

Table 12 - continued
Absolute and relative 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	3.63	0.60	61.5	10.1	1.36	0.23	3.59	0.59
		S.D.	±0.19	±0.05	±5.9	±1.1	±0.06	±0.03	±0.32	±0.06
	4 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	3.70	0.64	60.4	10.4	1.40	0.24	3.78	0.66
		S.D.	±0.45	±0.05	±10.8	±1.7	±0.09	±0.03	±0.62	±0.13
	20 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	3.69	0.62	58.3	9.8	1.35	0.23	3.45	0.58
		S.D.	±0.52	±0.07	±8.6	±1.2	±0.18	±0.02	±0.31	±0.05
	100 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	4.01	0.64	59.6	9.5	1.34	0.21	3.59	0.57
		S.D.	±0.55	±0.06	±4.9	±0.8	±0.13	±0.03	±0.34	±0.05
Female	Control	N	10	10	10	10				
		Mean	1.88	0.60	67.0	21.3				
		S.D.	±0.15	±0.05	±7.5	±2.6				
	4 mg/kg	N	10	10	10	10				
		Mean	1.87	0.61	64.9	21.1				
		S.D.	±0.14	±0.04	±9.4	±2.6				
	20 mg/kg	N	10	10	10	10				
		Mean	2.01	0.64	66.4	21.1				
		S.D.	±0.21	±0.04	±11.2	±2.0				
	100 mg/kg	N	10	10	10	10				
		Mean	2.01	0.65*	68.7	22.4				
		S.D.	±0.19	±0.05	±9.5	±2.5				

*: P<0.05 (significantly different from control).

One male in the 4 mg/kg group was imminently sacrificed when moribund and one male in the 100 mg/kg group died.

Table 12 - continued
Absolute and relative 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.				
	4 mg/kg	N				
		Mean				
		S. D.				
	20 mg/kg	N				
		Mean				
		S. D.				
	100 mg/kg	N				
		Mean				
		S. D.				
Female	Control	N	10	10	10	10
		Mean	77.7	24.6	0.65	0.21
		S. D.	±10.4	±3.4	±0.15	±0.06
	4 mg/kg	N	10	10	10	10
		Mean	77.7	25.4	0.72	0.24
		S. D.	±9.1	±3.0	±0.17	±0.06
	20 mg/kg	N	10	10	10	10
		Mean	82.4	26.4	0.64	0.21
		S. D.	±10.2	±4.1	±0.11	±0.03
	100 mg/kg	N	10	10	10	10
		Mean	81.3	26.5	0.61	0.20
		S. D.	±8.8	±2.5	±0.13	±0.06

Not significantly different from control.

Table 13 Absolute and relative 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	853.9	2.52	0.30	17.3	2.0	33.1	3.9	2.05	0.24
		S.D.	±106.6	±0.13	±0.04	±3.8	±0.4	±5.2	±0.7	±0.23	±0.02
	4 mg/kg	N	8	8	8	8	8	8	8	8	8
		Mean	801.5	2.44	0.31	16.0	2.0	37.3	4.7	1.89	0.24
		S.D.	±79.6	±0.08	±0.03	±1.9	±0.2	±7.2	±1.0	±0.15	±0.01
	20 mg/kg	N	8	8	8	8	8	8	8	8	8
		Mean	846.9	2.42	0.29	25.9	3.2	34.1	4.0	1.93	0.23
		S.D.	±138.4	±0.08	±0.04	±18.1	±2.8	±10.1	±0.7	±0.24	±0.01
	100 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	884.2	2.48	0.29	32.6	3.6	42.1*	4.8*	1.99	0.23
		S.D.	±135.7	±0.08	±0.04	±48.0	±4.9	±7.5	±0.5	±0.28	±0.02
Female	Control	N	10	10	10	10	10	10	10	10	10
		Mean	432.9	2.11	0.50	27.3	6.4	23.8	5.6	1.21	0.28
		S.D.	±77.3	±0.11	±0.08	±6.1	±1.6	±5.2	±1.2	±0.10	±0.03
	4 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	408.3	2.10	0.52	46.8	12.2	22.2	5.4	1.18	0.29
		S.D.	±53.6	±0.10	±0.07	±47.8	±14.4	±6.2	±1.3	±0.12	±0.04
	20 mg/kg	N	9	9	9	9	9	9	9	9	9
		Mean	435.3	2.12	0.49	36.3	8.3	23.8	5.5	1.22	0.28
		S.D.	±38.5	±0.06	±0.05	±15.3	±3.4	±1.6	±0.5	±0.11	±0.02
	100 mg/kg	N	10	10	10	10	10	10	10	10	10
		Mean	452.8	2.18	0.50	32.4	7.4	26.9	6.1	1.29	0.29
		S.D.	±93.4	±0.08	±0.11	±7.8	±2.4	±3.7	±0.9	±0.18	±0.03

*: P<0.05 (significantly different from control).

One male in the 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males and one female in the 20 mg/kg group died.

