

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ことから、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係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その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係のない変化と考え

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，2g）
- 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			
		1	2	3	1	2	3	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	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	
	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	
Total	10	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	5
	Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	normal	-	5	5	5	5	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	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	5
	Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	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		
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																		
		7			8			9			10			11			12			
		1	2	3	1	2	3	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	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	
	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	
Total	10	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	5
	Total	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	normal	-	5	5	5	5	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	5	5	5	5		
03 TCDAM 300	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	
	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		
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																				
		13----->			14----->			15----->			16----->			17----->			18----->					
		1	2	3	1	2	3	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	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		
	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		
	Total	10	10	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	5		
		Total	5	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	5		
	Total	5	5	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	5		
		Total	5	5	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	5	5	
	Total	5	5	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	10	
		Total	10	10	10	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	10	10	10
	Total	10	10	10	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----->						
		1	2	3	1	2	3	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	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	10	10	
	Emaciation	-	10	10	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	0	0	
	Total	10	10	10	10	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	5	5	5	
		Total	5	5	5	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	5	5	5	
	Total	5	5	5	5	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	5	5	5	
		Total	5	5	5	5	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	5	5	5	
	Total	5	5	5	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	10	10	
		Total	10	10	10	10	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	10	10	10	10
	Total	10	10	10	10	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												29		
		25----->			26----->			27----->			28----->					
		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	9	9	9	5
	Total	10	10	10	10	10	10	10	10	10	10	10	9	9	9	5
	Emaciation	-	10	10	10	10	10	10	10	10	10	10	9	9	9	5
	Total	10	10	10	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	5	5
	Total	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
	Total	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	5
	Total	10	10	10	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----->			4----->			5----->			6----->			
		1	2	3	1	2	3	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	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	10
02 TCDAM 100	normal	-	5	5	5	5	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	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	5
	Total	5	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	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----->			8----->			9----->			10----->			11----->			12----->			
		1	2	3	1	2	3	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	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	normal	-	5	5	5	5	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	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	5
		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: Female

Group No. Dose mg/kg	Finding Part	Day of experiment																		
		13----->			14----->			15----->			16----->			17----->			18----->			
		1	2	3	1	2	3	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	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	normal	-	5	5	5	5	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	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	5
		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: Female

Group No. Dose mg/kg	Finding Part	Day of experiment																		
		19			20			21			22			23			24			
		1	2	3	1	2	3	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	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	normal	-	5	5	5	5	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	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	5
		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: Female

