

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

Sex	Dose level (mg/kg)	No. of animals	Albumin (%)	Alpha-1 (%)	Alpha-2 (%)	Beta (%)	Gamma (%)	A/G
Male	0	5	52.9 ± 1.1	19.9 ± 0.9	8.1 ± 0.3	15.4 ± 0.7	3.8 ± 1.2	1.12 ± 0.05
	20	5	54.2 ± 0.7	17.9 ± 0.8*	8.2 ± 0.6	15.6 ± 0.4	4.2 ± 0.7	1.18 ± 0.03
	100	5	53.9 ± 0.7	19.1 ± 0.7	8.5 ± 1.2	14.7 ± 0.9	3.7 ± 0.8	1.17 ± 0.03
	500	5	51.4 ± 1.1	19.1 ± 1.8	10.5 ± 1.2**	15.7 ± 0.9	3.3 ± 0.7	1.06 ± 0.05
Female	0	5	53.8 ± 1.1	18.2 ± 0.9	7.7 ± 0.2	15.2 ± 1.1	5.0 ± 1.2	1.17 ± 0.05
	20	5	54.1 ± 0.9	18.5 ± 1.2	7.6 ± 0.5	15.3 ± 0.2	4.4 ± 0.7	1.18 ± 0.04
	100	5	55.9 ± 1.9	17.2 ± 2.5	8.2 ± 0.9	14.7 ± 0.6	3.9 ± 1.4	1.27 ± 0.10
	500	3	53.2 ± 4.0	19.3 ± 2.4	9.3 ± 1.6	15.1 ± 0.8	3.1 ± 0.3	1.15 ± 0.17

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

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

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	2.99 ± 0.08	1.12 ± 0.06	0.46 ± 0.03	0.87 ± 0.05	0.21 ± 0.08
	20	5	2.99 ± 0.08	0.99 ± 0.07*	0.45 ± 0.03	0.86 ± 0.02	0.23 ± 0.04
	100	5	2.98 ± 0.10	1.06 ± 0.05	0.47 ± 0.07	0.81 ± 0.03	0.21 ± 0.04
	500	5	2.96 ± 0.07	1.10 ± 0.13	0.60 ± 0.06**	0.90 ± 0.05	0.19 ± 0.04
Female	0	5	3.11 ± 0.11	1.05 ± 0.02	0.45 ± 0.02	0.88 ± 0.07	0.29 ± 0.08
	20	5	3.00 ± 0.05	1.03 ± 0.07	0.42 ± 0.03	0.85 ± 0.01	0.24 ± 0.04
	100	5	3.16 ± 0.08	0.97 ± 0.14	0.46 ± 0.05	0.83 ± 0.04	0.22 ± 0.08
	500	3	2.85 ± 0.35	1.02 ± 0.07	0.49 ± 0.08	0.81 ± 0.05	0.17 ± 0.01

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

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

Sex	Dose level (mg/kg)	No. of animals	Albumin (%)	Alpha-1 (%)	Alpha-2 (%)	Beta (%)	Gamma (%)	A/G
Male	0	5	47.6 ± 3.1	22.3 ± 3.8	9.2 ± 1.3	16.1 ± 0.9	4.9 ± 1.1	0.91 ± 0.12
	500	5	51.6 ± 2.1*	19.3 ± 2.2	8.8 ± 1.1	15.6 ± 0.9	4.7 ± 0.6	1.07 ± 0.09
Female	0	5	51.0 ± 4.2	19.1 ± 3.6	6.9 ± 0.6	17.1 ± 1.2	6.0 ± 1.3	1.05 ± 0.18
	500	5	50.8 ± 3.0	20.0 ± 1.6	8.2 ± 1.3	15.7 ± 1.0	5.3 ± 1.0	1.04 ± 0.13

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

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

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	2.85 ± 0.17	1.33 ± 0.24	0.55 ± 0.08	0.96 ± 0.04	0.29 ± 0.08
	500	5	2.91 ± 0.06	1.09 ± 0.16	0.49 ± 0.06	0.88 ± 0.07	0.27 ± 0.04
Female	0	5	2.96 ± 0.22	1.11 ± 0.23	0.40 ± 0.03	1.00 ± 0.09	0.35 ± 0.08
	500	5	2.94 ± 0.25	1.16 ± 0.10	0.47 ± 0.06	0.90 ± 0.05	0.30 ± 0.05

Mean ± S.D.