Table 13 - continued Absolute and relative 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	1.93	0.23	0.11	0.01	20.37	2.40	1.01	0.12
		S.D.	±0.19	±0.03	±0.03	±0.00	±1.92	±0.15	±0.16	±0.02
	4 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	1.88	0.24	0.09	0.01	19.58	2.42	1.05	0.13
		S.D.	±0.13	±0.02	±0.03	±0.00	±4.28	±0.33	±0.35	±0.03
	20 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	1.94	0.23	0.09	0.01	20.56	2.42	0.97	0.11
		S.D.	±0.20	±0.02	±0.02	±0.00	±5.01	±0.34	±0.19	±0.02
	100 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.97	0.23	0.10	0.01	25.21*	2.86**	1.32	0.15
		S.D.	±0.18	±0.02	±0.03	±0.00	±4.20	±0.27	±0.42	±0.06
Female	Control	N	10	10	10	10	10	10	10	10
		Mean	1.30	0.31	0.10	0.02	10.00	2.34	0.60	0.14
		S.D.	±0.08	±0.04	±0.03	±0.01	±1.17	±0.27	±0.09	±0.02
	4 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.32	0.33	0.08	0.02	11.09	2.73*	0.72	0.18
		S.D.	±0.09	±0.03	±0.02	±0.01	±1.61	±0.36	±0.30	±0.10
	20 mg/kg	N	9	9	9	9	9	9	9	9
		Mean	1.36	0.31	0.10	0.02	11.77*	2.71*	0.64	0.15
		S.D.	±0.08	±0.03	±0.03	±0.00	±1.20	±0.19	±0.15	±0.03
	100 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	1.37	0.32	0.08	0.02	15.66**	3.48**	0.74	0.17
		S.D.	±0.08	±0.07	±0.02	±0.01	±3.19	±0.41	±0.21	±0.05

*: P<0.05, **: P<0.01 (significantly different from control).

One male in the 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males and one female in the 20 mg/kg group died.

Table 13 - continued Absolute and relative 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	4.20	0.50	63.4	7.5	1.43	0.17	3.87	0.46
		S.D.	±0.38	±0.05	±7.3	±0.7	±0.18	±0.03	±0.39	±0.06
	4 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	4.10	0.51	65.7	8.2	1.43	0.18	3.87	0.49
		S.D.	±0.46	±0.03	±12.1	±0.8	±0.15	±0.02	±0.33	±0.06
	20 mg/kg	N	8	8	8	8	8	8	8	8
		Mean	4.23	0.50	64.1	7.7	1.27	0.15	3.56	0.42
		S.D.	±0.73	±0.05	±6.1	±1.5	±0.25	±0.03	±0.77	±0.08
	100 mg/kg	N	10	10	10	10	10	10	10	10
		Mean	4.61	0.53	68.0	7.8	1.31	0.15	3.83	0.44
		S.D.	±0.68	±0.08	±13.5	±1.4	±0.15	±0.03	±0.54	±0.05
Female	Control	N	10	10	10	10				
		Mean	2.29	0.54	83.8	19.7				
		S.D.	±0.26	±0.10	±18.3	±4.5				
	4 mg/kg	N	10	10	10	10				
		Mean	2.31	0.57	80.4	19.9				
		S.D.	±0.30	±0.07	±12.6	±3.3				
	20 mg/kg	N	9	9	9	9				
		Mean	2.45	0.56	77.1	17.9				
		S.D.	±0.30	±0.06	±13.3	±3.8				
	100 mg/kg	N	10	10	10	10				
		Mean	2.75**	0.63	81.3	18.6				
		S.D.	±0.33	±0.12	±17.3	±5.5				

** : P<0.01 (significantly different from control).

One male in the 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males and one female in the 20 mg/kg group died.

Table 13 - continued
Absolute and relative 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.				
	4 mg/kg	N				
Mean						
S.D.						
20 mg/kg	N					
	Mean					
	S.D.					
100 mg/kg	N					
	Mean					
	S.D.					
Female	Control	N	10	10	10	10
		Mean	51.4	12.2	0.95	0.23
		S.D.	±10.3	±3.1	±0.19	±0.07
	4 mg/kg	N	10	10	10	10
		Mean	48.7	11.9	1.22	0.30
		S.D.	±12.1	±2.3	±0.43	±0.11
	20 mg/kg	N	9	9	9	9
		Mean	52.1	12.0	1.03	0.24
		S.D.	±15.8	±4.0	±0.25	±0.06
	100 mg/kg	N	10	10	10	10
		Mean	56.8	13.1	1.03	0.24
		S.D.	±19.5	±5.2	±0.18	±0.06

Not significantly different from control.
One female in the 20 mg/kg group died.

Table 14 Histopathological findings
Male, Female, 13w

Organs and findings	Sex		Male														
	Group and dose		Control					4 mg/kg					20 mg/kg				
	Number of animals		10					9					10				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total		
Digestive system																	
Tongue																	
Esophagus																	
Stomach																	
Duodenum																	
Jejunum																	
Ileum																	
Cecum																	
Colon																	
Rectum																	
Submaxillary gland																	
Sublingual gland																	
Parotid gland																	
Liver																	
Degeneration, hepatocyte, fatty, centrilobular	10	0	0	0	0	9	0	0	0	0	8	2	0	0	2		
Degeneration, hepatocyte, fatty, periportal	7	3	0	0	3	6	3	0	0	3	5	5	0	0	5		
Necrosis, hepatocyte, focal	10	0	0	0	0	9	0	0	0	0	10	0	0	0	0		
Hypertrophy, hepatocyte, centrilobular	10	0	0	0	0	9	0	0	0	0	10	0	0	0	0		
Cellular infiltration, mononuclear cell	10	0	0	0	0	9	0	0	0	0	10	0	0	0	0		
Fibrosis	9	1	0	0	1	9	0	0	0	0	10	0	0	0	0		
Pancreas																	
Atrophy, acinus, focal	8	2	0	0	2												
Cellular infiltration, mixed	9	1	0	0	1												
Respiratory system																	
Trachea																	
Lung																	
Metaplasia, osseous	7	3	0	0	3												
Accumulation, foam cell, alveolus	9	1	0	0	1												
Mineralization, artery	9	1	0	0	1												
Hematopoietic system																	
Thymus																	
Submaxillary lymph node																	

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.

One male in the 4 mg/kg group was imminently sacrificed when moribund.

