1,3,5,7-テトラアザトリシクロ〔3.3.1.1 ^{3,7}〕デカンの
ラット及びマウスを用いた経口投与による
がん原性試験（混水試験）報告書

APPENDIX

（L1～R2）

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<12>				<11>				<16>				<20>			
	ulcer		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	thrombus		0 (0)	0 (0)	1 (8)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	4 (25)	1 (6)	0 (0)	0 (0)	4 (20)	4 (20)	0 (0)
	mineralization		5 (42)	0 (0)	0 (0)	0 (0)	9 (82)	0 (0)	0 (0)	0 (0)	4 (25)	0 (0)	0 (0)	0 (0)	11 (55)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		7 (58)	1 (8)	0 (0)	0 (0)	8 (73)	0 (0)	0 (0)	0 (0)	7 (44)	0 (0)	0 (0)	0 (0)	4 (20)	0 (0)	0 (0)	0 * (0)
	eosinophilic change:respiratory epithelium		2 (17)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)	0 (0)	5 (31)	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		4 (33)	2 (17)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	3 (15)	0 (0)	1 (5)	0 (0)
	inflammation:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		2 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<12>				<11>				<16>				<20>			
	respiratory metaplasia:gland		9	0	0	0	8	0	0	0	15	0	0	0	14	0	0	0
			(75)	(0)	(0)	(0)	(73)	(0)	(0)	(0)	(94)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
nasopharynx			<12>				<11>				<16>				<20>			
	inflammation		0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
larynx			<12>				<11>				<16>				<20>			
	inflammation		0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(5)	(0)	(0)
trachea			<12>				<11>				<16>				<20>			
	inflammation		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<12>				<11>				<16>				<20>			
	hemorrhage		0	0	0	0	0	0	1	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(9)	(0)	(6)	(0)	(0)	(0)	(0)	(5)	(0)	(0)
	edema		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
	thrombus		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			<12>				<11>				<16>				<20>			
	inflammation		0	0	0	0	2	0	1	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(18)	(0)	(9)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<12>				<11>				<16>				<20>			
	necrosis:focal		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
	increased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	erythropoiesis:increased		2	0	0	0	0	4	0	0 *	1	3	0	0	1	3	0	0
			(17)	(0)	(0)	(0)	(0)	(36)	(0)	(0)	(6)	(19)	(0)	(0)	(5)	(15)	(0)	(0)
	granulopoiesis:increased		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
lymph node			<12>				<11>				<16>				<20>			
	granulation		2 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphadenitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<12>				<11>				<16>				<20>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	2 (17)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	8 (40)	0 (0)	0 (0)
	fibrosis		0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	scar		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	1 (9)	0 (0)	1 (6)	1 (6)	3 (19)	0 (0)	0 (0)	1 (5)	1 (5)	0 (0)
[Circulatory system]																		
heart			<12>				<11>				<16>				<20>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<12>				<11>				<16>				<20>			
	mineralization		1 (8)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	3 (15)	6 (30)	2 (10)	0 (0)
	myocardial fibrosis		5 (42)	6 (50)	0 (0)	0 (0)	4 (36)	7 (64)	0 (0)	0 (0)	1 (6)	12 (75)	1 (6)	0 (0)	2 (10)	16 (80)	1 (5)	0 (0)
[Digestive system]																		
esophagus			<12>				<11>				<16>				<20>			
	necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
stomach			<12>				<11>				<16>				<20>			
	edema		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization		0 (0)	1 (8)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (15)	2 (10)	0 (0)	0 (0)
	erosion:forestomach		0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
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Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Digestive system]																		
stomach			<12>				<11>				<16>				<20>			
	ulcer:forestomach		0	0	3	0	0	1	0	0	1	0	0	1	1	0	0	0
			(0)	(0)	(25)	(0)	(0)	(9)	(0)	(0)	(6)	(0)	(0)	(6)	(5)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(9)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		3	1	0	0	1	1	0	0	2	0	0	0	1	0	0	0
			(25)	(8)	(0)	(0)	(9)	(9)	(0)	(0)	(13)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	ulcer:glandular stomach		0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(19)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<12>				<11>				<16>				<20>			
	herniation		0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	congestion		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	peliosis-like lesion		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)

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< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<12>				<11>				<16>				<20>			
	necrosis:central		1	0	0	0	0	0	0	0	0	2	0	0	1	2	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(5)	(10)	(0)	(0)
	necrosis:focal		1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)
	fatty change:central		0	0	0	1	0	0	0	0	0	0	0	0	1	1	1	0
			(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(5)	(5)	(0)
	fatty change:peripheral		1	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:central		0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(8)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	clear cell focus		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<12>				<11>				<16>				<20>			
	acidophilic cell focus		2 (17)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		1 (8)	1 (8)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)	0 (0)
	vacuolated cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	spongiosis hepatis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	2 (10)	1 (5)	0 (0)	0 (0)
	bile duct hyperplasia		9 (75)	3 (25)	0 (0)	0 (0)	7 (64)	2 (18)	0 (0)	0 (0)	6 (38)	8 (50)	0 (0)	0 (0)	14 (70)	4 (20)	1 (5)	0 (0)