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

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	7.6 ± 3.2	1761 ± 545	166 ± 59	303.6 ± 92.9	222.0 ± 71.1
	20	5	6.8 ± 2.4	2044 ± 364	183 ± 43	343.4 ± 72.5	249.1 ± 49.0
	100	5	7.0 ± 2.5	1915 ± 351	168 ± 39	231.9 ± 31.1	235.1 ± 59.1
	500	10	16.7 ± 10.6	874 ± 367**	29 ± 16##	88.3 ± 35.6##	100.8 ± 41.5**
Female	0	10	5.7 ± 2.2	1692 ± 471	125 ± 40	246.2 ± 64.3	181.7 ± 52.8
	20	5	6.2 ± 0.9	1625 ± 346	134 ± 26	223.4 ± 53.6	178.6 ± 49.0
	100	5	8.2 ± 6.0	1778 ± 928	122 ± 74	197.4 ± 90.5	193.1 ± 97.8
	500	8	13.1 ± 4.6##	925 ± 283##	41 ± 27**	93.8 ± 29.3**	122.1 ± 36.7

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

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

Sex	Dose level (mg/kg)	No. of animals	Sodium (mmol/day)	Potassium (mmol/day)	Chloride (mmol/day)
Male	0	10	1.11 ± 0.21	2.08 ± 0.39	1.51 ± 0.26
	20	5	1.17 ± 0.16	2.20 ± 0.25	1.60 ± 0.22
	100	5	1.13 ± 0.29	1.59 ± 0.45	1.58 ± 0.42
	500	10	0.44 ± 0.29**	1.27 ± 0.57**	1.36 ± 0.53
Female	0	10	0.69 ± 0.29	1.31 ± 0.38	0.98 ± 0.33
	20	5	0.81 ± 0.11	1.34 ± 0.19	1.07 ± 0.14
	100	5	0.68 ± 0.15	1.19 ± 0.25	1.14 ± 0.18
	500	8	0.53 ± 0.40	1.18 ± 0.45	1.49 ± 0.40**

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

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

Sex	Dose level (mg/kg)	No. of animals	Color											Occult blood												
			1	2	3	4	5	6	7	8	9	10	11	pH	5	6	7	8	8.5	9	-	+/-	1+	2+	3+	
Male	0	10														1	1	6	2						10	
	20	5													1			4							4	1
	100	5											1						3	1					5	
	500	10								2						1	2	2	3	2					10	
Female	0	10														1	1	1	6	1					9	1
	20	5																3	1	1					5	
	100	5											1			1	1	1	1					4	1	
	500	8									1					2	2	1	3					8		

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)

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

Sex	Dose level (mg/kg)	No. of animals	Ketone bodies			Glucose (g/dL)				Protein (mg/dL)		
			-	+	3+	-	0.1	0.25	0.5	≥ 1.0	-	+/-
Male	0	10	3	6	1	7	3				4	6
	20	5	1	2	2	5				1	3	1
	100	5	1	3	1	4	1			1	4	
	500	10	4	3	3	9	1			1	6	3
Female	0	10	6	2	2	10				3	4	3
	20	5	4	1		5				2	2	1
	100	5	2	1	2	5				1	2	2
	500	8	3	5		8				4	4	

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

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

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
Male	0	10	8	1	1				3	5	2
	20	5	1	4				1	3	1	
	100	5	1	3	1			1	3	1	
	500	10	2	4	4			6	4		
Female	0	10	9	1				6	3	1	
	20	5	4	1				4	1		
	100	5	4	1				2	3		
	500	8	3	5				5	3		

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

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

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		10		10	
	20	5	5		4	1		5	5	5		5		5	
	100	5	5		5		5		5	5		5		5	
	500	10	10		10		9	1	10	10		10		10	
Female	0	10	10		7	3		10	10	10		9	1	1	9
	20	5	5		5		5		5	5		5		5	
	100	5	5		5		4	1	5	5		5		2	3
	500	8	8		8		5	3	8	8		8		3	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)

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

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	5	13.4 ± 3.6	1535 ± 227	107 ± 10	228.5 ± 33.9	145.9 ± 17.5
	500	5	13.9 ± 4.4	1680 ± 489	120 ± 33	242.9 ± 73.5	156.1 ± 47.7
Female	0	5	15.8 ± 8.9	1216 ± 575	90 ± 45	165.6 ± 73.1	114.2 ± 55.3
	500	5	14.9 ± 7.1	1549 ± 542	118 ± 40	212.0 ± 66.9	146.8 ± 48.9

Mean ± S.D.