Table 14 - continued
Histopathological findings
Male, Female, 13w

Organs and findings	Sex	Group and dose	Number of animals	Male														
				Control					4 mg/kg					20 mg/kg				
				10					9					10				
				-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Hematopoietic system																		
Mesenteric lymph node																		
Accumulation, foam cell			(10)					(0)					(10)					
Spleen			NR(10)					(0)					(0)					
Bone marrow (sternum)			NR(10)					(0)					(0)					
Bone marrow (femur)			NR(10)					(0)					(0)					
Cardiovascular system																		
Heart																		
Cellular infiltration, mononuclear cell			(10)					(0)					(0)					
Fibrosis, myocardium	8	2	0	0	2													
Aorta	9	1	0	0	1													
NR(10)								(0)					(0)					
Urinary system																		
Kidney																		
Tubule, basophilic	6	4	0	0	4	6	3	0	0	3	8	2	0	0	2			
Droplet, epithelial cell, proximal tubule, hyaline	10	0	0	0	0	9	0	0	0	0	7	3	0	0	3			
Cast, proteinaceous	10	0	0	0	0	9	0	0	0	0	10	0	0	0	0			
Cyst, medulla	10	0	0	0	0	8	1	0	0	1	10	0	0	0	0			
Cellular infiltration, mononuclear cell, pelvis	10	0	0	0	0	9	0	0	0	0	10	0	0	0	0			
Fibrosis, medulla	10	0	0	0	0	9	0	0	0	0	9	1	0	0	1			
Mineralization, cortex	9	1	0	0	1	9	0	0	0	0	10	0	0	0	0			
Mineralization, medulla	9	1	0	0	1	8	1	0	0	1	9	1	0	0	1			
Urinary bladder			(10)					(0)					(0)					
Granuloma, adventitia	10	0	0	0	0													
Genital system																		
Testis			NR(10)					(0)					(0)					
Epididymis			NR(10)					(0)					(0)					
Prostate			(10)					(0)					(0)					
Cellular infiltration, mononuclear cell	7	3	0	0	3													
Seminal vesicle			NR(10)					(0)					(0)					
Ovary			NA					NA					NA					
Uterus			NA					NA					NA					

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.

One male in the 4 mg/kg group was imminently sacrificed when moribund.

Table 14 - continued
Histopathological findings
Male, Female, 13w

Organs and findings	Sex Group and dose Number of animals	Male														
		Control					4 mg/kg					20 mg/kg				
		10					9					10				
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Genital system																
Vagina																
Degeneration, epithelium, mucous																
Mammary gland																
Endocrine system																
Pituitary																
Cyst, anterior lobe																
Thyroid																
Remnant, ultimobranchial body																
Parathyroid																
Adrenal																
Hypertrophy, cortical cell, focal																
Nervous system																
Cerebrum																
Cerebellum																
Medulla oblongata																
Spinal cord																
Optic nerve																
Sciatic nerve																
Special sense organs																
Eye																
Dysplasia, retina																
Harderian gland																
Musculoskeletal system																
M. biceps femoris																
Sternum																
Femur																
Integumentary system																
Integument																

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.

One male in the 4 mg/kg group was imminently sacrificed when moribund.

Table 14 - continued

Histopathological findings
Male, Female, 13w

Organs and findings	Sex		Male					Female									
	Group and dose		100 mg/kg					Control					4 mg/kg				
	Number of animals		9					10					10				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total		
Digestive system																	
Tongue					NR (9)					NR (10)					(0)		
Esophagus					NR (9)					NR (10)					(0)		
Stomach					NR (9)					NR (10)					(0)		
Duodenum					NR (9)					NR (10)					(0)		
Jejunum					NR (9)					NR (10)					(0)		
Ileum					NR (9)					NR (10)					(0)		
Cecum					NR (9)					NR (10)					(0)		
Colon					NR (9)					NR (10)					(0)		
Rectum					NR (9)					NR (10)					(0)		
Submaxillary gland					NR (9)					NR (10)					(0)		
Sublingual gland					NR (9)					NR (10)					(0)		
Parotid gland					NR (9)					NR (10)					(0)		
Liver					(9)					(10)					(10)		
Degeneration, hepatocyte, fatty, centrilobular	9	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Degeneration, hepatocyte, fatty, periportal	6	3	0	0	3	9	1	0	0	1	9	1	0	0	1		
Necrosis, hepatocyte, focal	9	0	0	0	0	10	0	0	0	0	9	1	0	0	1		
Hyper trophy, hepatocyte, centrilobular	7	2	0	0	2	10	0	0	0	0	10	0	0	0	0		
Cellular infiltration, mononuclear cell	9	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Fibrosis	9	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Pancreas					(9)					(10)					(0)		
Atrophy, acinus, focal	9	0	0	0	0	9	1	0	0	1							
Cellular infiltration, mixed	9	0	0	0	0	10	0	0	0	0							
Respiratory system																	
Trachea					NR (9)					NR (10)					(0)		
Lung					(9)					(10)					(0)		
Metaplasia, osseous	7	2	0	0	2	10	0	0	0	0							
Accumulation, foam cell, alveolus	8	1	0	0	1	10	0	0	0	0							
Mineralization, artery	5	4	0	0	4	8	2	0	0	2							
Hematopoietic system																	
Thymus					NR (9)					NR (10)					(0)		
Submaxillary lymph node					NR (9)					NR (10)					(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.

One male in the 100 mg/kg group died.