	bile ductular proliferation		0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	biliary cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
pancreas			<12>				<11>				<16>				<20>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
pancreas			<12>				<11>				<16>				<20>			
	hyperplasia:acinar cell		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			<12>				<11>				<16>				<20>			
	congestion		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline droplet		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	chronic nephropathy		7	0	1	2	5	3	2	0	5	3	3	1	3	9	6	0 **
			(58)	(0)	(8)	(17)	(45)	(27)	(18)	(0)	(31)	(19)	(19)	(6)	(15)	(45)	(30)	(0)
	papillary necrosis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<12>				<11>				<16>				<20>			
	mineralization:papilla		1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortex		1 (8)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	8 (40)	3 (15)	0 (0)	0 (0)
	urothelial hyperplasia:pelivis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	1 (5)	2 (10)	0 (0)	0 (0)
urin bladd			<12>				<11>				<16>				<20>			
	simple hyperplasia:transitional epithelium		0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	nodular hyperplasia:transitional epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary			<12>				<11>				<16>				<20>			
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<12>				<11>				<16>				<20>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid			<12>				<11>				<16>				<20>			
	ultimibranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	1 (5)	1 (5)	0 (0)	0 (0)
adrenal			<12>				<11>				<16>				<20>			
	hyperplasia:cortical cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		1 (8)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	1 (5)	1 (5)	0 (0)	0 (0)
[Reproductive system]																		
testis			<12>				<11>				<16>				<20>			
	atrophy		1 (8)	1 (8)	5 (42)	0 (0)	0 (0)	1 (9)	6 (55)	0 (0)	1 (6)	2 (13)	8 (50)	0 (0)	1 (5)	1 (5)	11 (55)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
testis			<12>				<11>				<16>				<20>			
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	6 (30)	0 (0)	0 (0)	0 (0)
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	interstitial cell hyperplasia		5 (42)	0 (0)	0 (0)	0 (0)	3 (27)	0 (0)	0 (0)	0 (0)	7 (44)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 * (0)
prostate			<12>				<11>				<16>				<20>			
	inflammation		1 (8)	0 (0)	0 (0)	0 (0)	2 (18)	1 (9)	0 (0)	0 (0)	1 (6)	2 (13)	0 (0)	0 (0)	2 (10)	2 (10)	0 (0)	0 (0)
	hyperplasia		1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
mammary gl			<12>				<11>				<16>				<20>			
	duct ectasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	galactocele		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
prep/cli gl			<12>				<11>				<16>				<20>			
	duct ectasia		0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<12>				<11>				<16>				<20>			
	hemorrhage		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	gliosis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spinal cord			<12>				<11>				<16>				<20>			
	hemorrhage		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<12>				<11>				<16>				<20>			
	hemorrhage		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12 1 (%)	Control 12 2 (%)	Control 12 3 (%)	Control 12 4 (%)	7500 ppm 11 1 (%)	7500 ppm 11 2 (%)	7500 ppm 11 3 (%)	7500 ppm 11 4 (%)	15000 ppm 16 1 (%)	15000 ppm 16 2 (%)	15000 ppm 16 3 (%)	15000 ppm 16 4 (%)	30000 ppm 20 1 (%)	30000 ppm 20 2 (%)	30000 ppm 20 3 (%)	30000 ppm 20 4 (%)
[Special sense organs/appandage]																		
eye			<12>				<11>				<16>				<20>			
	cataract		0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
	retinal atrophy		3 (25)	6 (50)	2 (17)	0 (0)	4 (36)	5 (45)	2 (18)	0 (0)	0 (0)	12 (75)	4 (25)	0 (0)	5 (25)	7 (35)	8 (40)	0 (0)
	keratitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)
	iritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
Harder gl			<12>				<11>				<16>				<20>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		2 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
[Musculoskeletal system]																		
muscle			<12>				<11>				<16>				<20>			
	atrophy		1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Musculoskeletal system]																		
muscle			<12>				<11>				<16>				<20>			
	mineralization		0	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(8)	(0)	(0)	(18)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Sauere
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<3>				<11>				<15>				<36>			
	epidermal cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)
[Respiratory system]																		
nasal cavit			<3>				<11>				<15>				<36>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	1 (7)	0 (0)	2 (6)	4 (11)	0 (0)	0 (0)
	mineralization		1 (33)	0 (0)	0 (0)	0 (0)	5 (45)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	7 (19)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		1 (33)	0 (0)	1 (33)	0 (0)	4 (36)	0 (0)	0 (0)	0 (0)	7 (47)	3 (20)	0 (0)	0 (0)	4 (11)	4 (11)	0 (0)	0 (0) **
	eosinophilic change:respiratory epithelium		1 (33)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)
	inflammation:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<3>				<11>				<15>				<36>			
	respiratory metaplasia:gland		1	0	0	0	7	0	0	0	13	0	0	0	31	0	0	0
			(33)	(0)	(0)	(0)	(64)	(0)	(0)	(0)	(87)	(0)	(0)	(0)	(86)	(0)	(0)	(0)
	erythropoiesis:increased		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<3>				<11>				<15>				<36>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	edema		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	thrombus		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
	osseous metaplasia		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			< 3>				<11>				<15>				<36>			
