

Table 9 - continued Biochemical findings  
Male, Female, 13w

Sex	Group and dose		BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
Male	Control	N	10	10	10	10	10	10	10
		Mean	12.3	0.4	6.1	10.2	147.1	4.14	106.5
		S.D.	±1.1	±0.1	±0.6	±0.2	±0.6	±0.13	±1.0
	0.1 mg/kg	N	10	10	10	10	10	10	10
		Mean	11.8	0.4	6.4	10.3	147.3	4.36	105.7
		S.D.	±1.7	±0.0	±0.3	±0.3	±0.7	±0.21	±1.1
	0.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	14.2*	0.4	6.6	10.1	145.9*	4.53**	105.3
		S.D.	±1.7	±0.0	±0.5	±0.4	±0.9	±0.28	±1.8
	2.5 mg/kg	N	9	9	9	9	9	9	9
		Mean	14.8**	0.4	6.8*	10.0	144.9**	4.66**	105.7
		S.D.	±1.8	±0.0	±0.6	±0.3	±1.1	±0.32	±1.7
Female	Control	N	10	10	10	10	10	10	10
		Mean	14.5	0.5	4.9	10.4	145.7	4.02	108.6
		S.D.	±1.7	±0.1	±0.6	±0.2	±0.7	±0.17	±0.9
	0.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	14.3	0.5	5.1	10.4	145.8	4.14	108.6
		S.D.	±1.7	±0.1	±0.6	±0.2	±1.1	±0.20	±1.2
	2.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	13.6	0.5	5.2	10.5	145.6	3.98	108.5
		S.D.	±1.1	±0.1	±0.7	±0.4	±0.8	±0.13	±1.7
	12.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	14.1	0.4	5.4	10.7	145.1	3.98	108.9
		S.D.	±1.8	±0.1	±0.7	±0.3	±1.1	±0.19	±1.2

\*: P&lt;0.05, \*\*: P&lt;0.01 (significantly different from control).

Table 10 Biochemical findings  
Male, Female, 52w

Sex	Group and dose		T. Protein (g/dL)	A/G ratio	$\alpha_1$ -Globulin (%)	$\alpha_2$ -Globulin (%)	$\beta$ -Globulin (%)	$\gamma$ -Globulin (%)	Albumin (%)
Male	Control	N	10	10	10	10	10	10	10
		Mean	5.8	1.01	19.2	7.5	17.9	5.7	49.7
		S. D.	±0.2	±0.21	±2.2	±0.5	±2.3	±2.3	±5.4
	0.1 mg/kg	N	8	8	8	8	8	8	8
		Mean	5.8	1.01	18.2	7.1	18.5	6.9	49.3
		S. D.	±0.3	±0.29	±1.8	±1.4	±4.5	±3.1	±8.4
	0.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	5.8	1.42**	15.2**	6.1*	15.3	5.2	58.1**
		S. D.	±0.5	±0.31	±2.4	±1.3	±3.0	±1.7	±5.4
	2.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	5.8	1.75**	13.4**	5.0**	12.7**	5.8	63.2**
		S. D.	±0.2	±0.30	±2.0	±1.1	±2.2	±1.2	±4.7
Female	Control	N	10	10	10	10	10	10	10
		Mean	6.4	1.79	13.5	4.8	13.2	4.6	63.9
		S. D.	±0.3	±0.25	±1.6	±0.6	±1.5	±0.9	±3.1
	0.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	6.7	1.69	14.2	4.8	13.5	4.9	62.6
		S. D.	±0.2	±0.17	±1.6	±0.5	±0.7	±1.2	±2.5
	2.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	6.7	1.73	12.8	5.0	13.6	5.4	63.3
		S. D.	±0.3	±0.17	±1.4	±0.9	±1.6	±1.2	±2.3
	12.5 mg/kg	N	9	9	9	9	9	9	9
		Mean	6.5	2.00	12.1	4.1	12.2	5.0	66.5
		S. D.	±0.5	±0.19	±1.0	±0.4	±1.2	±1.2	±2.1

\*: P&lt;0.05, \*\*: P&lt;0.01 (significantly different from control).

Table 10 - continued  
Biochemical findings  
Male, Female, 52w

Sex	Group and dose		T. Bilirubin (mg/dL)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	T. Cholesterol (mg/dL)	Triglycerides (mg/dL)	Phospholipids (mg/dL)	Glucose (mg/dL)
Male	Control	N	10	10	10	10	10	10	10	10
		Mean	0.0	85	32	141	80	92	134	125
		S.D.	±0.0	±17	±15	±42	±11	±41	±12	±27
	0.1 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	0.0	91	31	165	78	69	123	115
		S.D.	±0.0	±18	±8	±56	±22	±28	±26	±11
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	0.0	89	42	364**	82	98	152	139
		S.D.	±0.0	±23	±31	±87	±21	±32	±33	±17
	2.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	0.0	77	36	565**	75	77	143	125
		S.D.	±0.0	±15	±11	±137	±13	±32	±15	±16
Female	Control	N	10	10	10	10	10	10	10	10
		Mean	0.1	112	37	57	100	95	196	103
		S.D.	±0.1	±98	±36	±26	±23	±71	±41	±9
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	0.0	92	27	59	104	92	207	110
		S.D.	±0.0	±48	±12	±16	±13	±51	±17	±9
	2.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	0.0	132	76	57	108	91	208	106
		S.D.	±0.0	±103	±103	±14	±22	±61	±36	±16
	12.5 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	0.0*	69	25	86**	99	77	196	119*
		S.D.	±0.0	±13	±8	±20	±21	±26	±31	±16

\*: P&lt;0.05, \*\*: P&lt;0.01 (significantly different from control).