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

Sex	Dose level (mg/kg)	No. of animals	Sodium (mmol/day)	Potassium (mmol/day)	Chloride (mmol/day)
Male	0	5	1.41 ± 0.25	2.98 ± 0.45	1.92 ± 0.37
	500	5	1.57 ± 0.32	3.15 ± 0.64	2.03 ± 0.47
Female	0	5	1.15 ± 0.12	2.18 ± 0.39	1.49 ± 0.32
	500	5	1.53 ± 0.33*	2.78 ± 0.64	1.91 ± 0.46

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

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

Sex	Dose level (mg/kg)	No. of animals	Color	1	2	3	4	5	6	7	8	9	10	11	pH	5	5.5	6	6.5	7	7.5	8	8.5	9	Occult blood																																
																									-	+/-	1+	2+	3+																												
Male	0	5	5																	1						3	1		5																												
	500	5	5																		3							2		5																											
Female	0	5	5																		3							1	1		5																										
	500	5	5																					1	4						5																										

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)

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

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	5		1	3	1	4	1			3	2
	500	5		3	2		5			1	2	2
Female	0	5	3	2		4	1			3	1	1
	500	5	2	3		5				1	2	2

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

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

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	5	4	1		2	3	
	500	5	2	3		2	3	
Female	0	5	5			3	2	
	500	5	5			2	3	

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

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

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	5	5	5	5	5	5	5	5
	500	5	5	5	5	5	5	5	5
Female	0	5	5	5	4 1	5	5	4 1	5
	500	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)

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

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (g)	Heart (g)	Liver (g)	Kidneys (g)
Male	0	5	307 ± 25	2.00 ± 0.07	1.14 ± 0.10	10.36 ± 0.95	2.33 ± 0.12
	20	5	316 ± 12	2.07 ± 0.05	1.15 ± 0.06	10.44 ± 0.29	2.47 ± 0.23
	100	5	295 ± 24	2.05 ± 0.06	1.07 ± 0.06	10.21 ± 1.10	2.50 ± 0.28
	500	5	225 ± 16**	1.96 ± 0.08	0.88 ± 0.11**	9.70 ± 0.75	2.00 ± 0.12*
Female	0	5	183 ± 11	1.90 ± 0.07	0.72 ± 0.04	5.88 ± 0.29	1.47 ± 0.12
	20	5	184 ± 11	1.90 ± 0.07	0.72 ± 0.08	5.87 ± 0.44	1.50 ± 0.13
	100	5	187 ± 15	1.90 ± 0.04	0.77 ± 0.06	6.68 ± 0.80	1.60 ± 0.13
	500	3	158 ± 4*	1.87 ± 0.06	0.81 ± 0.39	6.45 ± 0.43	1.49 ± 0.14

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

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

Sex	Dose level (mg/kg)	No. of animals	Spleen (g)	Adrenals (mg)	Testes (g)	Ovaries (mg)	Thymus (mg)
Male	0	5	0.59 ± 0.09	50 ± 9	3.02 ± 0.24		559 ± 95
	20	5	0.59 ± 0.07	44 ± 6	2.92 ± 0.28		492 ± 61
	100	5	0.55 ± 0.02	44 ± 3	2.84 ± 0.22		515 ± 136
	500	5	0.65 ± 0.20	51 ± 8	2.49 ± 0.50		389 ± 102*
Female	0	5	0.39 ± 0.02	55 ± 5		76 ± 5	427 ± 77
	20	5	0.36 ± 0.04	52 ± 10		77 ± 4	430 ± 90
	100	5	0.42 ± 0.08	58 ± 5		86 ± 19	415 ± 106
	500	3	0.47 ± 0.06	55 ± 15		63 ± 12	338 ± 46

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

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

Sex	Dose level (mg/kg)	No. of animals	Epididymides (mg)	Mandibular gland (mg)
Male	0	5	631 ± 42	490 ± 27
	20	5	673 ± 68	500 ± 39
	100	5	628 ± 63	511 ± 17
	500	5	473 ± 97**	420 ± 43*
Female	0	5		357 ± 27
	20	5		362 ± 27
	100	5		365 ± 23
	500	3		319 ± 22

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

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

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (g)	Heart (g)	Liver (g)	Kidneys (g)
Male	0	5	354 ± 23	2.12 ± 0.08	1.22 ± 0.04	10.69 ± 0.80	2.56 ± 0.09
	500	5	295 ± 44*	2.14 ± 0.07	1.06 ± 0.13*	8.86 ± 1.42*	2.23 ± 0.36
Female	0	5	198 ± 12	1.94 ± 0.06	0.73 ± 0.02	5.64 ± 0.30	1.59 ± 0.11
	500	5	200 ± 21	1.90 ± 0.06	0.79 ± 0.07	6.45 ± 1.02	1.60 ± 0.08

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

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

Exp. No. 9933 (115-212)

Sex	Dose level (mg/kg)	No. of animals	Spleen (g)	Adrenals (mg)	Testes (g)	Ovaries (mg)	Thymus (mg)
Male	0	5	0.63 ± 0.09	48 ± 6	3.23 ± 0.16		452 ± 127
	500	5	0.66 ± 0.10	47 ± 6	2.71 ± 0.82		499 ± 56
Female	0	5	0.45 ± 0.06	59 ± 5		76 ± 12	352 ± 66
	500	5	0.48 ± 0.10	65 ± 5		79 ± 22	393 ± 92

Mean ± S.D.