Group No. Dose mg/kg	Finding Part	Day of experiment															
		25			26			27			28			29			
		1	2	3	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	10	10	5
		Total	10	10	10	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	5	5	5
		Total	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
		Total	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	5
		Total	10	10	10	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: 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	4
		Total	4	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	4
		+	1	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	4
	Abdominal distention	-	5	5	5	5	5	5	5	4	4	4	4	4	4	4	4
	+	0	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	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	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	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	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	28		
01 control 0	N	10	10	10	10	10	10	10	9	9	9	
	Mean	151	173	200	220	243	263	285	304	319	168	
	S.D.	6	10	14	18	23	26	30	31	33	29	
02 TCDAM 100	N	5	5	5	5	5	5	5	5	5	5	
	Mean	150	172	199	219	246	264	283	300	318	168	
	S.D.	6	10	13	15	21	24	29	33	42	40	
03 TCDAM 300	N	5	5	5	5	5	5	5	5	5	5	
	Mean	149	171	198	223	248	272	296	313	333	183	
	S.D.	6	8	14	16	17	18	20	22	22	18	
04 TCDAM 1000	N	10	10	10	10	10	10	10	10	10	10	
	Mean	151	172	197	219	240	257	277	292	308	158	
	S.D.	6	9	13	17	20	22	24	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	28		
01 control 0	N	10	10	10	10	10	10	10	10	10	10	
	Mean	117	131	146	160	169	179	191	197	207	90	
	S.D.	5	6	6	9	10	9	11	10	10	10	
02 TCDAM 100	N	5	5	5	5	5	5	5	5	5	5	
	Mean	117	132	144	157	164	172	181	187	198	82	
	S.D.	5	7	9	11	12	12	12	15	15	11	
03 TCDAM 300	N	5	5	5	5	5	5	5	5	5	5	
	Mean	117	129	141	154	162	169	178	187	194	77	
	S.D.	5	7	10	13	16	21	23	25	26	24	
04 TCDAM 1000	N	10	10	10	10	10	10	10	10	10	10	
	Mean	117	131	143	155	163	173	185	190	196	80	
	S.D.	5	6	7	7	7	9	9	8	11	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	N	Day of experiment					Gain 29-42	Unit:g
			29	32	36	39	42		
01 control 0		4	4	4	4	4	4	4	
		Mean	339	355	375	390	404	65	
		S.D.	25	24	27	27	29	5	
04 TCDAM 1000		5	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	N	Day of experiment					Gain 29-42	Unit:g
			29	32	36	39	42		
01 control 0		5	5	5	5	5	5	5	
		Mean	210	219	227	234	240	30	
		S.D.	9	12	12	11	9	4	
04 TCDAM 1000		5	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
		1 => 8	8 => 15	15 => 22	22 => 28	28 => 36	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
		1 => 8	8 => 15	15 => 22	22 => 28	28 => 36	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)	B. G.	Administration period (Week)				Recovery period (Week)			
			1	2	3	4	1	2		
No. of animals	0	10	10	10	10	10	5	4		
	100	5	5	5	5	5	-	-		
	300	5	5	5	5	5	-	-		
	1000	10	10	10	10	10	5	5		
REMOVAL FROM CAGE Ease of removal	Very easy	0	10	10	10	10	5	4		
		100	5	4	5	5	2	-	-	
		300	5	5	5	5	4	-	-	
		1000	10	7	10	9	9	5	5	
	Easy	0	0	0	0	0	0	0	0	
		100	0	1	0	0	3	-	-	
		300	0	0	0	0	1	-	-	
		1000	0	3	0	1	1	0	0	
	Vocalization	None	0	10	10	10	10	5	4	
			100	5	5	5	5	5	-	-
			300	5	5	5	5	5	-	-
			1000	10	10	10	10	10	5	5

B. G. : Before grouping

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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		
HANDLING OBSERVATIONS Muscle tone	Normal	0	10	10	10	10	9	4	4	
		100	5	5	5	5	5	-	-	
		300	5	5	5	5	5	-	-	
		1000	10	10	10	10	10	5	5	
	Decrease or limp	0	0	0	0	0	1	1	0	
		100	0	0	0	0	0	-	-	
		300	0	0	0	0	0	-	-	
		1000	0	0	0	0	0	0	0	
	Subnormal temperature	Absent	0	10	10	10	10	10	5	4
			100	5	5	5	5	5	-	-
			300	5	5	5	5	5	-	-
			1000	10	10	10	10	10	5	5
Piloerection	Absent	0	10	10	10	10	10	5	4	
		100	5	5	5	5	5	-	-	
		300	5	5	5	5	5	-	-	
		1000	10	10	10	10	10	5	5	
Staining hair	Absent	0	10	10	10	10	10	5	4	
		100	5	5	5	5	5	-	-	
		300	5	5	5	5	5	-	-	
		1000	10	10	10	10	10	5	5	
Unkempt hair	Absent	0	10	10	10	10	10	4	4	
		100	5	5	5	5	5	-	-	
		300	5	5	5	5	5	-	-	
		1000	10	10	10	10	10	5	5	
	Rough fur	0	0	0	0	0	0	1	0	
		100	0	0	0	0	0	-	-	
		300	0	0	0	0	0	-	-	
		1000	0	0	0	0	0	0	0	

B. G. : Before grouping

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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
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
Lacrimation	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)	Administration period (Week)				Recovery period (Week)		
		B. G.	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	-	-
		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	-	-
		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	-	-
		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	-	-
		1000	10	10	10	10	5	5