Table 14 - continued
Histopathological findings
Male, Female, 13w

Organs and findings	Sex		Male					Female									
	Group and dose		100 mg/kg					Control					4 mg/kg				
	Number of animals		9					10					10				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total		
Hematopoietic system																	
Mesenteric lymph node			(9)					(10)						(0)			
Accumulation, foam cell	7	2	0	0	2	10	0	0	0	0							
Spleen			NR(9)					NR(10)						(0)			
Bone marrow (sternum)			NR(9)					NR(10)						(0)			
Bone marrow (femur)			NR(9)					NR(10)						(0)			
Cardiovascular system																	
Heart																	
Cellular infiltration, mononuclear cell	5	4	0	0	4	10	0	0	0	0				(0)			
Fibrosis, myocardium	7	2	0	0	2	10	0	0	0	0							
Aorta			NR(9)					NR(10)						(0)			
Urinary system																	
Kidney																	
Tubule, basophilic	5	4	0	0	4	10	0	0	0	0	10	0	0	0	0		
Droplet, epithelial cell, proximal tubule, hyaline	4	5	0	0	5**	10	0	0	0	0	10	0	0	0	0		
Cast, proteinaceous	9	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Cyst, medulla	9	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Cellular infiltration, mononuclear cell, pelvis	8	1	0	0	1	10	0	0	0	0	10	0	0	0	0		
Fibrosis, medulla	9	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Mineralization, cortex	6	3	0	0	3	10	0	0	0	0	10	0	0	0	0		
Mineralization, medulla	9	0	0	0	0	10	0	0	0	0	9	1	0	0	1		
Urinary bladder			(9)					(10)						(0)			
Granuloma, adventitia	9	0	0	0	0	9	1	0	0	1							
Genital system																	
Testis			NR(9)					NA						NA			
Epididymis			NR(9)					NA						NA			
Prostate			(9)					NA						NA			
Cellular infiltration, mononuclear cell	7	2	0	0	2												
Seminal vesicle			NR(9)					NA						NA			
Ovary			NA					NR(10)						(0)			
Uterus			NA					NR(10)						(0)			

** : P<0.01 (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.

One male in the 100 mg/kg group died.

Table 14 - continued
Histopathological findings
Male, Female, 13w

Organs and findings	Sex	Male					Female									
	Group and dose	100 mg/kg					Control					4 mg/kg				
	Number of animals	9					10					10				
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Genital system																
Vagina		NA					(10)					(0)				
Degeneration, epithelium, mucous							10	0	0	0	0					
Mammary gland		NR(9)					NR(10)					(0)				
Endocrine system																
Pituitary		(9)					(10)					(0)				
Cyst, anterior lobe		9	0	0	0	0	10	0	0	0	0					
Thyroid		(9)					(10)					(0)				
Remnant, ultimobranchial body		6	3	0	0	3	6	4	0	0	4					
Parathyroid		NR(9)					NR(10)					(0)				
Adrenal		(9)					(10)					(0)				
Hypertrophy, cortical cell, focal		9	0	0	0	0	10	0	0	0	0					
Nervous system																
Cerebrum		NR(9)					NR(10)					(0)				
Cerebellum		NR(9)					NR(10)					(0)				
Medulla oblongata		NR(9)					NR(10)					(0)				
Spinal cord		NR(9)					NR(10)					(0)				
Optic nerve		NR(9)					NR(10)					(0)				
Sciatic nerve		NR(9)					NR(10)					(0)				
Special sense organs																
Eye		(9)					(10)					(0)				
Dysplasia, retina		9	0	0	0	0	10	0	0	0	0					
Harderian gland		NR(9)					NR(10)					(0)				
Musculoskeletal system																
M. biceps femoris		NR(9)					NR(10)					(0)				
Sternum		NR(9)					NR(10)					(0)				
Femur		NR(9)					NR(10)					(0)				
Integumentary system																
Integument		NR(9)					NR(10)					(0)				

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.

One male in the 100 mg/kg group died.

Table 14 - continued
Histopathological findings
Male, Female, 13w

Organs and findings	Sex		Female							
	Group and dose		20 mg/kg		100 mg/kg					
	Number of animals		10		10					
	-	+	++	+++	Total	-	+	++	+++	Total
Digestive system										
Tongue			(0)							NR (10)
Esophagus			(0)							NR (10)
Stomach			(0)							NR (10)
Duodenum			(0)							NR (10)
Jejunum			(0)							NR (10)
Ileum			(0)							NR (10)
Cecum			(0)							NR (10)
Colon			(0)							NR (10)
Rectum			(0)							NR (10)
Submaxillary gland			(0)							NR (10)
Sublingual gland			(0)							NR (10)
Parotid gland			(0)							NR (10)
Liver			(10)							(10)
Degeneration, hepatocyte, fatty, centrilobular	10	0	0	0	0	10	0	0	0	0
Degeneration, hepatocyte, fatty, periportal	8	2	0	0	2	6	4	0	0	4
Necrosis, hepatocyte, focal	9	1	0	0	1	10	0	0	0	0
Hypertrophy, hepatocyte, centrilobular	8	2	0	0	2	1	8	1	0	9**
Cellular infiltration, mononuclear cell	9	1	0	0	1	10	0	0	0	0
Fibrosis	10	0	0	0	0	10	0	0	0	0
Pancreas			(0)							(10)
Atrophy, acinus, focal						10	0	0	0	0
Cellular infiltration, mixed						10	0	0	0	0
Respiratory system										
Trachea			(0)							NR (10)
Lung			(0)							(10)
Metaplasia, osseous						10	0	0	0	0
Accumulation, foam cell, alveolus						10	0	0	0	0
Mineralization, artery						8	2	0	0	2
Hematopoietic system										
Thymus			(0)							NR (10)
Submaxillary lymph node			(0)							NR (10)

** : P<0.01 (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 14 - continued
Histopathological findings
Male, Female, 13w

