of gross findings with statistical analysis
(sacrificed, administration period)

Exp. No. 9934 (115-213)

Dose level (mg/kg)	No. of animals necropsied	Organ	Male animals					Female animals					
			0	100	300	1,000	5	5	5	5	100	300	1,000
RESPIRATORY SYSTEM													
Lung	brown patch/zone		1	0	0	0		0	0	0	0	0	0
DIGESTIVE SYSTEM													
stomach	white patch/zone		0	1	0	0		0	0	0	0	0	0
liver	hepatodiaphragmatic nodule		0	0	0	0		0	0	1	0	0	0
	white patch/zone		0	0	0	1		0	0	0	0	0	0
URINARY SYSTEM													
kidney	cyst		0	0	1	0		0	1	0	0	0	0
	scarred		1	1	0	0		1	2	1	1	1	1
REPRODUCTIVE SYSTEM													
uterus	cyst		-	-	-	-		0	1	0	0	0	2
	dilated lumen		-	-	-	-		2	2	0	0	2	2
ENDOCRINE SYSTEM													
thyroid gland	nodule		0	0	0	0		0	1	0	0	0	0

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Table 16-2.

Summary of gross findings with statistical analysis
(sacrificed, recovery period)

Exp. No. 9934 (115-213)

Dose level (mg/kg)	No. of animals necropsied	Male animals			Female animals		
		0	1,000	5	0	1,000	5
Organ	Findings						
DIGESTIVE SYSTEM							
liver	adhesion with kidney	0	0		1	0	
URINARY SYSTEM							
kidney	cyst	0	1	0	0	1	0
	scarred	1	0				
REPRODUCTIVE SYSTEM							
uterus	dilated lumen	-	-		0	1	

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Table 17-1.

Summary of histological findings with statistical analysis
(sacrificed, administration period)

Exp. No. 9934 (115-213)

Dose level (mg/kg)	No. of animals necropsied	Male animals				Female animals			
		0	100	300	1,000	0	100	300	1,000
Organ	Findings	5	5	5	5	5	5	5	5
RESPIRATORY SYSTEM									
lung	accumulation of foamy cells	3	-	-	2	3	-	-	2
	bronchopneumonia	1	-	-	0	0	-	-	0
	osseous metaplasia	1	-	-	0	0	-	-	0
trachea	dilatation, gland	1	-	-	0	0	-	-	1
DIGESTIVE SYSTEM									
glandular stomach	dilatation, gland	0	0	-	0	1	-	-	0
	epidermal cyst	0	1	-	0	0	-	-	0
exocrine pancreas	degeneration, acinar cell	1	-	-	0	0	-	-	0
liver	fatty change, hepatocyte	1	1	0	0	3	2	2	2
	necrosis, hepatocyte, focal	0	0	1	1	0	0	0	0
	microgranuloma	5	4	5	4	5	4	4	4
	hepatodiaphragmatic nodule	0	0	0	0	0	0	1	0
	hypertrophy, hepatocyte, centrilobular	0	0	3	5**	0	0	1	5**
URINARY SYSTEM									
kidney	basophilic tubule	3	1	0	1	1	0	0	1
	cyst	0	0	0	1	1	1	0	1
	hyaline droplet	1	0	0	1	0	0	0	0
	mineralization	1	0	0	1	0	0	0	0
	fibrosis, focal	1	1	1	0	0	0	0	0
REPRODUCTIVE SYSTEM									
epididymis	cellular infiltration, lymphocyte	1	-	-	1	-	-	-	-
prostate	cell debris, lumen	1	-	-	0	-	-	-	-
	cellular infiltration, lymphocyte	5	-	-	2	-	-	-	-
uterus	cyst	-	-	-	-	0	1	-	0

Significantly different from control group; ** : P ≤ 0.01 (Fisher)

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Table 17-1. -continued Summary of histological findings with statistical analysis
(sacrificed, administration period)

Exp. No. 9934 (115-213)

Dose level (mg/kg)	Male animals				Female animals			
	0	100	300	1,000	0	100	300	1,000
No. of animals necropsied	5	5	5	5	5	5	5	5
Organ	Findings							
REPRODUCTIVE SYSTEM								
uterus	dilatation, lumen	-	-	-	-	2	1	-
vagina	epidermal cyst	-	-	-	-	1	-	-
ENDOCRINE SYSTEM								
thyroid gland	ectopic thymus	1	-	-	0	0	0	-
	ultimobranchial remnant	2	-	-	0	1	0	3

Table 17-2. Summary of histological findings with statistical analysis
(sacrificed, recovery period)

Exp. No. 9934 (115-213)

Dose level (mg/kg)	Male animals		Female animals	
	0	1,000	5	1,000
No. of animals necropsied	4	5	5	5
Organ	Findings			
RESPIRATORY SYSTEM				
lung	accumulation of foamy cells	3	2	1
trachea	dilatation, gland	1	1	0
DIGESTIVE SYSTEM				
exocrine pancreas	degeneration, acinar cell	0	1	1
	cellular infiltration, mononuclear	0	0	1
	focus, hypertrophic, basophilic	0	0	1
cecum	cellular infiltration, mononuclear	1	0	0
liver	adhesion with kidney	0	0	1
	fatty change, hepatocyte	1	0	3
	microgranuloma	4	4	5
URINARY SYSTEM				
kidney	basophilic tubule	2	2	1
	cyst	0	1	1
	hyaline droplet	1	1	0
	mineralization	3	1	2
	fibrosis, focal	1	2	0
	hyperplasia, renal tubule	0	0	1
urinary bladder	cellular infiltration, lymphocyte	0	0	0
REPRODUCTIVE SYSTEM				
prostate	cellular infiltration, lymphocyte	3	2	-

Table 17-2. -continued Summary of histological findings with statistical analysis
(sacrificed, recovery period)

Exp. No. 9934 (115-213)

Dose level (mg/kg)	Male animals		Female animals	
No. of animals necropsied	0	1,000	0	1,000
Organ	Findings			
REPRODUCTIVE SYSTEM				
uterus	dilatation, lumen	-	-	0 1
ENDOCRINE SYSTEM				
pituitary gland	cyst	0	1	0 0
thyroid gland	ultimobranchial remnant	1	4	3 2
adrenal gland	mineralization	0	0	1 0
SPECIAL SENSE SYSTEM				
eye	dysplasia, retina	0	0	1 0
INTEGUMENTARY SYSTEM				
skin	cellular infiltration, mononuclear	1	0	1 0