	necrosis:focal		0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(33)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(3)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	increased hematopoiesis		0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	erythropoiesis:increased		0	0	0	0	2	3	0	0	2	2	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(18)	(27)	(0)	(0)	(13)	(13)	(0)	(0)	(3)	(0)	(0)	(0)
	granulopoiesis:increased		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 3>				<11>				<15>				<36>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	hyaline droplet		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<3>				<11>				<15>				<36>			
	deposit of hemosiderin		0	1	0	0	0	1	0	0	0	3	0	0	1	26	0	0
			(0)	(33)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(20)	(0)	(0)	(3)	(72)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	1	2	0	0	4	3	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(9)	(18)	(0)	(0)	(27)	(20)	(0)	(0)	(0)	(0)	(0)
	capsule hyperplasia		0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(3)	(0)	(0)	(0)
[Circulatory system]																		
heart			<3>				<11>				<15>				<36>			
	mineralization		1	0	0	0	0	0	0	0	0	0	2	0	2	12	4	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(6)	(33)	(11)	(0)
	myocardial fibrosis		0	1	0	0	3	2	0	0	8	4	0	0	27	5	1	0 *
			(0)	(33)	(0)	(0)	(27)	(18)	(0)	(0)	(53)	(27)	(0)	(0)	(75)	(14)	(3)	(0)
[Digestive system]																		
tooth			<3>				<11>				<15>				<36>			
	inflammation		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach			<3>				<11>				<15>				<36>			
	edema		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		0	1	0	0	0	0	0	0	2	0	0	0	2	0	0	0 **
			(0)	(33)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	erosion:forestomach		0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)
	ulcer:forestomach		0	1	0	0	0	1	1	0	1	1	0	0	2	0	0	0 **
			(0)	(33)	(0)	(0)	(0)	(9)	(9)	(0)	(7)	(7)	(0)	(0)	(6)	(0)	(0)	(0)
	hyperplasia:forestomach		0	1	1	0	0	3	0	0	2	0	0	0 *	1	1	0	0 **
			(0)	(33)	(33)	(0)	(0)	(27)	(0)	(0)	(13)	(0)	(0)	(0)	(3)	(3)	(0)	(0)
	erosion:glandular stomach		1	1	0	0	2	0	0	0	2	1	0	0	4	0	0	0 **
			(33)	(33)	(0)	(0)	(18)	(0)	(0)	(0)	(13)	(7)	(0)	(0)	(11)	(0)	(0)	(0)
	ulcer:glandular stomach		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
large intes			<3>				<11>				<15>				<36>			
	epidermal cyst		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			< 3>				<11>				<15>				<36>			
	herniation		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	necrosis:central		0	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		1	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	fatty change		0	0	0	0	2	0	0	0	0	1	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(3)	(0)	(0)	(0)
	fatty change:central		0	0	0	0	0	0	0	0	0	1	0	0	3	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(8)	(0)	(3)	(0)
	fatty change:peripheral		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<3>				<11>				<15>				<36>			
	degeneration:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		1 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		1 (33)	0 (0)	0 (0)	0 (0)	2 (18)	1 (9)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	5 (14)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	clear cell focus		0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		2 (67)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 * (0)	4 (27)	0 (0)	0 (0)	0 (0)	6 (17)	2 (6)	0 (0)	0 (0)
	vacuolated cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mixed cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Digestive system]																		
liver			< 3>				<11>				<15>				<36>			
	bile duct hyperplasia		0	0	0	0	4	0	0	0	0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(36)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
pancreas			< 3>				<11>				<15>				<36>			
	atrophy		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 3>				<11>				<15>				<36>			
	deposit of hemosiderin		0	0	0	0	0	1	0	0	1	1	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(9)	(0)	(0)	(7)	(7)	(0)	(0)	(6)	(0)	(0)	(0)
	chronic nephropathy		1	0	1	1	2	2	1	1	4	2	2	1	7	4	4	0 **
			(33)	(0)	(33)	(33)	(18)	(18)	(9)	(9)	(27)	(13)	(13)	(7)	(19)	(11)	(11)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)
	tubular necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<3>				<11>				<15>				<36>			
	mineralization:cortico-medullary junction		1	0	0	0	7	0	0	0	7	1	0	0	12	1	1	0
			(33)	(0)	(0)	(0)	(64)	(0)	(0)	(0)	(47)	(7)	(0)	(0)	(33)	(3)	(3)	(0)
	mineralization:papilla		0	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	mineralization:cortex		1	0	0	0	1	0	0	0	0	0	1	0	10	9	6	1
			(33)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(28)	(25)	(17)	(3)
	urothelial hyperplasia:pelivis		0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)
urin bladd			<3>				<11>				<15>				<36>			
	simple hyperplasia:transitional epithelium		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	nodular hyperplasia:transitional epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<3>				<11>				<15>				<36>			
	angiectasis		0	0	0	0	0	0	0	0	2	0	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(8)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			< 3>				<11>				<15>				<36>			
	cyst		1 (33)	0 (0)	0 (0)	0 (0)	3 (27)	0 (0)	0 (0)	0 (0)	5 (33)	1 (7)	0 (0)	0 (0)	2 (6)	1 (3)	0 (0)	0 (0)
	hyperplasia		0 (0)	1 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	1 (7)	0 (0)	0 (0)	2 (6)	3 (8)	0 (0)	0 (0)
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
thyroid			< 3>				<10>				<15>				<36>			
	C-cell hyperplasia		1 (33)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	focal follicular cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
adrenal			< 3>				<11>				<15>				<36>			