Organs and findings	Sex		Female							
	Group and dose		20 mg/kg			100 mg/kg				
	Number of animals		10			10				
	-	+	++	+++	Total	-	+	++	+++	Total
Hematopoietic system										
Mesenteric lymph node			(10)					(10)		
Accumulation, foam cell	10	0	0	0	0	9	1	0	0	1
Spleen			(0)					NR	(10)	
Bone marrow (sternum)			(0)					NR	(10)	
Bone marrow (femur)			(0)					NR	(10)	
Cardiovascular system										
Heart			(0)					(10)		
Cellular infiltration, mononuclear cell						10	0	0	0	0
Fibrosis, myocardium						10	0	0	0	0
Aorta			(0)					NR	(10)	
Urinary system										
Kidney			(10)					(10)		
Tubule, basophilic	10	0	0	0	0	8	2	0	0	2
Droplet, epithelial cell, proximal tubule, hyaline	10	0	0	0	0	10	0	0	0	0
Cast, proteinaceous	10	0	0	0	0	9	1	0	0	1
Cyst, medulla	10	0	0	0	0	10	0	0	0	0
Cellular infiltration, mononuclear cell, pelvis	10	0	0	0	0	10	0	0	0	0
Fibrosis, medulla	10	0	0	0	0	10	0	0	0	0
Mineralization, cortex	10	0	0	0	0	10	0	0	0	0
Mineralization, medulla	8	2	0	0	2	10	0	0	0	0
Urinary bladder			(0)					(10)		
Granuloma, adventitia						10	0	0	0	0
Genital system										
Testis			NA					NA		
Epididymis			NA					NA		
Prostate			NA					NA		
Cellular infiltration, mononuclear cell										
Seminal vesicle			NA					NA		
Ovary			(0)					NR	(10)	
Uterus			(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.

Table 14 - continued Histopathological findings
Male, Female, 13w

Organs and findings	Sex	Female									
	Group and dose	20 mg/kg					100 mg/kg				
	Number of animals	10					10				
		-	+	++	+++	Total	-	+	++	+++	Total
Genital system											
Vagina				(0)					(10)		
Degeneration, epithelium, mucous						9	1	0	0	1	
Mammary gland				(0)					NR(10)		
Endocrine system											
Pituitary				(0)					(10)		
Cyst, anterior lobe						9	1	0	0	1	
Thyroid				(0)					(10)		
Remnant, ultimobranchial body						9	1	0	0	1	
Parathyroid				(0)					NR(10)		
Adrenal				(0)					(10)		
Hypertrophy, cortical cell, focal						10	0	0	0	0	
Nervous system											
Cerebrum				(0)					NR(10)		
Cerebellum				(0)					NR(10)		
Medulla oblongata				(0)					NR(10)		
Spinal cord				(0)					NR(10)		
Optic nerve				(0)					NR(10)		
Sciatic nerve				(0)					NR(10)		
Special sense organs											
Eye				(0)					(10)		
Dysplasia, retina						10	0	0	0	0	
Harderian gland				(0)					NR(10)		
Musculoskeletal system											
M. biceps femoris				(0)					NR(10)		
Sternum				(0)					NR(10)		
Femur				(0)					NR(10)		
Integumentary system											
Integument				(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 15 Histopathological findings
Male, Female, 52w

Organs and findings	Sex		Male												
	Group and dose		Control				4 mg/kg				20 mg/kg				
	Number of animals		10				8				8				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Digestive system															
Tongue															
Esophagus															
Stomach															
Dilatation, glandular space, glandular stomach	5	5	0	0	5										
Duodenum															
Accumulation, foam cell, lamina propria	10	0	0	0	0						8	0	0	0	0
Jejunum															
Accumulation, foam cell, lamina propria	10	0	0	0	0						8	0	0	0	0
Ileum															
Accumulation, foam cell, lamina propria	10	0	0	0	0						8	0	0	0	0
Accumulation, foam cell, peyer's patch	10	0	0	0	0						8	0	0	0	0
Cecum															
Colon															
Rectum															
Submaxillary gland															
Sublingual gland															
Parotid gland															
Liver															
Degeneration, hepatocyte, fatty, centrilobular	9	1	0	0	1	7	1	0	0	1	8	0	0	0	0
Degeneration, hepatocyte, fatty, periportal	4	5	1	0	6	7	1	0	0	1*	4	3	1	0	4
Necrosis, hepatocyte, focal	10	0	0	0	0	5	2	1	0	3*	8	0	0	0	0
Hypertrophy, hepatocyte, centrilobular	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Hyperplasia, bile duct	9	1	0	0	1	8	0	0	0	0	6	2	0	0	2
Hematopoiesis, extramedullary	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Focus, altered cell, basophilic	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Focus, altered cell, clear	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Angiectasis	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Hemorrhage	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Cellular infiltration, mononuclear cell	8	2	0	0	2	8	0	0	0	0	5	3	0	0	3
Accumulation, foam cell, sinusoid ⁶⁰	10	0	0	0	0	8	0	0	0	0	6	2	0	0	2
Cholangioma	9	1	0	0	1	8	0	0	0	0	8	0	0	0	0

*: P<0.05 (significantly different from control).

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

NR: no remarkable changes.

a) with lymphocyte infiltration.

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

One male in the 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males in the 20 mg/kg group died.