Table 10 - continued      Biochemical findings  
Male, Female, 52w

Sex	Group and dose		BUN	Creatinine	IP	Ca	Na	K	Cl
			(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mEq/L)	(mEq/L)	(mEq/L)
Male	Control	N	10	10	10	10	10	10	10
		Mean	9.1	0.5	5.2	10.0	147.4	4.40	107.7
		S. D.	±1.5	±0.1	±0.6	±0.2	±1.3	±0.20	±1.1
	0.1 mg/kg	N	8	8	8	8	8	8	8
		Mean	8.8	0.4	5.2	10.0	147.3	4.54	108.0
		S. D.	±0.9	±0.1	±0.5	±0.3	±0.9	±0.16	±2.1
	0.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	10.4	0.4	5.8*	10.2	146.5	4.64	107.6
		S. D.	±1.9	±0.0	±0.5	±0.5	±0.8	±0.32	±1.8
	2.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	12.8**	0.4	5.6	9.9	146.2	4.63	107.1
		S. D.	±1.5	±0.1	±0.6	±0.3	±1.3	±0.26	±1.7
Female	Control	N	10	10	10	10	10	10	10
		Mean	13.4	0.5	4.7	10.6	145.8	4.04	107.2
		S. D.	±2.7	±0.1	±1.0	±0.4	±1.2	±0.27	±1.6
	0.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	12.6	0.5	4.6	10.9	146.4	3.80	107.0
		S. D.	±2.8	±0.0	±0.7	±0.3	±1.1	±0.33	±2.5
	2.5 mg/kg	N	10	10	10	10	10	10	10
		Mean	12.7	0.5	4.6	10.6	146.0	4.19	107.4
		S. D.	±3.1	±0.1	±0.6	±0.3	±1.5	±0.32	±1.8
	12.5 mg/kg	N	9	9	9	9	9	9	9
		Mean	12.1	0.4	5.0	10.5	145.7	3.96	107.9
		S. D.	±2.0	±0.1	±0.8	±0.4	±1.1	±0.21	±1.9

\*: P&lt;0.05, \*\*: P&lt;0.01 (significantly different from control).

Table 11 Necropsy findings  
Male, Female, 13w

Organs and findings	Sex	Male				Female			
	Group and dose	Control	0.1 mg/kg	0.5 mg/kg	2.5 mg/kg	Control	0.5 mg/kg	2.5 mg/kg	12.5 mg/kg
	Number of animals	10	10	10	9	10	10	10	10
Digestive system									
Liver									
Enlargement		0	0	0	5*	0	0	0	1
Hematopoietic system									
Thymus									
Coloration, dark red		0	0	0	0	1	0	0	0
Urinary system									
Kidney									
Pit		1	0	0	0	0	0	0	0
Dilatation, pelvic cavity		0	0	0	0	0	1	0	0
Mass, light gray		0	0	0	0	1	0	0	0
Integumentary system									
Integument									
Loss, hair		0	0	0	0	0	0	0	1

\*:  $P < 0.05$  (significantly different from control).  
 No appreciable changes in all other organs and tissues.  
 One male in the 2.5 mg/kg group died.

Table 12 Necropsy findings  
Male, Female, 52w

Organs and findings	Sex Group and dose Number of animals	Male				Female			
		Control	0.1 mg/kg	0.5 mg/kg	2.5 mg/kg	Control	0.5 mg/kg	2.5 mg/kg	12.5 mg/kg
		10	8	10	10	10	10	10	9
Digestive system									
Liver									
Macule, light gray		0	0	0	2	0	0	0	1
Macule, dark red		0	0	0	1	0	0	1	0
Discoloration		2	0	0	0	0	0	0	0
Enlargement		0	0	7**	9**	0	0	0	5*
Hernia, diaphragmatic		0	0	0	0	1	0	0	1
Respiratory system									
Lung									
Spot, white		1	0	0	4	1	0	0	0
Coloration, dark red		0	0	0	1	0	0	0	0
Hematopoietic system									
Thymus									
Small		10	8	10	9	8	8	10	9
Popliteal lymph node									
Enlargement		1	0	1	1	0	0	0	0
Spleen									
Macule, light gray		1	1	0	0	0	0	0	0
Cardiovascular system									
Heart									
Coloration, light gray		1	0	1	1	0	0	0	0
Urinary system									
Kidney									
Pit		0	0	1	0	0	0	0	0
Genital system									
Testis									
Small		0	0	0	1	NA	NA	NA	NA
Epididymis									
Small		0	0	0	1	NA	NA	NA	NA
Prostate									
Spot, dark red		0	0	0	1	NA	NA	NA	NA
Ovary									
Enlargement		NA	NA	NA	NA	0	0	2	0
Dilatation, ovarian bursa						0	0	0	1
Cyst						2	3	1	2

\*: P&lt;0.05, \*\*: P&lt;0.01 (significantly different from control).

NA: not applicable.

No appreciable changes in all other organs and tissues.

Two males in the 0.1 mg/kg group and one female in the 12.5 mg/kg group died.