	peliosis-like lesion		1 (33)	0 (0)	0 (0)	0 (0)	2 (18)	1 (9)	0 (0)	0 (0)	2 (13)	1 (7)	0 (0)	0 (0)	6 (17)	2 (6)	0 (0)	0 (0)
	necrosis		0 (0)	0 (0)	1 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<3>				<11>				<15>				<36>			
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:cortical cell		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	hyperplasia:medulla		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	focal fatty change:cortex		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	increased lipid:cortex		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Reproductive system]																		
ovary			<3>				<11>				<15>				<36>			
	cyst		0	0	0	0	0	0	0	0	2	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
uterus			<3>				<11>				<15>				<36>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
uterus			<3>				<11>				<15>				<36>			
	cystic endometrial hyperplasia		0	0	0	0	1	0	0	0	0	1	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(6)	(0)	(0)	(0)
mammary gl			<3>				<11>				<15>				<36>			
	hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(33)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<3>				<11>				<15>				<36>			
	vacuolic change		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<3>				<11>				<15>				<36>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Grade	Control 3				7500 ppm 11				15000 ppm 15				30000 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			< 3>				<11>				<15>				<36>			
	cataract		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	1 (3)	0 (0)	1 (3)	0 (0)
	retinal atrophy		0 (0)	2 (67)	1 (33)	0 (0)	0 (0)	6 (55)	3 (27)	1 (9)	4 (27)	4 (27)	6 (40)	1 (7)	8 (22)	7 (19)	16 (44)	1 (3)
	keratitis		0 (0)	0 (0)	1 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	1 (3)	1 (3)	1 (3)	0 (0)
	iritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	1 (3)	1 (3)	0 (0)
Harder gl			< 3>				<11>				<15>				<36>			
	degeneration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	1 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
[Musculoskeletal system]																		
bone			< 3>				<11>				<15>				<36>			
	osteosclerosis		1 (33)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)	3 (20)	1 (7)	0 (0)	0 (0)	4 (11)	2 (6)	2 (6)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<38>				<39>				<34>				<30>			
	inflammation		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
[Respiratory system]																		
nasal cavit			<38>				<39>				<34>				<30>			
	thrombus		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	mineralization		16	0	0	0	32	0	0	0 **	9	0	0	0	11	0	0	0
			(42)	(0)	(0)	(0)	(82)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(37)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		29	5	0	0	26	2	0	0	18	7	0	0	13	7	0	0 *
			(76)	(13)	(0)	(0)	(67)	(5)	(0)	(0)	(53)	(21)	(0)	(0)	(43)	(23)	(0)	(0)
	eosinophilic change:respiratory epithelium		14	0	0	0	12	0	0	0	8	0	0	0	6	0	0	0
			(37)	(0)	(0)	(0)	(31)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	inflammation:foreign body		10	2	0	0	11	4	0	0	7	0	0	0	7	1	0	0
			(26)	(5)	(0)	(0)	(28)	(10)	(0)	(0)	(21)	(0)	(0)	(0)	(23)	(3)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<38>				<39>				<34>				<30>			
	inflammation:respiratory epithelium		3 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		7 (18)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	5 (15)	0 (0)	0 (0)	0 (0)	4 (13)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		35 (92)	0 (0)	0 (0)	0 (0)	34 (87)	0 (0)	0 (0)	0 (0)	29 (85)	0 (0)	0 (0)	0 (0)	29 (97)	0 (0)	0 (0)	0 (0)
larynx			<38>				<39>				<34>				<30>			
	inflammation		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
trachea			<38>				<39>				<34>				<30>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung			<38>				<39>				<34>				<30>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	osseous metaplasia		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			<38>				<39>				<34>				<30>			
	accumulation of foamy cells		1	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0
			(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	bronchopneumonia		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		2	0	0	0	7	0	0	0	2	2	0	0	1	2	0	0
			(5)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(6)	(6)	(0)	(0)	(3)	(7)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<38>				<39>				<34>				<30>			
	atrophy		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	granulation		1	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	fibrosis		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<38>				<39>				<34>				<30>			
	increased hematopoiesis		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erythropoiesis:increased		2	1	0	0	1	1	0	0	0	1	0	0	1	1	0	0
			(5)	(3)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(3)	(3)	(0)	(0)
lymph node			<38>				<39>				<34>				<30>			
	dilatation		0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	0	3	0	0	3	0	0	0	3	2	0	0
			(3)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(9)	(0)	(0)	(0)	(10)	(7)	(0)	(0)
spleen			<38>				<39>				<34>				<30>			
	ectopic tissue		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	deposit of hemosiderin		2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<38>				<39>				<34>				<30>			
	fibrosis		1	0	0	0	5	0	0	0	2	1	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(6)	(3)	(0)	(0)	(3)	(0)	(0)	(0)
	extramedullary hematopoiesis		2	0	1	0	0	1	0	0	1	0	0	0	0	0	1	0
			(5)	(0)	(3)	(0)	(0)	(3)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(3)	(0)
	capsule hyperplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]																		
heart			<38>				<39>				<34>				<30>			
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	myocardial fibrosis		8	29	1	0	8	31	0	0	3	30	1	0	5	24	1	0