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

Sex	Dose level (mg/kg)	No. of animals	Epididymides (mg)	Mandibular gland (mg)
Male	0	5	903 ± 86	581 ± 71
	500	5	704 ± 236	506 ± 84
Female	0	5		362 ± 17
	500	5		388 ± 69

Mean ± S.D.

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

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (%)	Heart (%)	Liver (%)	Kidneys (%)
Male	0	5	307 ± 25	0.658 ± 0.073	0.374 ± 0.033	3.378 ± 0.124	0.763 ± 0.042
	20	5	316 ± 12	0.656 ± 0.035	0.366 ± 0.017	3.309 ± 0.106	0.782 ± 0.075
	100	5	295 ± 24	0.699 ± 0.068	0.365 ± 0.038	3.455 ± 0.187	0.846 ± 0.049*
	500	5	225 ± 16**	0.874 ± 0.056**	0.392 ± 0.039	4.314 ± 0.097**	0.889 ± 0.022**
Female	0	5	183 ± 11	1.042 ± 0.039	0.397 ± 0.027	3.225 ± 0.117	0.809 ± 0.070
	20	5	184 ± 11	1.037 ± 0.049	0.389 ± 0.025	3.198 ± 0.122	0.818 ± 0.057
	100	5	187 ± 15	1.018 ± 0.071	0.414 ± 0.032	3.557 ± 0.161*	0.854 ± 0.065
	500	3	158 ± 4*	1.187 ± 0.066**	0.511 ± 0.229	4.089 ± 0.382**	0.943 ± 0.115

Mean ± S.D.

Significantly different from control group;

*: P ≤ 0.05

**: P ≤ 0.01 (Dunnett)

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

Exp. No. 9933 (115-212)

Sex	Dose Level (mg/kg)	No. of animals	Spleen (%)	Adrenals (%)	Testes (%)	Ovaries (%)	Thymus (%)
Male	0	5	0.192 ± 0.028	0.016 ± 0.003	0.987 ± 0.072		0.184 ± 0.040
	20	5	0.186 ± 0.028	0.014 ± 0.002	0.926 ± 0.117		0.156 ± 0.018
	100	5	0.188 ± 0.014	0.015 ± 0.000	0.969 ± 0.133		0.176 ± 0.052
	500	5	0.286 ± 0.073#	0.023 ± 0.003#	1.102 ± 0.144		0.173 ± 0.041
Female	0	5	0.213 ± 0.017	0.030 ± 0.002		0.042 ± 0.004	0.234 ± 0.040
	20	5	0.196 ± 0.024	0.028 ± 0.005		0.042 ± 0.003	0.233 ± 0.036
	100	5	0.225 ± 0.027	0.031 ± 0.002		0.046 ± 0.009	0.221 ± 0.056
	500	3	0.296 ± 0.044**	0.035 ± 0.010		0.040 ± 0.008	0.214 ± 0.029

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

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

Exp. No. 9933 (115-212)

Sex	Dose level (mg/kg)	No. of animals	Epididymides (%)	Mandibular gland (%)
Male	0	5	0.206 ± 0.007	0.160 ± 0.011
	20	5	0.213 ± 0.017	0.158 ± 0.011
	100	5	0.214 ± 0.029	0.174 ± 0.018
	500	5	0.209 ± 0.033	0.187 ± 0.015*
Female	0	5		0.196 ± 0.007
	20	5		0.198 ± 0.017
	100	5		0.195 ± 0.010
	500	3		0.202 ± 0.009

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

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

Sex	Dose level (mg/kg)	No. of animals	Body weight (g)	Brain (%)	Heart (%)	Liver (%)	Kidneys (%)
Male	0	5	354 ± 23	0.603 ± 0.052	0.345 ± 0.023	3.024 ± 0.129	0.728 ± 0.060
	500	5	295 ± 44*	0.736 ± 0.110*	0.362 ± 0.018	2.996 ± 0.108	0.755 ± 0.019
Female	0	5	198 ± 12	0.983 ± 0.060	0.372 ± 0.019	2.855 ± 0.091	0.803 ± 0.032
	500	5	200 ± 21	0.958 ± 0.083	0.395 ± 0.014	3.215 ± 0.256*	0.804 ± 0.054

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

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

Exp. No. 9933 (115-212)