Table 12 - continued

Necropsy findings  
Male, Female, 52w

Organs and findings	Sex	Male				Female			
	Group and dose	Control	0.1 mg/kg	0.5 mg/kg	2.5 mg/kg	Control	0.5 mg/kg	2.5 mg/kg	12.5 mg/kg
	Number of animals	10	8	10	10	10	10	10	9
Genital system									
Uterus		NA	NA	NA	NA				
Polyp, endometrium						0	0	0	1
Mammary gland									
Retention, milk		0	0	0	0	2	2	3	3
Endocrine system									
Pituitary									
Spot, dark red		0	0	0	0	2	1	3	1
Enlargement		0	0	0	0	1	1	2	1
Nodule, light gray		0	0	0	0	0	0	1	1
Thyroid									
Defect, left		0	1	0	0	0	0	0	0
Enlargement, right		0	1	0	0	0	0	0	0
Adrenal									
Spot, brown		0	0	0	0	1	2	1	1
Enlargement		0	0	0	0	0	0	1	0
Integumentary system									
Integument									
Nodule, cutis, white		0	0	1	0	0	0	0	0
Nodule, subcutis, white		0	0	0	0	0	0	0	1
Mass, subcutis, light gray		0	0	0	0	3	0	1	3
Others									
Extremity									
Swelling, hindlimb		0	0	0	1	0	0	0	0
Corn, hindlimb		5	5	7	1	1	0	2	2

Not significantly different from control.

NA: not applicable.

No appreciable changes in all other organs and tissues.

Two males in the 0.1 mg/kg group and one female in the 12.5 mg/kg group died.

Table 13 Organ weights  
Male, Female, 13w

Sex	Group and dose		Final body weight	Brain		Pituitary		Thyroids		Heart	
			(g)	(g)	(g/100 gB.W.)	(mg)	(mg/100 gB.W.)	(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N	10	10	10	10	10	10	10	10	10
		Mean	530.1	2.22	0.42	14.0	2.7	20.4	3.8	1.54	0.29
		S.D.	±32.1	±0.08	±0.02	±1.6	±0.3	±5.8	±1.0	±0.19	±0.03
	0.1 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	566.3	2.28	0.40	13.9	2.5	26.6*	4.7	1.61	0.29
		S.D.	±42.2	±0.05	±0.03	±1.3	±0.2	±5.2	±0.8	±0.13	±0.02
	0.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	546.5	2.29	0.42	14.2	2.6	24.5	4.5	1.63	0.30
		S.D.	±40.3	±0.07	±0.03	±1.2	±0.2	±5.7	±1.1	±0.10	±0.02
	2.5 mg/kg	N	9	9	9	9	9	9	9	9	9
		Mean	450.1**	2.19	0.49**	12.8	2.8	18.7	4.1	1.49	0.33**
		S.D.	±27.8	±0.07	±0.03	±0.5	±0.2	±4.1	±0.7	±0.09	±0.02
Female	Control	N	10	10	10	10	10	10	10	10	10
		Mean	304.1	2.05	0.68	16.9	5.6	16.7	5.5	0.96	0.32
		S.D.	±26.9	±0.06	±0.06	±1.7	±0.5	±4.1	±1.1	±0.07	±0.02
	0.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	303.0	2.06	0.69	18.4	6.1	17.7	5.9	0.91	0.30
		S.D.	±31.0	±0.09	±0.05	±1.9	±0.7	±2.2	±0.8	±0.08	±0.02
	2.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	297.0	2.09	0.70	19.1	6.4*	19.2	6.5*	0.95	0.32
		S.D.	±17.5	±0.08	±0.03	±2.5	±1.0	±2.7	±1.1	±0.06	±0.02
	12.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	299.8	2.09	0.70	18.6	6.2	18.7	6.2	0.94	0.32
		S.D.	±23.1	±0.07	±0.05	±2.9	±0.8	±2.4	±0.7	±0.07	±0.03

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\*: P<0.05, \*\*: P<0.01 (significantly different from control).  
One male in the 2.5 mg/kg group died.



Table 13 - continued

Organ weights  
Male, Female, 13w

Sex	Group and dose		Lungs		Thymus		Liver		Spleen	
			(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N	10	10	10	10	10	10	10	10
		Mean	1.54	0.29	0.28	0.06	14.56	2.75	0.77	0.14
		S.D.	±0.11	±0.02	±0.05	±0.01	±0.81	±0.10	±0.12	±0.02
	0.1 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.59	0.28	0.31	0.05	15.96	2.82	0.84	0.15
		S.D.	±0.13	±0.03	±0.08	±0.02	±2.02	±0.23	±0.10	±0.01
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.62	0.30	0.26	0.05	20.25**	3.71**	0.76	0.14
		S.D.	±0.11	±0.02	±0.07	±0.02	±2.00	±0.21	±0.06	±0.01
	2.5 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	1.41	0.31	0.25	0.05	23.16**	5.12**	0.68	0.15
		S.D.	±0.09	±0.03	±0.05	±0.01	±4.45	±0.72	±0.07	±0.01
66 Female	Control	N	10	10	10	10	10	10	10	10
		Mean	1.11	0.37	0.25	0.08	7.97	2.63	0.54	0.18
		S.D.	±0.09	±0.03	±0.04	±0.01	±0.70	±0.14	±0.06	±0.02
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.12	0.37	0.28	0.09	7.97	2.63	0.45**	0.15**
		S.D.	±0.09	±0.02	±0.07	±0.02	±0.94	±0.18	±0.06	±0.01
	2.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.08	0.36	0.27	0.09	8.32	2.80	0.50	0.17
		S.D.	±0.06	±0.02	±0.04	±0.01	±0.52	±0.18	±0.07	±0.02
	12.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.14	0.38	0.27	0.09	11.63**	3.88**	0.49	0.17
		S.D.	±0.11	±0.03	±0.06	±0.02	±1.72	±0.50	±0.05	±0.01

\*\* : P<0.01 (significantly different from control).  
One male in the 2.5 mg/kg group died.