			(21)	(76)	(3)	(0)	(21)	(79)	(0)	(0)	(9)	(88)	(3)	(0)	(17)	(80)	(3)	(0)
artery/aort			<38>				<39>				<34>				<30>			
	arteritis		0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tooth			<38>				<39>				<34>				<30>			
	dysplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
stomach			<38>				<39>				<34>				<30>			
	atrophy		0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	ulcer:forestomach		1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)
	erosion:glandular stomach		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)
liver			<38>				<39>				<34>				<30>			
	herniation		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	peliosis-like lesion		1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:zonal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<38>				<39>				<34>				<30>			
	necrosis:central		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		5	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change:peripheral		0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		15	0	0	0	18	1	0	0	14	0	0	0	10	0	0	0
			(39)	(0)	(0)	(0)	(46)	(3)	(0)	(0)	(41)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
	clear cell focus		14	4	0	0	8	4	0	0	10	4	0	0	4	0	0	0 **
			(37)	(11)	(0)	(0)	(21)	(10)	(0)	(0)	(29)	(12)	(0)	(0)	(13)	(0)	(0)	(0)
	acidophilic cell focus		6	1	0	0	9	2	0	0	9	0	0	0	2	0	0	0
			(16)	(3)	(0)	(0)	(23)	(5)	(0)	(0)	(26)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	basophilic cell focus		15	1	0	0	9	5	1	0	8	2	0	0	4	1	0	0
			(39)	(3)	(0)	(0)	(23)	(13)	(3)	(0)	(24)	(6)	(0)	(0)	(13)	(3)	(0)	(0)
	vacuolated cell focus		3	1	0	0	1	0	0	0	3	0	0	0	1	0	0	0
			(8)	(3)	(0)	(0)	(3)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(3)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<38>				<39>				<34>				<30>			
	mixed cell focus		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	spongiosis hepatis		3	1	0	0	5	0	0	0	7	0	0	0	4	0	0	0
			(8)	(3)	(0)	(0)	(13)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
	bile duct hyperplasia		23	15	0	0	23	16	0	0	17	17	0	0	16	14	0	0
			(61)	(39)	(0)	(0)	(59)	(41)	(0)	(0)	(50)	(50)	(0)	(0)	(53)	(47)	(0)	(0)
pancreas			<38>				<39>				<34>				<30>			
	atrophy		6	0	0	0	5	1	0	0	10	0	0	0	3	0	0	0
			(16)	(0)	(0)	(0)	(13)	(3)	(0)	(0)	(29)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	basophilic change		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Urinary system]																		
kidney			<38>				<39>				<34>				<30>			
	deposit of hemosiderin		1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<38>				<39>				<34>				<30>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	chronic nephropathy		1 (3)	16 (42)	17 (45)	4 (11)	0 (0)	14 (36)	22 (56)	3 (8)	2 (6)	12 (35)	20 (59)	0 (0)	4 (13)	17 (57)	9 (30)	0 (0)
	mineralization:papilla		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)
	mineralization:cortex		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)
	urothelial hyperplasia:pelivis		1 (3)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	1 (3)	3 (10)	0 (0)	0 (0)
urin bladd			<38>				<39>				<34>				<30>			
	simple hyperplasia:transitional epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary			<38>				<39>				<34>				<30>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
pituitary			<38>				<39>				<34>				<30>			
	cyst		1	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(3)	(3)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia		4	5	0	0	10	3	0	0	2	2	0	0	11	2	0	0 *
			(11)	(13)	(0)	(0)	(26)	(8)	(0)	(0)	(6)	(6)	(0)	(0)	(37)	(7)	(0)	(0)
	Rathke pouch		0	0	0	0	2	1	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(5)	(3)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<38>				<39>				<34>				<30>			
	ultimibranchial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	C-cell hyperplasia		8	1	0	0	7	0	0	0	6	2	0	0	4	0	0	0
			(21)	(3)	(0)	(0)	(18)	(0)	(0)	(0)	(18)	(6)	(0)	(0)	(13)	(0)	(0)	(0)
	focal follicular cell hyperplasia		0	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<38>				<39>				<34>				<30>			
	hemorrhage		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<38>				<39>				<34>				<30>			
	cyst		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:cortical cell		1	0	0	0	3	0	0	0	1	1	0	0	2	0	0	0
			(3)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(7)	(0)	(0)	(0)
	hyperplasia:medulla		3	1	0	0	3	4	0	0	1	2	0	0	3	0	0	0
			(8)	(3)	(0)	(0)	(8)	(10)	(0)	(0)	(3)	(6)	(0)	(0)	(10)	(0)	(0)	(0)
	focal fatty change:cortex		7	0	0	0	5	0	0	0	8	0	0	0	3	0	0	0
			(18)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Reproductive system]																		
testis			<38>				<39>				<34>				<30>			
	atrophy		2	3	30	0	3	3	31	0	2	3	28	0	3	1	22	0
			(5)	(8)	(79)	(0)	(8)	(8)	(79)	(0)	(6)	(9)	(82)	(0)	(10)	(3)	(73)	(0)
	mineralization		3	1	0	0	2	0	0	0	3	0	0	0	3	0	0	0
			(8)	(3)	(0)	(0)	(5)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	arteritis		1	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(5)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
testis			<38>				<39>				<34>				<30>			
	interstitial cell hyperplasia		3	0	0	0	2	0	0	0	4	1	0	0	3	0	0	0
			(8)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(12)	(3)	(0)	(0)	(10)	(0)	(0)	(0)
epididymis			<38>				<39>				<34>				<30>			
	inflammation		0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
prostate			<38>				<39>				<34>				<30>			
	inflammation		9	3	0	0	8	2	0	0	8	3	0	0	6	2	0	0
			(24)	(8)	(0)	(0)	(21)	(5)	(0)	(0)	(24)	(9)	(0)	(0)	(20)	(7)	(0)	(0)
	hyperplasia		4	0	0	0	9	0	0	0	4	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(23)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
mammary gl			<38>				<39>				<34>				<30>			
	duct ectasia		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	galactocele		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
prep/cli gl			<38>				<39>				<34>				<30>			