Sex	Dose level (mg/kg)	No. of animals	Spleen (%)	Adrenals (%)	Testes (%)	Ovaries (%)	Thymus (%)
Male	0	5	0.177 ± 0.018	0.014 ± 0.001	0.918 ± 0.094		0.128 ± 0.035
	500	5	0.225 ± 0.025**	0.016 ± 0.002	0.902 ± 0.202		0.171 ± 0.027
Female	0	5	0.227 ± 0.025	0.030 ± 0.003		0.039 ± 0.005	0.178 ± 0.030
	500	5	0.239 ± 0.026	0.033 ± 0.005		0.039 ± 0.009	0.196 ± 0.037

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

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

Sex	Dose level (mg/kg)	No. of animals	Epididymides (%)	Mandibular gland (%)
Male	0	5	0.257 ± 0.034	0.164 ± 0.018
	500	5	0.234 ± 0.064	0.172 ± 0.017
Female	0	5		0.184 ± 0.010
	500	5		0.193 ± 0.019

Mean ± S.D.

Table 16-1.

Summary of gross findings
(sacrificed, administration period)

Exp. No. 9933 (115-212)

Dose level (mg/kg) No. of animals necropsied Organ	Male animals			Female animals		
	0	20	500	0	20	500
CARDIOVASCULAR SYSTEM						
heart	0	0	0	0	0	1
hypertrophic nodule	0	0	0	0	0	1
scarred	0	0	0	0	0	1
HEMATOPOIETIC SYSTEM						
spleen	0	0	2	0	0	2
dark	0	0	0	0	0	1
white patch/zone						
RESPIRATORY SYSTEM						
lung	0	0	0	0	0	1
brown patch/zone						
DIGESTIVE SYSTEM						
stomach	0	0	0	0	0	0
black patch/zone	0	0	0	0	0	1
red patch/zone	0	0	1	0	0	1
white patch/zone	0	0	3	0	0	0
dark	0	0	0	0	0	1
white patch/zone	0	0	0	0	0	1
URINARY SYSTEM						
kidney	0	1	0	0	0	0
cyst	0	0	1	0	0	0
dark	0	0	0	0	0	0
scarred	0	0	1	0	0	0
REPRODUCTIVE SYSTEM						
testis	0	0	0	0	0	0
small	0	0	1	0	0	0
small	0	0	4*	0	0	0
seminal vesicle	0	0	0	0	0	0
small	0	0	0	0	0	0
dilated lumen	0	0	4*	0	1	0
ENDOCRINE SYSTEM						
adrenal gland	0	0	0	0	0	0
scarred	0	0	1	0	0	0

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

Table 16-2. Summary of gross findings (dead, administration period)

Dose level (mg/kg)	No. of animals necropsied	Organ Findings	Female animals		
			0	20	100
			0	0	500
			0	0	2
HEMATOPOIETIC SYSTEM					
		spleen small	-	-	2
		thymus atrophic	-	-	1
DIGESTIVE SYSTEM					
		stomach autolysis	-	-	1
		small intestine black patch/zone	-	-	1
		large intestine autolysis	-	-	2
		liver autolysis	-	-	2
			-	-	2
ENDOCRINE SYSTEM					
		adrenal gland hypertrophic	-	-	2
NERVOUS SYSTEM					
		brain autolysis	-	-	2

Table 16-3. Summary of gross findings (sacrificed, recovery period)

Exp. No. 9933 (115-212)

Dose level (mg/kg) No. of animals necropsied Organ	Male animals		Female animals	
	0	500	0	500
Findings	5	5	5	5
RESPIRATORY SYSTEM				
lung	0	1	0	0
black patch/zone				
DIGESTIVE SYSTEM				
stomach	1	0	0	0
nodule				
white patch/zone	1	1	0	0
liver	0	0	1	0
hepatodiaphragmatic nodule				
URINARY SYSTEM				
kidney	1	0	0	0
scarred				
white patch/zone	0	0	1	0
REPRODUCTIVE SYSTEM				
testis	0	1	-	-
small				
prostate	0	1	-	-
small				
seminal vesicle	0	1	-	-
small				