Table 13 - continued

Organ weights  
Male, Female, 13w

Sex	Group and dose		Kidneys		Adrenals		Epididymides		Testes	
			(g)	(g/100 gB. W.)	(mg)	(mg/100 gB. W.)	(g)	(g/100 gB. W.)	(g)	(g/100 gB. W.)
Male	Control	N	10	10	10	10	10	10	10	10
		Mean	3.30	0.62	57.1	10.8	1.39	0.26	3.46	0.65
		S.D.	±0.28	±0.04	±7.0	±1.5	±0.14	±0.02	±0.28	±0.07
	0.1 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	3.49	0.62	61.0	10.8	1.39	0.25	3.47	0.62
		S.D.	±0.29	±0.02	±6.1	±1.0	±0.15	±0.02	±0.23	±0.07
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	3.64	0.67	58.0	10.7	1.24*	0.23*	3.31	0.61
		S.D.	±0.29	±0.06	±3.9	±0.8	±0.08	±0.02	±0.39	±0.06
	2.5 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	3.16	0.70*	50.5*	11.2	1.27	0.28	3.65	0.81**
		S.D.	±0.45	±0.07	±5.3	±1.1	±0.11	±0.03	±0.15	±0.07
Female	Control	N	10	10	10	10				
		Mean	2.12	0.70	66.0	21.8				
		S.D.	±0.72	±0.25	±7.8	±2.6				
	0.5 mg/kg	N	10	10	10	10				
		Mean	1.93	0.64	66.5	22.1				
		S.D.	±0.29	±0.07	±6.4	±2.4				
	2.5 mg/kg	N	10	10	10	10				
		Mean	1.89	0.64	64.7	21.8				
		S.D.	±0.11	±0.05	±6.1	±2.5				
	12.5 mg/kg	N	10	10	10	10				
		Mean	1.96	0.66	61.8	20.6				
		S.D.	±0.15	±0.06	±6.7	±1.6				

\*, P<0.05, \*\*: P<0.01 (significantly different from control).  
One male in the 2.5 mg/kg group died.

Table 13 - continued

Organ weights  
Male, Female, 13w

Sex	Group and dose		Ovaries		Uterus	
			(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N				
		Mean				
		S.D.				
	0.1 mg/kg	N				
		Mean				
		S.D.				
	0.5 mg/kg	N				
		Mean				
		S.D.				
	2.5 mg/kg	N				
		Mean				
		S.D.				
Female	Control	N	10	10	10	10
		Mean	78.5	26.1	0.58	0.19
		S.D.	±7.8	±4.0	±0.09	±0.03
	0.5 mg/kg	N	10	10	10	10
		Mean	79.8	26.5	0.65	0.22
		S.D.	±8.9	±3.2	±0.08	±0.04
	2.5 mg/kg	N	10	10	10	10
		Mean	79.3	26.9	0.56	0.19
		S.D.	±11.9	±4.6	±0.06	±0.03
	12.5 mg/kg	N	10	10	10	10
		Mean	80.4	27.0	0.63	0.21
		S.D.	±10.9	±4.0	±0.08	±0.03

Not significantly different from control.

Table 14 Organ weights  
Male, Female, 52w

Sex	Group and dose		Final body weight	Brain		Pituitary		Thyroids		Heart	
			(g)	(g)	(g/100 gB.W.)	(mg)	(mg/100 gB.W.)	(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N	10	10	10	10	10	10	10	10	10
		Mean	819.9	2.41	0.30	15.8	2.0	31.5	3.8	1.89	0.23
		S.D.	±145.4	±0.12	±0.04	±1.8	±0.2	±11.3	±0.9	±0.25	±0.02
	0.1 mg/kg	N	8	8	8	8	8	8	8	8	8
		Mean	792.5	2.41	0.31	15.7	2.0	31.4	3.9	1.93	0.25
		S.D.	±140.4	±0.08	±0.07	±1.7	±0.5	±11.9	±1.0	±0.19	±0.04
	0.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	842.4	2.41	0.29	16.2	1.9	34.0	4.1	2.05	0.25
		S.D.	±136.1	±0.07	±0.04	±1.3	±0.3	±6.0	±0.8	±0.17	±0.03
	2.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	614.2**	2.36	0.39**	16.8	2.8**	29.7	4.9*	1.87	0.31**
		S.D.	±97.3	±0.10	±0.05	±3.1	±0.3	±5.7	±0.9	±0.27	±0.03
Female	Control	N	10	10	10	10	10	10	10	10	10
		Mean	423.2	2.17	0.54	27.9	6.6	24.0	5.7	1.15	0.28
		S.D.	±87.2	±0.08	±0.12	±11.9	±2.3	±5.8	±1.1	±0.16	±0.04
	0.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	441.8	2.20	0.51	30.9	7.0	24.6	5.5	1.23	0.28
		S.D.	±71.4	±0.09	±0.07	±16.5	±3.8	±8.7	±1.3	±0.16	±0.04
	2.5 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	481.0	2.16	0.47	32.8	7.1	27.6	5.9	1.23	0.26
		S.D.	±104.7	±0.06	±0.10	±13.6	±3.2	±4.7	±1.1	±0.17	±0.04
	12.5 mg/kg	N	9	9	9	9	9	9	9	9	9
		Mean	425.8	2.17	0.52	30.5	7.4	26.5	6.4	1.24	0.29
		S.D.	±71.4	±0.07	±0.08	±9.9	±2.4	±4.1	±1.4	±0.09	±0.03

#: P<0.05, \*\*: P<0.01 (significantly different from control).  
Two males in the 0.1 mg/kg group and one female in the 12.5 mg/kg group died.