	duct ectasia		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<38>				<39>				<34>				<30>			
	necrosis:focal		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<38>				<39>				<34>				<30>			
	cataract		1	2	0	0	0	3	1	0	0	5	0	0	0	0	0	0
			(3)	(5)	(0)	(0)	(0)	(8)	(3)	(0)	(0)	(15)	(0)	(0)	(0)	(0)	(0)	(0)
	retinal atrophy		7	14	15	1	2	14	23	0	0	13	20	1	2	12	16	0
			(18)	(37)	(39)	(3)	(5)	(36)	(59)	(0)	(0)	(38)	(59)	(3)	(7)	(40)	(53)	(0)
	keratitis		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
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Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<38>				<39>				<34>				<30>			
	iritis		1 (3)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Harder gl			<38>				<39>				<34>				<30>			
	degeneration		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		2 (5)	1 (3)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
[Musculoskeletal system]																		
muscle			<38>				<39>				<34>				<30>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	47				39				35				14			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<47>				<39>				<35>				<14>			
	ulcer		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	scab		0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)
[Respiratory system]																		
nasal cavit			<47>				<39>				<35>				<14>			
	mineralization		6	0	0	0	15	0	0	0 *	2	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		18	16	3	0	20	10	1	0	12	15	3	0	2	6	4	0
			(38)	(34)	(6)	(0)	(51)	(26)	(3)	(0)	(34)	(43)	(9)	(0)	(14)	(43)	(29)	(0)
	eosinophilic change:respiratory epithelium		15	0	0	0	16	0	0	0	14	0	0	0	4	0	0	0
			(32)	(0)	(0)	(0)	(41)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(29)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 47 1 (%)	Control 47 2 (%)	Control 47 3 (%)	Control 47 4 (%)	7500 ppm 39 1 (%)	7500 ppm 39 2 (%)	7500 ppm 39 3 (%)	7500 ppm 39 4 (%)	15000 ppm 35 1 (%)	15000 ppm 35 2 (%)	15000 ppm 35 3 (%)	15000 ppm 35 4 (%)	30000 ppm 14 1 (%)	30000 ppm 14 2 (%)	30000 ppm 14 3 (%)	30000 ppm 14 4 (%)
[Respiratory system]																		
nasal cavit			<47>				<39>				<35>				<14>			
	inflammation:foreign body		5 (11)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		43 (91)	0 (0)	0 (0)	0 (0)	35 (90)	0 (0)	0 (0)	0 (0)	34 (97)	0 (0)	0 (0)	0 (0)	14 (100)	0 (0)	0 (0)	0 (0)
larynx			<47>				<39>				<35>				<14>			
	inflammation		3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung			<47>				<39>				<35>				<14>			
	accumulation of foamy cells		3 (6)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<47>				<39>				<35>				<14>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 47				7500 ppm 39				15000 ppm 35				30000 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<47>				<39>				<35>				<14>			
	granulation		2 (4)	1 (2)	0 (0)	0 (0)	3 (8)	2 (5)	0 (0)	0 (0)	1 (3)	2 (6)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	histiocytosis		1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	3 (9)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	increased hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)
lymph node			<47>				<39>				<35>				<14>			
	granulation		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
thymus			<47>				<39>				<35>				<14>			
	glandular metaplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<47>				<39>				<35>				<14>			
	hyaline droplet		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	47				39				35				14			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<47>				<39>				<35>				<14>			
	deposit of hemosiderin		0	22	0	0	1	16	0	0	1	11	0	0	0	6	0	0
			(0)	(47)	(0)	(0)	(3)	(41)	(0)	(0)	(3)	(31)	(0)	(0)	(0)	(43)	(0)	(0)
	extramedullary hematopoiesis		0	2	1	0	0	0	0	0	0	2	0	0	0	0	0	0
			(0)	(4)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
	capsule hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]																		
heart			<47>				<39>				<35>				<14>			
	mineralization		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)
	myocardial fibrosis		24	12	0	0	23	7	0	0	22	4	0	0	13	0	0	0 *
			(51)	(26)	(0)	(0)	(59)	(18)	(0)	(0)	(63)	(11)	(0)	(0)	(93)	(0)	(0)	(0)
artery/aort			<47>				<39>				<35>				<14>			
	arteritis		0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	47				39				35				14			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<47>				<39>				<35>				<14>			
	ulcer:forestomach		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:forestomach		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver			<47>				<39>				<35>				<14>			
	herniation		4 (9)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		1 (2)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	fatty change:central		0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	fatty change:peripheral		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		30 (64)	3 (6)	1 (2)	0 (0)	18 (46)	0 (0)	0 (0)	0 * (0)	25 (71)	0 (0)	0 (0)	0 (0)	6 (43)	2 (14)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 47				7500 ppm 39				15000 ppm 35				30000 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<47>				<39>				<35>				<14>			
	clear cell focus		2 (4)	1 (2)	0 (0)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	acidophilic cell focus		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		20 (43)	0 (0)	0 (0)	0 (0)	21 (54)	0 (0)	0 (0)	0 (0)	19 (54)	1 (3)	0 (0)	0 (0)	6 (43)	1 (7)	0 (0)	0 (0)
	vacuolated cell focus		4 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mixed cell focus		1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		12 (26)	0 (0)	0 (0)	0 (0)	14 (36)	0 (0)	0 (0)	0 (0)	13 (37)	0 (0)	0 (0)	0 (0)	5 (36)	0 (0)	0 (0)	0 (0)
	cholangiofibrosis		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
pancreas			<47>				<39>				<35>				<14>			