Sex: Male	Dose level (mg/kg)	No. of animals examined histologically					No. of animals examined histologically														
		0	5	5	5	5	0	100	500	5	5										
Organ	Findings	1	2	3	T	1	2	3	T	1	2	3	T								
CARDIOVASCULAR SYSTEM																					
heart	cellular infiltration, mononuclear	(5)	0	0	0	0	(5)	3	0	0	3	(5)	1	1	0	2	(5)	0	1	0	1
HEMATOPOIETIC SYSTEM																					
spleen	congestion	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	0	0	1
	deposit, pigment		0	0	0	0		0	0	0	0		0	0	0	0		3	0	0	3
	increase, extramedullary hematopoiesis		0	0	0	0		1	0	0	1		0	0	0	0		1	0	0	1
RESPIRATORY SYSTEM																					
lung	accumulation of foamy cells	(5)	1	0	0	1	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	0	0	1
	cellular infiltration, mixed		0	0	0	0		0	0	0	0		0	0	0	0		1	0	0	1
	osseous metaplasia		0	0	0	0		0	0	0	0		0	0	0	0		1	0	0	1
DIGESTIVE SYSTEM																					
forestomach	edema, intraepithelial	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	0	0	1	(5)	0	0	0	0
	hemorrhage		0	0	0	0		0	0	0	0		0	0	0	0		1	0	0	1
	fibrosis		0	0	0	0		0	0	0	0		0	0	0	0		1	0	0	1
	squamous hyperplasia		0	0	0	0		0	0	0	0		0	0	0	0		3	0	0	3
cecum	basophilic change	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	2	0	3
	cellular infiltration, eosinophile		0	0	0	0		0	0	0	0		1	0	0	1		1	0	0	1
	cellular infiltration, mixed		0	0	0	0		0	0	0	0		0	0	0	0		1	0	0	1
	increase in mitosis		0	0	0	0		0	0	0	0		0	0	0	0		5	0	0	5***##
colon	hemorrhage	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	0	0	1
	basophilic change		0	0	0	0		0	0	0	0		0	0	0	0		3	1	0	4*#
	cellular infiltration, eosinophile		0	0	0	0		0	0	0	0		1	0	0	1		0	0	0	0
	increase in mitosis		0	0	0	0		0	0	0	0		1	0	0	1		5	0	0	5***##
rectum	cellular infiltration, mixed	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	0	0	1
liver	eosinophilic change, hepatocyte	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	4	0	0	4*#
	microgranuloma		3	0	0	3		3	0	0	3		3	0	0	3		2	0	0	2
	hypertrophy, hepatocyte, centrilobular		0	0	0	0		0	0	0	0		0	0	0	0		4	0	0	4*#

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site.
 Significantly different from control group; #: P<0.05
 Significantly different from control group; #: P<0.01 (Mann-Whitney)
 -: Not applicable.
 **: P<0.01 (Fisher)
 ##: P<0.01 (Mann-Whitney)

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

Exp. No. 9933 (115-212)

Sex: Male

Dose level (mg/kg)	20					100					500									
	1	2	3	T		1	2	3	T		1	2	3	T						
No. of animals necropsied	0	5	5	5		0	5	5	5		0	5	5	5						
No. of animals examined histologically	1	2	3	T		1	2	3	T		1	2	3	T						
Organ																				
Findings																				
URINARY SYSTEM																				
kidney	(5)	1	0	0	1	(1)	0	0	0	0	(1)	1	0	0	1	(5)	0	0	0	0
basophilic tubule																				
degeneration, vacuolar, tubule																				
dilatation, tubule																				
cellular infiltration, lymphocyte																				
REPRODUCTIVE SYSTEM																				
prostate	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	3	0	0	3
atrophy																				
cellular infiltration, lymphocyte																				
seminal vesicle	(5)	0	0	0	0	(5)	1	0	0	1	(5)	1	0	0	1	(5)	1	0	0	1
atrophy																				
ENDOCRINE SYSTEM																				
adrenal gland	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(5)	1	1	0	2
angiectasis																				
degeneration, vacuolar																				
necrosis																				
accumulation of macrophage																				
hypertrophy, cortex																				

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site.
 * : P<0.05 (Fisher)
 # : P<0.05 (Mann-Whitney)

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

Exp. No. 9933 (115-212)