Table 14 - continued  
Organ weights  
Male, Female, 52w

Sex	Group and dose		Lungs		Thymus		Liver		Spleen	
			(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N	10	10	10	10	10	10	10	10
		Mean	1.88	0.23	0.08	0.01	18.35	2.22	0.99	0.12
		S.D.	±0.16	±0.02	±0.02	±0.00	±4.61	±0.25	±0.24	±0.02
	0.1 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	1.86	0.24	0.08	0.01	17.79	2.26	0.96	0.13
		S.D.	±0.05	±0.05	±0.03	±0.00	±2.65	±0.20	±0.07	±0.03
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.88	0.23	0.07	0.01	24.85**	2.95**	1.06	0.13
		S.D.	±0.22	±0.02	±0.02	±0.00	±5.23	±0.47	±0.15	±0.03
	2.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.79	0.29**	0.09	0.01	25.09**	4.13**	0.89	0.15
		S.D.	±0.16	±0.03	±0.02	±0.00	±3.69	±0.62	±0.19	±0.02
Female	Control	N	10	10	10	10	10	10	10	10
		Mean	1.34	0.33	0.09	0.02	10.55	2.48	0.62	0.15
		S.D.	±0.17	±0.07	±0.03	±0.01	±3.14	±0.39	±0.15	±0.02
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.29	0.30	0.10	0.02	10.70	2.42	0.60	0.14
		S.D.	±0.12	±0.05	±0.03	±0.01	±2.03	±0.14	±0.09	±0.02
	2.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.35	0.29	0.10	0.02	11.66	2.45	0.62	0.13
		S.D.	±0.12	±0.07	±0.02	±0.00	±2.41	±0.32	±0.10	±0.03
	12.5 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	1.33	0.32	0.09	0.02	15.04**	3.54**	0.60	0.14
		S.D.	±0.08	±0.05	±0.02	±0.01	±2.96	±0.41	±0.06	±0.02

\*\* : P&lt;0.01 (significantly different from control).

Two males in the 0.1 mg/kg group and one female in the 12.5 mg/kg group died.

Table 14 - continued  
Organ weights  
Male, Female, 52w

Sex	Group and dose		Kidneys		Adrenals		Epididymides		Testes	
			(g)	(g/100 gB.W.)	(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N	10	10	10	10	10	10	10	10
		Mean	3.78	0.47	63.7	7.9	1.30	0.16	3.60	0.45
		S.D.	±0.50	±0.05	±8.7	±1.2	±0.10	±0.03	±0.33	±0.06
	0.1 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	3.76	0.48	61.6	8.0	1.35	0.18	3.61	0.47
		S.D.	±0.46	±0.08	±8.3	±1.9	±0.08	±0.04	±0.36	±0.10
	0.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	4.29	0.51	60.9	7.3	1.37	0.17	3.78	0.46
		S.D.	±0.63	±0.06	±10.9	±1.1	±0.13	±0.02	±0.31	±0.07
	2.5 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	4.12	0.68**	55.6	9.1	1.28	0.22*	3.65	0.61**
		S.D.	±0.40	±0.09	±8.8	±0.9	±0.26	±0.06	±0.73	±0.15
Female	Control	N	10	10	10	10				
		Mean	2.29	0.55	76.3	18.4				
		S.D.	±0.43	±0.08	±16.8	±4.0				
	0.5 mg/kg	N	10	10	10	10				
		Mean	2.35	0.54	79.6	18.0				
		S.D.	±0.33	±0.06	±25.3	±4.7				
	2.5 mg/kg	N	10	10	10	10				
		Mean	2.39	0.52	81.2	17.6				
		S.D.	±0.29	±0.13	±32.9	±8.1				
	12.5 mg/kg	N	9	9	9	9				
		Mean	2.63	0.63	73.9	17.7				
		S.D.	±0.26	±0.09	±10.2	±3.4				

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\*: P<0.05, \*\*: P<0.01 (significantly different from control).  
Two males in the 0.1 mg/kg group and one female in the 12.5 mg/kg group died.

Table 14 - continued  
Organ weights  
Male, Female, 52w

Sex	Group and dose		Ovaries		Uterus	
			(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)
Male	Control	N				
		Mean				
		S.D.				
	0.1 mg/kg	N				
		Mean				
		S.D.				
	0.5 mg/kg	N				
		Mean				
		S.D.				
	2.5 mg/kg	N				
		Mean				
		S.D.				
Female	Control	N	10	10	10	10
		Mean	67.0	16.0	0.97	0.24
		S.D.	±17.0	±3.3	±0.25	±0.08
	0.5 mg/kg	N	10	10	10	10
		Mean	62.2	14.3	0.96	0.22
		S.D.	±17.5	±4.4	±0.24	±0.06
	2.5 mg/kg	N	10	10	10	10
		Mean	64.5	13.5	0.97	0.22
		S.D.	±32.6	±5.5	±0.26	±0.09
	12.5 mg/kg	N	8	8	9	9
		Mean	60.9	14.3	1.03	0.25
		S.D.	±18.2	±2.5	±0.22	±0.08

Not significantly different from control.