B. G. : Before grouping

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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
SENSORIMOTOR FUNCTION							
Approach contact	Normal a)	0				9	4
		100				5	-
		300				5	-
		1000				10	5
Freezing		0				1	0
		100				0	-
		300				0	-
		1000				0	0
Touch response	Moderate reaction	0				9	4
		100				4	-
		300				5	-
		1000				10	5
Vocalization, energetically reaction		0				0	0
		100				1	-
		300				0	-
		1000				0	0
Freezing		0				1	0
		100				0	-
		300				0	-
		1000				0	0
Pinna response	Normal	0				10	4
		100				5	-
		300				5	-
		1000				10	5

B. G. : Before grouping

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

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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	
Normal	0				7	4		
	100				5	-		
	300				4	-		
	1000				10	4		
Pupillary reflex	Normal	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	5		
	100	5	5	5	5	5	-	-		
	300	5	5	5	5	5	-	-		
	1000	10	10	10	10	10	5	5		
REMOVAL FROM CAGE Ease of removal	Very easy	0	6	7	9	9	7	5	5	
		100	3	5	5	5	3	-	-	
		300	3	5	5	5	5	-	-	
		1000	6	10	10	10	9	5	4	
	Easy	0	4	3	1	1	3	0	0	
		100	2	0	0	0	2	-	-	
		300	2	0	0	0	0	-	-	
		1000	4	0	0	0	1	0	1	
	Vocalization	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	
HANDLING OBSERVATIONS									
Muscle tone	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
Subnormal temperature	Absent	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
Piloerection	Absent	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
Staining hair	Absent	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
Unkempt hair	Absent	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
Skin color	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

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	
Lacrimation	Absent	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
Exophthalmos	Absent	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
Pupillary size	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
Salivation	Absent	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	
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)	B. G.	Administration period (Week)				Recovery period (Week)		
			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

Sex: Female

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

B. G. : Before grouping

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

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	1	2
	0	10	0.0 ± 0.0 a)	0.3 ± 0.9	0.0 ± 0.0	0.2 ± 0.6	0.3 ± 1.0 (9)	0.0 ± 0.0 (4)	0.0 ± 0.0 (4)
Male	100	5	0.4 ± 0.9	1.0 ± 1.4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0		
	300	5	0.4 ± 0.9	0.4 ± 0.9	0.0 ± 0.0	0.2 ± 0.4	0.6 ± 1.3		
	1,000	10	0.6 ± 1.1	0.8 ± 1.1	0.2 ± 0.6	0.3 ± 0.9	0.1 ± 0.3	0.4 ± 0.9 (5)	0.0 ± 0.0 (5)
	0	10	0.2 ± 0.6	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (5)	0.0 ± 0.0 (5)
Female	100	5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0		
	300	5	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0		
	1,000	10	0.1 ± 0.3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0 (5)	0.0 ± 0.0 (5)
	0	10	0.2 ± 0.6	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	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 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	
Male	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)
	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	
Male	0	9	1338 ± 147 a)	703 ± 139	
	100	5	1457 ± 206	822 ± 228	
	300	5	1370 ± 211	721 ± 129	
	1,000	10	1281 ± 170	739 ± 205	
Female	0	10	620 ± 171	321 ± 77	
	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	Forelimb		Hindlimb
Male	0	4	1381 ± 408 a)		707 ± 284
	1,000	5	1604 ± 241		1027 ± 155
Female	0	5	1080 ± 291		574 ± 190
	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									
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	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
	1,000	10	204 ± 17	169 ± 26	157 ± 25	130 ± 35	105 ± 64	74 ± 57	838 ± 146
Female	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
	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

a) interval time (minutes)

b) Mean ± S.D.

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

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.

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 (pg)	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)

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 (%)						
				NEUT	LYMPH	MONO	EOSN	BASO	LUC	
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)

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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 ($\times 10^3/\text{mm}^3$)	
			Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
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.