Sex: Female

Organ	Dose level (mg/kg)	No. of animals necropsied	No. of animals examined histologically	1			20			100			500		
				1	2	3	T	1	2	3	T	1	2	3	T
CARDIOVASCULAR SYSTEM															
heart				(5)				(5)				(5)			(3)
	myxoid change	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	cellular infiltration, mononuclear	2	0	0	2	0	0	0	0	0	0	0	0	0	1
	pericarditis	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	fibrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	hypertrophy, myocardium	0	0	0	0	0	0	0	0	0	0	0	0	0	1
HEMATOPOIETIC SYSTEM															
spleen				(5)				(5)				(5)			(3)
	congestion	0	0	0	0	0	0	0	0	0	0	0	0	0	3**
	atrophy	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	deposit, pigment	0	0	0	0	0	0	0	0	0	0	0	0	0	3**
	capulitis	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	increase, extramedullary hematopoiesis	0	0	0	0	0	0	0	0	0	0	0	0	0	1
RESPIRATORY SYSTEM															
lung				(5)				(0)				(0)			(3)
	accumulation of foamy cells	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	accumulation of macrophage	1	0	0	1	0	0	0	0	0	0	0	0	0	0
DIGESTIVE SYSTEM															
forestomach				(5)				(5)				(5)			(3)
	edema	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	ulcer	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	squamous hyperplasia	0	0	0	0	0	0	0	0	0	0	0	0	0	1
glandular stomach				(5)				(5)				(5)			(3)
	edema	0	0	0	0	0	0	0	0	0	0	0	0	0	1
colon				(5)				(5)				(5)			(3)
	basophilic change	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	hyperplasia, lymphoid tissue	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	increase in mitosis	0	0	0	0	0	0	0	0	0	0	0	0	0	2
liver				(5)				(5)				(5)			(3)
	congestion	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	eosinophilic change, hepatocyte	0	0	0	0	0	0	0	0	0	0	0	0	0	3**
	vacuolation in hepatocyte	4	0	0	4	1	0	0	1	0	0	0	0	0	1
	microgranuloma	5	0	0	5	5	0	0	5	3	0	0	0	0	2
	hypertrophy, hepatocyte, centrilobular	0	0	0	0	0	0	0	0	0	0	0	0	0	1

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site.
 Significantly different from control group; * : P<0.05
 Significantly different from control group; # : P<0.05 (Mann-Whitney)

-: Not applicable.

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

Exp. No. 9933 (115-212)

Sex: Female

Dose level (mg/kg)	20					100					500									
	No. of animals necropsied					No. of animals examined histologically					No. of animals examined histologically					No. of animals examined histologically				
Organ	1	2	3	T		1	2	3	T		1	2	3	T		1	2	3	T	
URINARY SYSTEM																				
kidney					(5)					(0)					(3)					
basophilic tubule	2	0	0	2		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
dilatation, tubule	2	0	0	2		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
mineralization	1	0	0	1		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
REPRODUCTIVE SYSTEM																				
uterus	(5)	0	0	0	0	(1)	1	0	0	1	(1)	1	0	0	1	(3)	0	0	0	0
dilatation, lumen																				
ENDOCRINE SYSTEM																				
adrenal gland	(5)	0	0	0	0	(5)	0	0	0	0	(5)	0	0	0	0	(3)	1	1	0	2
angiectasis	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
degeneration, vacuolar	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
necrosis	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
accumulation of macrophage	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
hypertrophy, cortex	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site. - : Not applicable.
 Significantly different from control group; * : P<0.05 (Fisher)
 Significantly different from control group; # : P<0.05 (Mann-Whitney)

Table 17-2. Summary of histological findings (dead, administration period)

Sex: Female	Dose level (mg/kg)	0			20			100			500			
		1	2	3	T	1	2	3	T	1	2	3	T	
No. of animals necropsied														
No. of animals examined histologically														
Organ Findings														
CARDIOVASCULAR SYSTEM														
heart		-	-	-	-	-	-	-	-	-	-	-	-	(2)
	cellular infiltration, mononuclear													1 0 0 1
HEMATOPOIETIC SYSTEM														
spleen	atrophy	-	-	-	-	-	-	-	-	-	-	-	-	(2)
thymus	atrophy	-	-	-	-	-	-	-	-	-	-	-	-	(2)
														1 0 0 1
RESPIRATORY SYSTEM														
lung	accumulation of foamy cells	-	-	-	-	-	-	-	-	-	-	-	-	(2)
														1 0 0 1
DIGESTIVE SYSTEM														
glandular stomach	ulcer	-	-	-	-	-	-	-	-	-	-	-	-	(2)
mandibular gland	decrease, eosinophilic granule	-	-	-	-	-	-	-	-	-	-	-	-	(2)
														1 0 0 1
														(2)
														2 0 0 2
ENDOCRINE SYSTEM														
adrenal gland	congestion	-	-	-	-	-	-	-	-	-	-	-	-	(2)
	degeneration, vacuolar	-	-	-	-	-	-	-	-	-	-	-	-	1 0 0 1
	necrosis	-	-	-	-	-	-	-	-	-	-	-	-	0 1 0 1
	hypertrophy, cortex	-	-	-	-	-	-	-	-	-	-	-	-	1 0 0 1

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site.

-: Not applicable.