	atrophy		4 (9)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 47				7500 ppm 39				15000 ppm 35				30000 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<47>				<39>				<35>				<14>			
	necrosis:zonal		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)
	cyst		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	chronic nephropathy		12	20	8	2	9	17	7	2	4	22	9	0 *	4	8	0	0
			(26)	(43)	(17)	(4)	(23)	(44)	(18)	(5)	(11)	(63)	(26)	(0)	(29)	(57)	(0)	(0)
	mineralization:cortico-medullary junction		16	1	0	0	24	0	1	0 *	22	0	0	0 *	13	0	0	0 **
			(34)	(2)	(0)	(0)	(62)	(0)	(3)	(0)	(63)	(0)	(0)	(0)	(93)	(0)	(0)	(0)
	mineralization:papilla		2	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	mineralization:cortex		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<46>				<39>				<35>				<14>			
	angiectasis		1	2	0	0	0	0	1	0	0	0	0	0	0	1	0	0
			(2)	(4)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 47 1 (%)	Control 47 2 (%)	Control 47 3 (%)	Control 47 4 (%)	7500 ppm 39 1 (%)	7500 ppm 39 2 (%)	7500 ppm 39 3 (%)	7500 ppm 39 4 (%)	15000 ppm 35 1 (%)	15000 ppm 35 2 (%)	15000 ppm 35 3 (%)	15000 ppm 35 4 (%)	30000 ppm 14 1 (%)	30000 ppm 14 2 (%)	30000 ppm 14 3 (%)	30000 ppm 14 4 (%)
[Endocrine system]																		
pituitary			<46>				<39>				<35>				<14>			
	cyst		6 (13)	2 (4)	0 (0)	0 (0)	9 (23)	2 (5)	1 (3)	0 (0)	7 (20)	1 (3)	0 (0)	0 (0)	3 (21)	1 (7)	0 (0)	0 (0)
	hyperplasia		9 (20)	6 (13)	0 (0)	0 (0)	2 (5)	5 (13)	0 (0)	0 (0)	6 (17)	8 (23)	0 (0)	0 (0)	3 (21)	2 (14)	0 (0)	0 (0)
	Rathke pouch		1 (2)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (7)	1 (7)	0 (0)	0 (0)
thyroid			<47>				<39>				<35>				<14>			
	ultimibranchial body remanet		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		4 (9)	0 (0)	0 (0)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	focal follicular cell hyperplasia		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal			<47>				<39>				<35>				<14>			
	peliosis-like lesion		23 (49)	6 (13)	1 (2)	0 (0)	18 (46)	8 (21)	0 (0)	0 (0)	18 (51)	6 (17)	0 (0)	0 (0)	6 (43)	1 (7)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	47				39				35				14			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			<47>				<39>				<35>				<14>			
	hyperplasia:cortical cell		4 (9)	2 (4)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		7 (15)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 * (0)	1 (7)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<47>				<38>				<35>				<14>			
	cyst		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
uterus			<47>				<39>				<35>				<14>			
	cystic endometrial hyperplasia		1 (2)	1 (2)	2 (4)	0 (0)	2 (5)	1 (3)	0 (0)	0 (0)	6 (17)	1 (3)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
mammary gl			<47>				<39>				<35>				<14>			
	hyperplasia		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	47				39				35				14			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Nervous system]																		
brain			<47>				<39>				<35>				<14>			
	vacuolic change		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<47>				<39>				<35>				<14>			
	cataract		0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)
	retinal atrophy		3	6	38	0	0	9	29	0	0	7	25	2	0	6	8	0 *
			(6)	(13)	(81)	(0)	(0)	(23)	(74)	(0)	(0)	(20)	(71)	(6)	(0)	(43)	(57)	(0)
	keratitis		1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(3)	(0)	(0)	(0)	(0)	(0)
Harder gl			<47>				<39>				<35>				<14>			
	degeneration		3	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0
			(6)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)
	inflammatory infiltration		0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	47				39				35				14			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
Harder gl			<47>				<39>				<35>				<14>			
	lymphocytic infiltration		4 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		2 (4)	0 (0)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Musculoskeletal system]																		
bone			<47>				<39>				<35>				<14>			
	osteosclerosis		3 (6)	3 (6)	2 (4)	0 (0)	7 (18)	3 (8)	0 (0)	0 (0)	4 (11)	3 (9)	3 (9)	0 (0)	2 (14)	2 (14)	1 (7)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

MOSUE : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	16				15				20				25			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<16>				<15>				<20>				<25>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
subcutis			<16>				<15>				<20>				<25>			
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
[Respiratory system]																		
nasal cavit			<16>				<15>				<20>				<25>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		2 (13)	0 (0)	0 (0)	0 (0)	4 (27)	0 (0)	0 (0)	0 (0)	5 (25)	0 (0)	0 (0)	0 (0)	4 (16)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		5 (31)	1 (6)	0 (0)	0 (0)	3 (20)	2 (13)	0 (0)	0 (0)	2 (10)	1 (5)	0 (0)	0 (0)	4 (16)	2 (8)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		2 (13)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	8 (40)	0 (0)	0 (0)	0 (0)	12 (48)	2 (8)	0 (0)	0 * (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<16>				<15>				<20>				<25>			
	respiratory metaplasia:gland		3 (19)	1 (6)	0 (0)	0 (0)	4 (27)	0 (0)	0 (0)	0 (0)	7 (35)	1 (5)	0 (0)	0 (0)	14 (56)	2 (8)	0 (0)	0 * (0)
	duct ectasia:olfactory gland		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	18 (72)	0 (0)	0 (0)	0 ** (0)
nasopharynx			<16>				<15>				<20>				<25>			
	eosinophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
lung			<16>				<15>				<20>				<25>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<16>				<15>				<20>				<25>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		1 (6)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<16>				<15>				<20>				<25>			
	hyperplasia:vascular		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<16>				<15>				<20>				<25>			