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

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	PLT ($\times 10^9/\text{mm}^3$)	Reticulocyte (%)
Male	0	5	1153 \pm 164	2.7 \pm 0.5
	100	5	1135 \pm 178	2.7 \pm 0.5
	300	5	1218 \pm 58	3.0 \pm 0.1
	1,000	5	1169 \pm 178	3.0 \pm 0.4
Female	0	5	1382 \pm 185	2.6 \pm 0.8
	100	5	1284 \pm 136	2.2 \pm 0.3
	300	5	1226 \pm 152	2.4 \pm 0.3
	1,000	5	1264 \pm 190	3.2 \pm 0.7

Mean \pm 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 \pm 2.0	15.6 \pm 0.6	8.06 \pm 0.19	52.9 \pm 1.5	19.4 \pm 0.4	36.5 \pm 0.3
	1,000	5	42.2 \pm 1.6	15.3 \pm 0.7	8.03 \pm 0.54	52.6 \pm 2.2	19.1 \pm 0.7	36.3 \pm 0.5
Female	0	5	41.9 \pm 2.6	15.7 \pm 1.0	7.91 \pm 0.42	53.0 \pm 1.4	19.9 \pm 0.3	37.5 \pm 0.8
	1,000	5	40.3 \pm 2.4	15.0 \pm 0.8	7.62 \pm 0.58	52.9 \pm 1.7	19.7 \pm 0.7	37.3 \pm 0.4

Mean \pm 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 (%)					
				NEUT	LYMPH	MONO	EOSN	BASO	LUC
Male	0	4	10.00 \pm 2.46	16.7 \pm 3.6	79.8 \pm 3.7	1.8 \pm 0.2	1.0 \pm 0.5	0.1 \pm 0.0	0.6 \pm 0.1
	1,000	5	10.20 \pm 2.74	11.9 \pm 4.7	84.4 \pm 5.2	1.9 \pm 0.6	1.0 \pm 0.4	0.2 \pm 0.1	0.6 \pm 0.1
Female	0	5	6.69 \pm 2.02	19.4 \pm 7.4	77.4 \pm 6.9	1.7 \pm 0.4	1.0 \pm 0.3	0.1 \pm 0.0	0.6 \pm 0.2
	1,000	5	5.81 \pm 2.87	16.3 \pm 5.8	79.7 \pm 6.2	1.8 \pm 0.4	1.6 \pm 0.7	0.0 \pm 0.1	0.6 \pm 0.2

NEUT: Neutrophil LYMPH: Lymphocyte MONO: Monocyte EOSN: Eosinophil BASO: Basophil LUC: Large unstained cells
 Mean \pm 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	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 ($\times 10^3/\text{mm}^3$)	
			Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Male	0	4	1.62 \pm 0.28		8.03 \pm 2.17		0.18 \pm 0.06		0.10 \pm 0.06		0.01 \pm 0.00		0.06 \pm 0.02	
	1,000	5	1.15 \pm 0.25*		8.69 \pm 2.66		0.18 \pm 0.03		0.10 \pm 0.06		0.02 \pm 0.01		0.06 \pm 0.02	
Female	0	5	1.33 \pm 0.83		5.14 \pm 1.38		0.11 \pm 0.04		0.06 \pm 0.03		0.00 \pm 0.01		0.04 \pm 0.02	
	1,000	5	0.92 \pm 0.45		4.66 \pm 2.53		0.10 \pm 0.03		0.08 \pm 0.03		0.00 \pm 0.00		0.04 \pm 0.04	

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

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

Exp. No. 9934 (115-213)

Sex	Dose level (mg/kg)	No. of animals	PLT (x10 ⁹ /mm 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 ≤ 0.05 (Dunnett)

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

Exp. No. 9934 (115-213)

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.

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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 \pm 0.7	0.21 \pm 0.02	0.04 \pm 0.01	42.3 \pm 23.9
	100	5	12.1 \pm 1.2	0.22 \pm 0.03	0.03 \pm 0.01	13.4 \pm 5.0
	300	5	11.6 \pm 1.2	0.22 \pm 0.00	0.03 \pm 0.01	10.8 \pm 4.6
	1,000	5	13.2 \pm 2.4	0.21 \pm 0.02	0.03 \pm 0.01	19.4 \pm 15.8
Female	0	5	15.5 \pm 1.7	0.27 \pm 0.03	0.03 \pm 0.01	16.8 \pm 4.1
	100	5	13.3 \pm 1.1	0.23 \pm 0.03	0.03 \pm 0.01	11.8 \pm 7.8
	300	5	15.7 \pm 2.0	0.25 \pm 0.01	0.04 \pm 0.01	13.2 \pm 5.8
	1,000	5	14.5 \pm 1.6	0.24 \pm 0.02	0.04 \pm 0.01	8.8 \pm 1.6