Table 17-3. Summary of histological findings (sacrificed, recovery period)

Sex: Male

Dose level (ng/kg)	No. of animals necropsied					500	
	1	2	3	T	5		
No. of animals examined histologically	5					5	
	1	2	3	T	5		
Organ	1	2	3	T	5	1 2 3 T	
CARDIOVASCULAR SYSTEM							
heart	(5)	1	0	0	1	(5)	0 0 0 0
necrosis							0 0 0 0
cellular infiltration, mononuclear		2	0	0	2		0 0 0 0
fibrosis		1	0	0	1		0 0 0 0
HEMATOPOIETIC SYSTEM							
spleen	(5)	0	0	0	0	(5)	5 0 0 5***
deposit, pigment							
RESPIRATORY SYSTEM							
lung	(5)	2	0	0	2	(5)	1 0 0 1
accumulation of foamy cells		0	0	0	0		1 0 0 1
cellular infiltration, mixed							
DIGESTIVE SYSTEM							
glandular stomach	(5)	1	0	0	1	(5)	0 0 0 0
ectopic tissue		1	0	0	1		0 0 0 0
epidermal cyst	(5)	1	0	0	1	(5)	0 0 0 0
jejunum							
mineralization	(5)	1	0	0	1	(5)	0 0 0 0
colon	(5)	0	0	0	0	(5)	1 0 0 1
hyperplasia, lymphoid tissue							
liver	(5)	4	0	0	4	(5)	5 0 0 5
microgranuloma							
URINARY SYSTEM							
kidney	(5)	1	0	0	1	(5)	0 0 0 0
dilatation, tubule		3	0	0	3		1 0 0 1
mineralization		1	0	0	1		1 0 0 1
cellular infiltration, lymphocyte							
REPRODUCTIVE SYSTEM							
epididymals	(5)	0	0	0	0	(5)	1 0 0 1
decrease, sperm							
prostate	(5)	1	1	0	2	(5)	1 0 0 1
cellular infiltration, lymphocyte							

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site. --: Not applicable.
 Significantly different from control group; **: P<0.01 (Fisher)
 Significantly different from control group; #: P<0.01 (Mann-Whitney)

Table 17-3. -continued Summary of histological findings (sacrificed, recovery period)

Sex: Male	Dose level (mg/kg)	NO. of animals necropsied					T				
		0	500	5	5	5					
Organ	Findings	1	2	3	T	1	2	3	T		
REPRODUCTIVE SYSTEM											
seminal vesicle	atrophy	(5)	0	0	0	0	(5)	1	0	0	1
ENDOCRINE SYSTEM											
adrenal gland	angiectasis	(5)	0	0	0	0	(5)	1	0	0	1
	degeneration, vacuolar		0	0	0	0		3	0	0	3
	necrosis		0	0	0	0		0	1	0	1
	accumulation of macrophage		0	0	0	0		5	0	0	5***##
	hypertrophy, cortex		0	0	0	0		1	0	0	1

1: slight 2: moderate 3: marked T: total
 (): No of animals examined microscopically at this site. --: Not applicable.
 Significantly different from control group; **: P<0.01 (Fisher)
 Significantly different from control group; ##: P<0.01 (Mann-Whitney)

Table 17-3. -continued Summary of histological findings
(sacrificed, recovery period)

Exp. No. 9933 (115-212)

Sex: Female											
Dose level (mg/kg)	No. of animals necropsied	500									
No. of animals examined histologically											
Organ	Findings	1	2	3	T						
HEMATOPOIETIC SYSTEM											
spleen	deposit, pigment	(5)	0	0	0	0	(5)	4	0	0	4**
RESPIRATORY SYSTEM											
lung	accumulation of foamy cells	(5)	2	0	0	2	(5)	0	0	0	0
	osseous metaplasia		2	0	0	2		0	0	0	0
DIGESTIVE SYSTEM											
liver	vacuolation in hepatocyte	(5)	1	0	0	1	(5)	0	0	0	0
	microgranuloma		5	0	0	5		5	0	0	5
	hepatodiaphragmatic nodule		1	0	0	1		0	0	0	0
URINARY SYSTEM											
kidney	mineralization	(5)	2	0	0	2	(5)	0	0	0	0
	fibrosis		1	0	0	1		0	0	0	0
ENDOCRINE SYSTEM											
thyroid gland	ultimobranchial remnant	(5)	0	0	0	0	(5)	1	0	0	1
adrenal gland	angiectasis	(5)	0	0	0	0	(5)	3	2	0	5***
	degeneration, vacuolar		0	0	0	0		3	0	0	3
	accumulation of macrophage		0	0	0	0		2	0	0	2

1: slight 2: moderate 3: marked T: total
 (): No. of animals examined microscopically at this site.
 Significantly different from control group; * : P<0.05
 Significantly different from control group; #: P<0.05
 -: Not applicable.
 **: P<0.01 (Fisher)
 #: P<0.01 (Mann-Whitney)