Table 15 - continued
Histopathological findings
Male, Female, 52w

Organs and findings	Sex	Group and dose	Male														
			Control					4 mg/kg					20 mg/kg				
			10					8					8				
			-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Digestive system																	
Pancreas																	
			(10)					(0)					(0)				
Atrophy, acinus, focal			10	0	0	0	0										
Hyperplasia, acinar cell, focal			8	2	0	0	2										
Focus, acinar cell, basophilic			8	2	0	0	2										
Metaplasia, hepatocyte			10	0	0	0	0										
Hemorrhage			9	1	0	0	1										
Polyarteritis			10	0	0	0	0										
Respiratory system																	
Trachea																	
			NR(10)					(0)					(0)				
Lung																	
			(10)					(0)					(0)				
Metaplasia, osseous			8	2	0	0	2										
Accumulation, foam cell, alveolus			9	1	0	0	1										
Mineralization, artery			6	4	0	0	4										
Hematopoietic system																	
Thymus																	
			(10)					(0)					(0)				
Atrophy			0	7	3	0	10										
Submaxillary lymph node																	
			NR(10)					(0)					(0)				
Mesenteric lymph node																	
			(10)					(8)					(8)				
Accumulation, foam cell			10	0	0	0	0	8	0	0	0	0	3	5	0	0	5**
Spleen																	
			(10)					(8)					(8)				
Hematopoiesis, extramedullary			10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Cyst, capsule			10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Accumulation, foam cell, white pulp			10	0	0	0	0	8	0	0	0	0	7	1	0	0	1
Accumulation, foam cell, red pulp			10	0	0	0	0	8	0	0	0	0	7	1	0	0	1
Bone marrow (sternum)																	
			NR(10)					(0)					(0)				
Bone marrow (femur)																	
			NR(10)					(0)					(0)				
Cardiovascular system																	
Heart																	
			(10)					(0)					(0)				
Cellular infiltration, mononuclear cell			4	6	0	0	6										
Fibrosis, myocardium			5	5	0	0	5										

** : P<0.01 (significantly different from control).

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

NR: no remarkable changes.

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

One male in the 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males in the 20 mg/kg group died.

Table 15 - continued
Histopathological findings
Male, Female, 52w

Organs and findings	Sex		Male												
	Group and dose		Control				4 mg/kg				20 mg/kg				
	Number of animals		10				8				8				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Cardiovascular system															
Aorta					NR (10)					(0)					(0)
Urinary system															
Kidney					(10)					(8)					(8)
Hyperplasia, transitional epithelium, pelvis	9	1	0	0	1	6	2	0	0	2	8	0	0	0	0
Tubule, basophilic	5	4	1	0	5	3	4	1	0	5	3	5	0	0	5
Karyomegaly, epithelial cell, proximal tubule	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Droplet, epithelial cell, proximal tubule, hyaline	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Cast, proteinaceous	8	2	0	0	2	6	2	0	0	2	4	4	0	0	4
Dilatation, distal tubule	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Dilatation, pelvic cavity	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Cyst, medulla	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Hemorrhage, pelvis	10	0	0	0	0	8	0	0	0	0	8	0	0	0	0
Cellular infiltration, mononuclear cell, pelvis	9	1	0	0	1	5	3	0	0	3	5	3	0	0	3
Cellular infiltration, mononuclear cell, cortex	9	1	0	0	1	6	2	0	0	2	7	1	0	0	1
Cellular exudation, pelvic cavity, neutrophil	9	1	0	0	1	6	2	0	0	2	5	3	0	0	3
Mineralization, pelvis	9	1	0	0	1	8	0	0	0	0	8	0	0	0	0
Mineralization, cortex	10	0	0	0	0	7	1	0	0	1	4	4	0	0	4*
Mineralization, medulla	10	0	0	0	0	8	0	0	0	0	7	1	0	0	1
Urinary bladder					NR (10)					(0)					(0)
Genital system															
Testis					(10)					(0)					(0)
Atrophy, seminiferous tubule	9	0	0	1	1										
Edema, interstitium	9	0	0	1	1										
Epididymis					(10)					(0)					(0)
Decrease, sperm, lumen	9	0	1	0	1										
Prostate					(10)					(0)					(0)
Cellular infiltration, mononuclear cell	9	1	0	0	1										
Fibrosis, interstitium	10	0	0	0	0										
Seminal vesicle					NR (10)					(0)					(0)
Ovary					NA					NA					NA

*: P<0.05 (significantly different from control).

Grade sign: -, none; +, mild (existence 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 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males in the 20 mg/kg group died.

Table 15 - continued Histopathological findings
Male, Female, 52w

Organs and findings	Sex Group and dose Number of animals	Male														
		Control					4 mg/kg					20 mg/kg				
		10					8					8				
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Genital system																
Uterus					NA					NA					NA	
Metaplasia, epithelial cell, gland, squamous																
Cyst, endometrium																
Vagina					NA					NA					NA	
Degeneration, epithelium, mucous																
Mammary gland					(10)					(0)					(0)	
Ectasia, alveolus/duct		10	0	0	0	0										
Adenoma		10	0	0	0	0										
Endocrine system																
Pituitary					(10)					(0)					(0)	
Hyperplasia, anterior lobe, focal		9	1	0	0	1										
Cyst, anterior lobe		10	0	0	0	0										
Hemorrhage, Rathke's pouch		10	0	0	0	0										
Gliosis, posterior lobe		9	1	0	0	1										
Ectopic tissue, posterior lobe		10	0	0	0	0										
Adenoma, anterior lobe		10	0	0	0	0										
Thyroid					(10)					(0)					(0)	
Hyperplasia, C cell, focal		9	1	0	0	1										
Remnant, ultimobranchial body		8	2	0	0	2										
Parathyroid					NR (10)					(0)					(0)	
Adrenal					(10)					(0)					(0)	
Hypertrophy, cortical cell, focal		9	1	0	0	1										
Hyperplasia, cortical cell, focal		10	0	0	0	0										
Angiectasis		10	0	0	0	0										
Nervous system																
Cerebrum					NR (10)					(0)					(0)	
Cerebellum					NR (10)					(0)					(0)	
Medulla oblongata					NR (10)					(0)					(0)	
Spinal cord					NR (10)					(0)					(0)	
Optic nerve					NR (10)					(0)					(0)	
Sciatic nerve					NR (10)					(0)					(0)	

Not significantly different from control.

Grade sign: -, none; +, mild (existence 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 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males in the 20 mg/kg group died.