Mean \pm 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 \pm 3	29 \pm 6	860 \pm 126	0.4 \pm 0.1
	100	5	83 \pm 7	31 \pm 5	818 \pm 84	0.3 \pm 0.1
	300	5	78 \pm 9	29 \pm 3	762 \pm 131	0.3 \pm 0.1
	1,000	5	85 \pm 10	31 \pm 5	804 \pm 172	0.4 \pm 0.1
Female	0	5	84 \pm 13	24 \pm 7	409 \pm 75	0.7 \pm 0.1
	100	5	95 \pm 15	22 \pm 3	384 \pm 40	0.8 \pm 0.4
	300	5	88 \pm 12	23 \pm 6	397 \pm 50	0.8 \pm 0.1
	1,000	5	71 \pm 10	21 \pm 3	427 \pm 108	0.8 \pm 0.2

Mean \pm 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)	I.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)

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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.

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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	BUN (mg/dL)	Creatinine (mg/dL)	T.bilirubin (mg/dL)	Total bile acid (μ mol/L)
Male	0	4	11.5 \pm 1.1	0.27 \pm 0.02	0.04 \pm 0.02	23.2 \pm 21.4
	1,000	5	11.6 \pm 1.4	0.26 \pm 0.04	0.03 \pm 0.01	20.9 \pm 14.3
Female	0	5	15.6 \pm 1.2	0.30 \pm 0.03	0.05 \pm 0.01	18.7 \pm 20.2
	1,000	5	15.6 \pm 2.6	0.27 \pm 0.04	0.05 \pm 0.01	16.4 \pm 6.3

Mean \pm 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 \pm 15	31 \pm 3	486 \pm 70	0.4 \pm 0.1
	1,000	5	84 \pm 6	30 \pm 4	565 \pm 76	0.4 \pm 0.1
Female	0	5	86 \pm 20	25 \pm 3	358 \pm 79	0.9 \pm 0.4
	1,000	5	78 \pm 10	25 \pm 2	375 \pm 31	0.9 \pm 0.2

Mean \pm 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)	I. 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.

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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)

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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)

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.

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	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			Leukocytes			Epithelial cells			Casts		Fat globules		Mucous threads		Crystals	
			-	1+	2+ 3+	-	1+	2+ 3+	-	1+	2+ 3+	-	+	-	+	-	+	-	+
Male	0	10			10			10			10			10					10
	100	5			5			5			5			5					5
	300	5			5			5			5			5		4	1		5
	1,000	10			10			10			10			10					4 6
Female	0	10			10			10			10			10					2 8
	100	5			5			5		4 1	5			5					5
	300	5			5			5		5				5					5
	1,000	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 \pm 1.7	2102 \pm 146	179 \pm 5	316.1 \pm 25.0	232.4 \pm 17.4
	1,000	5	13.3 \pm 3.6	1611 \pm 374*	128 \pm 24#	243.1 \pm 48.9*	164.1 \pm 31.0**
Female	0	5	13.8 \pm 5.0	1552 \pm 480	122 \pm 46	221.6 \pm 66.1	151.4 \pm 52.2
	1,000	5	14.2 \pm 6.9	1536 \pm 611	119 \pm 51	223.6 \pm 88.5	155.6 \pm 66.3

Mean \pm S.D.
 Significantly different from control group; *: P \leq 0.05 **; P \leq 0.01 (Dunnett)
 Significantly different from control group; #: P \leq 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																						4				
	1,000	5	5																						5				
Female	0	5	5																						2 3				
	1,000	5	5																						1 4				