One female in the 12.5 mg/kg group died.

The ovaries in one female in the 12.5 mg/kg group were not weighed due to the dilatation of paraovarian bursa, prevents obtaining the actual ovary weights.

Table 15 Histopathological findings  
Male, Female, 13w

Organs and findings	Sex		Male																		
	Group and dose		Control				0.1 mg/kg				0.5 mg/kg				2.5 mg/kg						
	Number of animals		10				10				10				9						
			-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++
Digestive system																					
Tongue		NR (10)				(0)				(0)				NR (9)							
Esophagus		(10)				(0)				(0)				(9)							
Fibrosis, muscular layer		9	1	0	0	1									9	0	0	0	0		
Stomach		NR (10)				(0)				(0)				NR (9)							
Duodenum		NR (10)				(0)				(0)				NR (9)							
Jejunum		NR (10)				(0)				(0)				NR (9)							
Ileum		NR (10)				(0)				(0)				NR (9)							
Cecum		NR (10)				(0)				(0)				NR (9)							
Colon		NR (10)				(0)				(0)				NR (9)							
Rectum		NR (10)				(0)				(0)				NR (9)							
Submaxillary gland		NR (10)				(0)				(0)				NR (9)							
Sublingual gland		NR (10)				(0)				(0)				NR (9)							
Parotid gland		NR (10)				(0)				(0)				NR (9)							
Liver		(10)				(10)				(10)				(9)							
Degeneration, hepatocyte, fatty, midzonal		10	0	0	0	0	9	1	0	0	1	10	0	0	0	0	9	0	0	0	0
Degeneration, hepatocyte, fatty, periportal		10	0	0	0	0	10	0	0	0	0	10	0	0	0	0	9	0	0	0	0
Necrosis, hepatocyte, focal		9	1	0	0	1	10	0	0	0	0	9	1	0	0	1	7	2	0	0	2
Hypertrophy, hepatocyte <sup>1)</sup> , centrilobular		10	0	0	0	0	10	0	0	0	0	7	3	0	0	3	0	6	3	0	9**
Cellular infiltration, mononuclear cell		9	1	0	0	1	7	3	0	0	3	8	2	0	0	2	9	0	0	0	0
Pancreas		(10)				(0)				(0)				(9)							
Atrophy, acinus, focal		10	0	0	0	0									9	0	0	0	0		
Respiratory system																					
Trachea		NR (10)				(0)				(0)				NR (9)							
Lung		(10)				(0)				(0)				(9)							
Accumulation, foam cell, alveolus		9	1	0	0	1									6	3	0	0	3		
Mineralization, artery		9	1	0	0	1									8	1	0	0	1		
Hematopoietic system																					
Thymus		(10)				(0)				(0)				(9)							
Hemorrhage		10	0	0	0	0									9	0	0	0	0		
Submaxillary lymph node		NR (10)				(0)				(0)				NR (9)							
Mesenteric lymph node		NR (10)				(0)				(0)				NR (9)							

\*\* : P &lt; 0.01 (significantly different from control).

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

NR: no remarkable changes.

1) with eosinophilic granular cytoplasm.

Figures in parentheses are number of animals with tissues examined histopathologically.

One male in the 2.5 mg/kg group died.



Table 15 - continued  
Histopathological findings  
Male, Female, 13w

Organs and findings	Sex Group and dose Number of animals	Male																			
		Control					0.1 mg/kg					0.5 mg/kg					2.5 mg/kg				
		10					10					10					9				
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Hematopoietic system																					
Spleen		NR (10)					(0)					(0)					NR (9)				
Bone marrow (sternum)		NR (10)					(0)					(0)					NR (9)				
Bone marrow (femur)		NR (10)					(0)					(0)					NR (9)				
Cardiovascular system																					
Heart		(10)					(0)					(0)					(9)				
Cellular infiltration, mononuclear cell		8	2	0	0	2											5	4	0	0	4
Aorta		NR (10)					(0)					(0)					NR (9)				
Urinary system																					
Kidney		(10)					(0)					(0)					(9)				
Tubule, basophilic		10	0	0	0	0											8	1	0	0	1
Cast, proteinaceous		9	1	0	0	1											9	0	0	0	0
Cellular infiltration, pelvis, neutrophil		10	0	0	0	0											8	1	0	0	1
Mineralization, corticomedullary		10	0	0	0	0											9	0	0	0	0
Nephroblastoma		10	0	0	0	0											9	0	0	0	0
Urinary bladder		NR (10)					(0)					(0)					NR (9)				
Genital system																					
Testis		NR (10)					(0)					(0)					NR (9)				
Epididymis		NR (10)					(0)					(0)					NR (9)				
Prostate		(10)					(0)					(0)					(9)				
Cellular infiltration, mononuclear cell		8	2	0	0	2											7	2	0	0	2
Seminal vesicle		NR (10)					(0)					(0)					NR (9)				
Ovary		NA					NA					NA					NA				
Uterus		NA					NA					NA					NA				
Vagina		NA					NA					NA					NA				
Mammary gland		NR (10)					(0)					(0)					NR (9)				
Endocrine system																					
Pituitary		NR (10)					(0)					(0)					NR (9)				
Thyroid		(10)					(0)					(0)					(9)				
Remnant, ultimobranchial body		10	0	0	0	0											8	1	0	0	1

Not significantly different from control.

Grade sign: -, none; +, mild(existent of tumor); ++, moderate; +++, marked.