Table 15 - continued
Histopathological findings
Male, Female, 52w

Organs and findings	Sex Group and dose Number of animals	Male														
		Control					4 mg/kg					20 mg/kg				
		10					8					8				
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Special sense organs																
Eye																
		(10)					(0)					(0)				
	Atrophy, retina, focal	10	0	0	0	0										
	Dysplasia, retina	10	0	0	0	0										
	Mineralization, cornea	10	0	0	0	0										
	Harderian gland	NR(10)					(0)					(0)				
Musculoskeletal system																
	M. biceps femoris	NR(10)					(0)					(0)				
	Sternum	NR(10)					(0)					(0)				
	Femur	NR(10)					(0)					(0)				
Integumentary system																
	Integument	(10)					(0)					(0)				
	Cellular infiltration, mononuclear cell, subcutis	10	0	0	0	0										
	Keratoacanthoma	9	1	0	0	1										
Others																
	Extremity	(4)					(0)					(0)				
	Formation, callus, hindlimb	4	0	0	0	0										
	Ulcer, hindlimb	0	4	0	0	4										

Not significantly different from control.

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

NR: no remarkable changes.

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

One male in the 4 mg/kg group died and one male in the 4 mg/kg group was imminently sacrificed when moribund.

Two males in the 20 mg/kg group died.

Table 15 - continued
Histopathological findings
Male, Female, 52w

Organs and findings	Sex		Male					Female									
	Group and dose		100 mg/kg					Control					4 mg/kg				
	Number of animals		10					10					10				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total		
Digestive system																	
Tongue																	
Esophagus																	
Stomach																	
Dilatation, glandular space, glandular stomach	7	3	0	0	3	8	2	0	0	2							
Duodenum																	
Accumulation, foam cell, lamina propria	9	1	0	0	1	10	0	0	0	0							
Jejunum																	
Accumulation, foam cell, lamina propria	2	8	0	0	8**	10	0	0	0	0							
Ileum																	
Accumulation, foam cell, lamina propria	4	6	0	0	6**	10	0	0	0	0							
Accumulation, foam cell, peyer's patch	7	3	0	0	3	10	0	0	0	0							
Cecum																	
Colon																	
Rectum																	
Submaxillary gland																	
Sublingual gland																	
Parotid gland																	
Liver																	
Degeneration, hepatocyte, fatty, centrilobular	10	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Degeneration, hepatocyte, fatty, periportal	5	3	2	0	5	7	3	0	0	3	9	1	0	0	1		
Necrosis, hepatocyte, focal	8	2	0	0	2	9	1	0	0	1	9	1	0	0	1		
Hypertrophy, hepatocyte, centrilobular	8	2	0	0	2	10	0	0	0	0	10	0	0	0	0		
Hyperplasia, bile duct	3	5	2	0	7**	9	1	0	0	1	10	0	0	0	0		
Hematopoiesis, extramedullary	10	0	0	0	0	10	0	0	0	0	9	1	0	0	1		
Focus, altered cell, basophilic	10	0	0	0	0	9	1	0	0	1	9	1	0	0	1		
Focus, altered cell, clear	9	1	0	0	1	10	0	0	0	0	10	0	0	0	0		
Angiectasis	9	1	0	0	1	9	1	0	0	1	10	0	0	0	0		
Hemorrhage	10	0	0	0	0	10	0	0	0	0	8	2	0	0	2		
Cellular infiltration, mononuclear cell	10	0	0	0	0	10	0	0	0	0	10	0	0	0	0		
Accumulation, foam cell, sinusoid ^{a)}	0	2	8	0	10**	10	0	0	0	0	10	0	0	0	0		
Cholangioma	10	0	0	0	0	10	0	0	0	0	10	0	0	0	0		

** : P<0.01 (significantly different from control).

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

NR: no remarkable changes.

a) with lymphocyte infiltration.

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

Table 15 - continued
Histopathological findings
Male, Female, 52w

Organs and findings	Sex		Male					Female									
	Group and dose		100 mg/kg					Control					4 mg/kg				
	Number of animals		10					10					10				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total		
Digestive system																	
Pancreas			(10)					(10)					(0)				
Atrophy, acinus, focal	9	1	0	0	1	7	3	0	0	3							
Hyperplasia, acinar cell, focal	9	1	0	0	1	10	0	0	0	0							
Focus, acinar cell, basophilic	10	0	0	0	0	10	0	0	0	0							
Metaplasia, hepatocyte	9	1	0	0	1	10	0	0	0	0							
Hemorrhage	10	0	0	0	0	10	0	0	0	0							
Polyarteritis	10	0	0	0	0	9	1	0	0	1							
Respiratory system																	
Trachea			NR (10)					NR (10)					(0)				
Lung			(10)					(10)					(0)				
Metaplasia, osseous	10	0	0	0	0	10	0	0	0	0							
Accumulation, foam cell, alveolus	8	2	0	0	2	9	1	0	0	1							
Mineralization, artery	8	2	0	0	2	10	0	0	0	0							
Hematopoietic system																	
Thymus			(10)					(10)					(0)				
Atrophy	0	6	4	0	10	1	8	1	0	9							
Submaxillary lymph node			NR (10)					NR (10)					(0)				
Mesenteric lymph node			(10)					(10)					(10)				
Accumulation, foam cell	0	3	6	1	10**	10	0	0	0	0	10	0	0	0	0		
Spleen			(10)					(10)					(10)				
Hematopoiesis, extramedullary	10	0	0	0	0	10	0	0	0	0	8	1	1	0	2		
Cyst, capsule	10	0	0	0	0	9	1	0	0	1	10	0	0	0	0		
Accumulation, foam cell, white pulp	6	3	1	0	4*	10	0	0	0	0	10	0	0	0	0		
Accumulation, foam cell, red pulp	6	3	1	0	4*	10	0	0	0	0	10	0	0	0	0		
Bone marrow (sternum)			NR (10)					NR (10)					(0)				
Bone marrow (femur)			NR (10)					NR (10)					(0)				
Cardiovascular system																	
Heart			(10)					(10)					(0)				
Cellular infiltration, mononuclear cell	5	5	0	0	5	9	1	0	0	1							
Fibrosis, myocardium	5	4	1	0	5	10	0	0	0	0							

*: P<0.05, **: P<0.01 (significantly different from control).