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			Leukocytes			Epithelial cells			Casts		Fat globules		Mucous threads		Crystals	
			-	1+	2+ 3+	-	1+	2+ 3+	-	1+	2+ 3+	-	+	-	+	-	+	-	+
Male	0	4		4			4			4			4			4			4
	1,000	5		5			5			5			5			5			5
Female	0	5		5			5			5			5			5			5
	1,000	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 \pm 30	2.12 \pm 0.03	1.03 \pm 0.10	8.56 \pm 1.05	2.34 \pm 0.15
	100	5	293 \pm 35	2.08 \pm 0.08	1.07 \pm 0.11	9.48 \pm 1.97	2.40 \pm 0.23
	300	5	306 \pm 23	2.12 \pm 0.08	1.10 \pm 0.07	9.76 \pm 0.80	2.59 \pm 0.11
	1,000	5	272 \pm 22	2.00 \pm 0.09	1.00 \pm 0.11	8.64 \pm 1.30	2.35 \pm 0.32
Female	0	5	189 \pm 8	1.96 \pm 0.06	0.72 \pm 0.04	5.85 \pm 0.29	1.62 \pm 0.15
	100	5	182 \pm 14	1.88 \pm 0.08	0.69 \pm 0.06	5.63 \pm 0.64	1.46 \pm 0.17
	300	5	181 \pm 24	1.90 \pm 0.05	0.70 \pm 0.07	5.75 \pm 0.52	1.58 \pm 0.16
	1,000	5	186 \pm 6	1.88 \pm 0.10	0.73 \pm 0.07	6.42 \pm 0.63	1.57 \pm 0.06

Mean \pm 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)

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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	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.

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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	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	brown patch/zone	1	0	0	0	0	0	0	0	
DIGESTIVE SYSTEM										
stomach	white patch/zone	0	1	0	0	0	0	0	0	
liver	hepatodiaphragmatic nodule	0	0	0	0	0	0	1	0	
	white patch/zone	0	0	0	1	0	0	0	0	
URINARY SYSTEM										
kidney	cyst	0	0	1	0	0	1	0	0	
	scarred	1	1	0	0	1	2	1	1	
REPRODUCTIVE SYSTEM										
uterus	cyst	-	-	-	-	0	1	0	0	
	dilated lumen	-	-	-	-	2	2	0	2	
ENDOCRINE SYSTEM										
thyroid gland	nodule	0	0	0	0	0	1	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	0	1,000
Organ	Findings	4	5	5	5
DIGESTIVE SYSTEM					
liver	adhesion with kidney	0	0	1	0
URINARY SYSTEM					
kidney	cyst	0	1	0	1
	scarred	1	0	0	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				
		5	100	300	1,000	5	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	0	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	1	0	0	2	
	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)	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
REPRODUCTIVE SYSTEM									
uterus	dilatation, lumen	-	-	-	-	2	1	-	2
vagina	epidermal cyst	-	-	-	-	1	-	-	0
ENDOCRINE SYSTEM									
thyroid gland	ectopic thymus	1	-	-	0	0	0	-	0
	ultimobranchial remnant	2	-	-	0	1	0	-	3

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Table 17-2. Summary of histological 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	0	1,000
Organ	Findings	4	5	5	5
RESPIRATORY SYSTEM					
lung	accumulation of foamy cells	3	2	1	2
trachea	dilatation, gland	1	1	0	0
DIGESTIVE SYSTEM					
exocrine pancreas	degeneration, acinar cell	0	1	1	0
	cellular infiltration, mononuclear	0	0	1	0
	focus, hypertrophic, basophilic	0	0	1	0
cecum	cellular infiltration, mononuclear	1	0	0	0
liver	adhesion with kidney	0	0	1	0
	fatty change, hepatocyte	1	0	3	2
	microgranuloma	4	4	5	5
URINARY SYSTEM					
kidney	basophilic tubule	2	2	1	0
	cyst	0	1	1	1
	hyaline droplet	1	1	0	0
	mineralization	3	1	2	0
	fibrosis, focal	1	2	1	0
	hyperplasia, renal tubule	0	0	1	0
urinary bladder	cellular infiltration, lymphocyte	0	0	1	0
REPRODUCTIVE SYSTEM					
prostate	cellular infiltration, lymphocyte	3	2	-	-

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

Exp. No. 9934 (115-213)

Dose level (mg/kg)	No. of animals necropsied	Male animals		Female animals	
		4	5	5	5
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

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