NR: no remarkable changes.

NA: not applicable.

Figures in parentheses are number of animals with tissues examined histopathologically.

One male in the 2.5 mg/kg group died.



Table 15 - continued Histopathological findings  
Male, Female, 13w

Organs and findings	Sex	Group and dose	Female																			
			Control					0.5 mg/kg					2.5 mg/kg					12.5 mg/kg				
			10					10					10					10				
			-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
<b>Digestive system</b>																						
Tongue																						
Esophagus																						
Fibrosis, muscular layer																						
Stomach																						
Duodenum																						
Jejunum																						
Ileum																						
Cecum																						
Colon																						
Rectum																						
Submaxillary gland																						
Sublingual gland																						
Parotid gland																						
Liver																						
Degeneration, hepatocyte, fatty, midzonal																						
Degeneration, hepatocyte, fatty, periportal																						
Necrosis, hepatocyte, focal																						
Hypertrophy, hepatocyte <sup>1)</sup> , centrilobular																						
Cellular infiltration, mononuclear cell																						
Pancreas																						
Atrophy, acinus, focal																						
<b>Respiratory system</b>																						
Trachea																						
Lung																						
Accumulation, foam cell, alveolus																						
Mineralization, artery																						
<b>Hematopoietic system</b>																						
Thymus																						
Hemorrhage																						
Submaxillary lymph node																						
Mesenteric lymph node																						

\*\* : P<0.01 (significantly different from control).  
Grade sign: -, none; +, mild; ++, moderate; +++, marked.  
NR: no remarkable changes.

1) with eosinophilic granular cytoplasm.  
Figures in parentheses are number of animals with tissues examined histopathologically.

Table 15 - continued

Histopathological findings  
Male, Female, 13w

Organs and findings	Sex		Female																	
	Group and dose		Control				0.5 mg/kg				2.5 mg/kg				12.5 mg/kg					
	Number of animals		10				10				10				10					
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Hematopoietic system																				
Spleen																				
Bone marrow (sternum)																				
Bone marrow (femur)																				
Cardiovascular system																				
Heart																				
Cellular infiltration, mononuclear cell																				
Aorta																				
Urinary system																				
Kidney																				
Tubule, basophilic																				
Cast, proteinaceous																				
Cellular infiltration, pelvis, neutrophil																				
Mineralization, corticomedullary																				
Nephroblastoma																				
Urinary bladder																				
Genital system																				
Testis																				
Epididymis																				
Prostate																				
Cellular infiltration, mononuclear cell																				
Seminal vesicle																				
Ovary																				
Uterus																				
Vagina																				
Mammary gland																				
Endocrine system																				
Pituitary																				
Thyroid																				
Remnant, ultimobranchial body																				

Not significantly different from control.  
 Grade sign: -, none; +, mild(existent of tumor); ++, moderate; +++, marked.  
 NR: no remarkable changes.  
 NA: not applicable.  
 Figures in parentheses are number of animals with tissues examined histopathologically.

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Table 15 - continued

Histopathological findings  
Male, Female, 13w

Organs and findings	Sex		Female																							
	Group and dose		Control					0.5 mg/kg					2.5 mg/kg					12.5 mg/kg								
	Number of animals		10					10					10					10								
			-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total				
Endocrine system																										
Parathyroid		NR(10)					(0)					(0)					NR(10)									
Adrenal		(10)					(0)					(0)					(10)									
Hypertrophy, cortical cell, focal		10	0	0	0	0																10	0	0	0	0
Nervous system																										
Cerebrum		(10)					(0)					(0)					(10)									
Dilatation, lateral ventricle		10	0	0	0	0																10	0	0	0	0
Cerebellum		NR(10)					(0)					(0)					NR(10)									
Medulla oblongata		NR(10)					(0)					(0)					NR(10)									
Spinal cord		NR(10)					(0)					(0)					NR(10)									
Optic nerve		NR(10)					(0)					(0)					NR(10)									
Sciatic nerve		NR(10)					(0)					(0)					NR(10)									
Special sense organs																										
Eye		NR(10)					(0)					(0)					NR(10)									
Harderian gland		NR(10)					(0)					(0)					NR(10)									
Musculoskeletal system																										
M. biceps femoris		NR(10)					(0)					(0)					NR(10)									
Sternum		NR(10)					(0)					(0)					NR(10)									
Femur		NR(10)					(0)					(0)					NR(10)									
Integumentary system																										
Integument		NR(10)					(0)					(0)					NR(10)									

Not significantly different from control.

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

NR: no remarkable changes.

Figures in parentheses are number of animals with tissues examined histopathologically.