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

NR: no remarkable changes.

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

Table 15 - continued

Histopathological findings
Male, Female, 52w

Organs and findings	Sex	Male					Female									
	Group and dose	100 mg/kg					Control					4 mg/kg				
	Number of animals	10					10					10				
		-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total
Cardiovascular system																
Aorta					NR(10)					NR(10)						(0)
Urinary system																
Kidney					(10)					(10)						(10)
Hyperplasia, transitional epithelium, pelvis	10	0	0	0	0	9	1	0	0	1	8	2	0	0	2	
Tubule, basophilic	1	7	2	0	9	10	0	0	0	0	7	3	0	0	3	
Karyomegaly, epithelial cell, proximal tubule	9	1	0	0	1	10	0	0	0	0	10	0	0	0	0	
Droplet, epithelial cell, proximal tubule, hyaline	7	3	0	0	3	10	0	0	0	0	10	0	0	0	0	
Cast, proteinaceous	7	3	0	0	3	9	1	0	0	1	8	2	0	0	2	
Dilatation, distal tubule	10	0	0	0	0	10	0	0	0	0	10	0	0	0	0	
Dilatation, pelvic cavity	10	0	0	0	0	9	1	0	0	1	10	0	0	0	0	
Cyst, medulla	10	0	0	0	0	9	1	0	0	1	10	0	0	0	0	
Hemorrhage, pelvis	10	0	0	0	0	10	0	0	0	0	10	0	0	0	0	
Cellular infiltration, mononuclear cell, pelvis	10	0	0	0	0	9	1	0	0	1	10	0	0	0	0	
Cellular infiltration, mononuclear cell, cortex	10	0	0	0	0	10	0	0	0	0	10	0	0	0	0	
Cellular exudation, pelvic cavity, neutrophil	10	0	0	0	0	9	1	0	0	1	10	0	0	0	0	
Mineralization, pelvis	10	0	0	0	0	10	0	0	0	0	8	2	0	0	2	
Mineralization, cortex	8	2	0	0	2	10	0	0	0	0	10	0	0	0	0	
Mineralization, medulla	10	0	0	0	0	8	2	0	0	2	6	4	0	0	4	
Urinary bladder					NR(10)					NR(10)					(0)	
Genital system																
Testis					(10)					NA					NA	
Atrophy, seminiferous tubule	10	0	0	0	0											
Edema, interstitium	10	0	0	0	0											
Epididymis					(10)					NA					NA	
Decrease, sperm, lumen	10	0	0	0	0											
Prostate					(10)					NA					NA	
Cellular infiltration, mononuclear cell	9	1	0	0	1											
Fibrosis, interstitium	9	1	0	0	1											
Seminal vesicle					NR(10)					NA					NA	
Ovary					NA					NR(10)					(0)	

Not significantly different from control.

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

NR: no remarkable changes.

NA: not applicable.

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

Table 15 - continued
Histopathological findings
Male, Female, 52w

Organs and findings	Sex		Male					Female									
	Group and dose		100 mg/kg					Control					4 mg/kg				
	Number of animals		10					10					10				
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total		
Genital system																	
Uterus			NA					(10)					(0)				
Metaplasia, epithelial cell, gland, squamous						7	3	0	0	3							
Cyst, endometrium						10	0	0	0	0							
Vagina			NA					(10)					(0)				
Degeneration, epithelium, mucous						6	4	0	0	4							
Mammary gland			(10)					(10)					(0)				
Ectasia, alveolus/duct	9	1	0	0	1	2	2	6	0	8							
Adenoma	10	0	0	0	0	10	0	0	0	0							
Endocrine system																	
Pituitary			(10)					(10)					(0)				
Hyperplasia, anterior lobe, focal	9	1	0	0	1	8	2	0	0	2							
Cyst, anterior lobe	9	1	0	0	1	10	0	0	0	0							
Hemorrhage, Rathke's pouch	10	0	0	0	0	9	1	0	0	1							
Giosis, posterior lobe	10	0	0	0	0	10	0	0	0	0							
Ectopic tissue, posterior lobe	10	0	0	0	0	10	0	0	0	0							
Adenoma, anterior lobe	9	1	0	0	1	10	0	0	0	0							
Thyroid			(10)					(10)					(0)				
Hyperplasia, C cell, focal	10	0	0	0	0	10	0	0	0	0							
Remnant, ultimobranchial body	10	0	0	0	0	8	2	0	0	2							
Parathyroid			NR (10)					NR (9)					(0)				
Adrenal			(10)					(10)					(0)				
Hypertrophy, cortical cell, focal	10	0	0	0	0	10	0	0	0	0							
Hyperplasia, cortical cell, focal	9	1	0	0	1	4	6	0	0	6							
Angiectasis	10	0	0	0	0	3	7	0	0	7							
Nervous system																	
Cerebrum			NR (10)					NR (10)					(0)				
Cerebellum			NR (10)					NR (10)					(0)				
Medulla oblongata			NR (10)					NR (10)					(0)				
Spinal cord			NR (10)					NR (10)					(0)				
Optic nerve			NR (10)					NR (10)					(0)				
Sciatic nerve			NR (10)					NR (10)					(0)				

Not significantly different from control.

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

NR: no remarkable changes.

NA: not applicable.

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