Table 16 - continued Histopathological findings  
Male, Female, 52w

Organs and findings	Sex		Male																	
	Group and dose		Control				0.1 mg/kg				0.5 mg/kg				2.5 mg/kg					
	Number of animals		10				8				10				10					
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Hematopoietic system																				
Bone marrow (femur)																				
(10)																				
Atrophy, focal																				
	10	0	0	0	0	(0)				(0)				(10)						
Hematopoiesis, increased																				
	9	1	0	0	1									10 0 0 0 0						
Cardiovascular system																				
Heart																				
(10)																				
Cellular infiltration, mononuclear cell																				
	7	3	0	0	3	(0)				(0)				6 4 0 0 4						
Fibrosis, myocardium																				
	6	4	0	0	4	(0)				(0)				8 2 0 0 2						
Aorta																				
NR(10)																				
(0)																				
(0)																				
NR(10)																				
Urinary system																				
Kidney																				
(10)																				
(0)																				
(0)																				
(10)																				
Hyperplasia, epithelial cell, tubule																				
	10	0	0	0	0									10 0 0 0 0						
Hyperplasia, transitional cell, pelvis																				
	10	0	0	0	0									10 0 0 0 0						
Tubule, basophilic																				
	6	4	0	0	4									8 2 0 0 2						
Cast, proteinaceous																				
	6	4	0	0	4									8 2 0 0 2						
Hemorrhage, pelvis																				
	9	1	0	0	1									10 0 0 0 0						
Cellular infiltration, mononuclear cell, pelvis																				
	8	2	0	0	2									10 0 0 0 0						
Cellular infiltration, mononuclear cell, cortex																				
	8	2	0	0	2									9 1 0 0 1						
Cellular infiltration, pelvis, neutrophil																				
	9	1	0	0	1									10 0 0 0 0						
Cellular infiltration, cortex, neutrophil																				
	10	0	0	0	0									10 0 0 0 0						
Cellular exudation, pelvic cavity, neutrophil																				
	9	1	0	0	1									10 0 0 0 0						
Mineralization, papilla																				
	10	0	0	0	0									8 2 0 0 2						
Mineralization, pelvis																				
	9	1	0	0	1									10 0 0 0 0						
Urinary bladder																				
(10)																				
(0)																				
(0)																				
(10)																				
Cellular infiltration, muscular layer, neutrophil																				
	9	1	0	0	1									10 0 0 0 0						

Not significantly different from control.  
Grade sign: -, none; +, mild; ++, moderate; +++, marked.  
NR: no remarkable changes.  
Figures in parentheses are number of animals with tissues examined histopathologically.  
Two males in the 0.1 mg/kg group died.



Table 16 - continued Histopathological findings  
Male, Female, 52w

Organs and findings	Sex Group and dose Number of animals	Male																				
		Control					0.1 mg/kg					0.5 mg/kg					2.5 mg/kg					
		10					8					10					10					
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	
Genital system																						
Testis				(10)				(0)						(0)				(10)				
Atrophy, seminiferous tubule	10	0	0	0	0													8	0	1	1	2
Hyperplasia, leydig cell, focal	10	0	0	0	0													9	1	0	0	1
Epididymis			(10)						(0)					(0)						(10)		
Decrease, sperm, lumen	10	0	0	0	0													9	0	0	1	1
Cellular infiltration, mononuclear cell	9	1	0	0	1													10	0	0	0	0
Prostate			(10)						(0)					(0)						(10)		
Atrophy	6	4	0	0	4													5	3	2	0	5
Hemorrhage	10	0	0	0	0													9	1	0	0	1
Cellular infiltration, mononuclear cell	9	1	0	0	1													8	2	0	0	2
Seminal vesicle			NR	(10)					(0)					(0)						NR	(10)	
Ovary			NA						NA					NA						NA		
Dilatation, ovarian bursa																						
Cyst																						
Uterus			NA						NA					NA						NA		
Metaplasia, epithelial cell, gland, squamous																						
Polyp, endometrial stromal																						
Vagina			NA						NA					NA						NA		
Degeneration, epithelium, mucous																						
Mammary gland			(10)						(0)					(0)						(10)		
Hyperplasia, lobular	10	0	0	0	0													10	0	0	0	0
Ectasia, alveolus/duct	10	0	0	0	0													10	0	0	0	0
Adenoma	10	0	0	0	0													10	0	0	0	0
Fibroadenoma	10	0	0	0	0													10	0	0	0	0
Adenocarcinoma	10	0	0	0	0													10	0	0	0	0

Not significantly different from control.  
Grade sign: -, none; +, mild(existent of tumor); ++, moderate; +++, marked.  
NR: no remarkable changes.  
NA: not applicable.  
Figures in parentheses are number of animals with tissues examined histopathologically.  
Two males in the 0.1 mg/kg group died.

Table 16 - continued  
Histopathological findings  
Male, Female, 52w

Organs and findings	Sex Group and dose Number of animals	Male																	
		Control				0.1 mg/kg				0.5 mg/kg				2.5 mg/kg					
		10				8				10				10					
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++
Endocrine system																			
Pituitary																			
		(10)				(0)				(0)				(10)					
		7	3	0	0	3													
		10	0	0	0	0													
Thyroid																			
		(10)				(0)				(0)				(10)					
		10	0	0	0	0													
		10	0	0	0	0													
		9	1	0	0	1													
Parathyroid																			
		NR (10)				(0)				(0)				NR (10)					
Adrenal																			
		(10)				(0)				(0)				(10)					
		8	2	0	0	2													
		9	1	0	0	1													
		10	0	0	0	0													
Nervous system																			
		NR (10)				(0)				(0)				NR (10)					
		NR (10)				(0)				(0)				NR (10)					
		NR (10)				(0)				(0)				NR (10)					
		NR (10)				(0)				(0)				NR (10)					
		NR (10)				(0)				(0)				NR (10)					
		NR (10)				(0)				(0)				NR (10)					
Special sense organs																			
		NR (10)				(0)				(0)				NR (10)					
		(10)				(0)				(0)				(10)					
		10	0	0	0	0													
Musculoskeletal system																			
		NR (10)				(0)				(0)				NR (10)					

Not significantly different from control.

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

NR: no remarkable changes.

NA: not applicable.

Figures in parentheses are number of animals with tissues examined histopathologically.

Two males in the 0.1 mg/kg group died.