	thrombus		0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		2 (13)	2 (13)	2 (13)	0 (0)	1 (7)	4 (27)	3 (20)	0 (0)	0 (0)	3 (15)	4 (20)	0 (0)	1 (4)	1 (4)	2 (8)	0 (0)
	hyperplasia:vascular		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Circulatory system]																		
heart			<16>				<15>				<20>				<25>			
	necrosis		0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<16>				<15>				<20>				<25>			
	mineralization		0	1	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
[Digestive system]																		
tooth			<16>				<15>				<20>				<25>			
	dysplasia		5	1	0	0	6	0	0	0	7	3	0	0	8	1	0	0
			(31)	(6)	(0)	(0)	(40)	(0)	(0)	(0)	(35)	(15)	(0)	(0)	(32)	(4)	(0)	(0)
tongue			<16>				<15>				<20>				<25>			
	arteritis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
salivary gl			<16>				<15>				<20>				<25>			
	mineralization		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<16>				<15>				<20>				<25>			
	mineralization		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:forestomach		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	16				15				20				25			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<16>				<15>				<20>				<25>			
	erosion:glandular stomach		1 (6)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		1 (6)	2 (13)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	4 (20)	1 (5)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
liver			<16>				<15>				<20>				<25>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	necrosis:central		0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)
	necrosis:focal		0 (0)	1 (6)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
	fatty change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	fatty change:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<16>				<15>				<20>				<25>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic cell focus		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<16>				<15>				<20>				<25>			
	necrosis		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	islet cell hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
[Urinary system]																		
kidney			<16>				<15>				<20>				<25>			
	cyst		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<16>				<15>				<20>				<25>			
	hyaline droplet		0 (0)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	1 (5)	2 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hydronephrosis		0 (0)	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
	tubular necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
	papillary necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	mineralization:cortico-medullary junction		6 (38)	0 (0)	0 (0)	0 (0)	8 (53)	0 (0)	0 (0)	0 (0)	8 (40)	0 (0)	0 (0)	0 (0)	13 (52)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<16>				<15>				<20>				<25>			
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortex		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
	glomerulosclerosis		0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
urethra			<16>				<15>				<20>				<25>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary			<16>				<15>				<20>				<24>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			<16>				<15>				<20>				<25>			
	spindle-cell hyperplasia		3 (19)	0 (0)	0 (0)	0 (0)	5 (33)	0 (0)	0 (0)	0 (0)	8 (40)	0 (0)	0 (0)	0 (0)	9 (36)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
testis			<16>				<15>				<20>				<25>			
	atrophy		2 (13)	1 (6)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)
	mineralization		7 (44)	0 (0)	0 (0)	0 (0)	11 (73)	1 (7)	0 (0)	0 (0)	13 (65)	1 (5)	0 (0)	0 (0)	17 (68)	2 (8)	0 (0)	0 (0)
epididymis			<16>				<15>				<20>				<25>			
	inflammation		1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	spermatogenic granuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
semin ves			<16>				<15>				<20>				<25>			
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
prostate			<16>				<15>				<20>				<25>			
	inflammation		0	0	0	0	2	0	1	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(7)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)
prep/cli gl			<16>				<15>				<20>				<25>			
	duct ectasia		0	0	0	0	0	2	0	0	0	3	1	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(15)	(5)	(0)	(0)	(8)	(0)	(0)
[Nervous system]																		
brain			<16>				<15>				<20>				<25>			
	hemorrhage		1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(6)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		7	0	0	0	8	0	0	0	11	0	0	0	11	0	0	0
			(44)	(0)	(0)	(0)	(53)	(0)	(0)	(0)	(55)	(0)	(0)	(0)	(44)	(0)	(0)	(0)
spinal cord			<16>				<15>				<20>				<24>			
	hemorrhage		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl			<16>				<15>				<20>				<25>			
	hyperplasia		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Musculoskeletal system]																		
muscle			<16>				<15>				<20>				<25>			
	mineralization		2 (13)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
[Body cavities]																		
peritoneum			<16>				<15>				<20>				<25>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
subcutis			<21>				<26>				<31>				<22>			
	inflammation		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Respiratory system]																		
nasal cavit			<21>				<26>				<31>				<22>			
	bacteria		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)
	embolus		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		0	0	1	0	0	1	0	0	2	1	0	0	3	1	0	0
			(0)	(0)	(5)	(0)	(0)	(4)	(0)	(0)	(6)	(3)	(0)	(0)	(14)	(5)	(0)	(0)
	eosinophilic change:respiratory epithelium		4	1	0	0	7	1	1	0	8	2	0	0	9	1	0	0
			(19)	(5)	(0)	(0)	(27)	(4)	(4)	(0)	(26)	(6)	(0)	(0)	(41)	(5)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		1	0	0	0	2	0	0	0	3	0	0	0	4	0	0	0
			(5)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(18)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	21				26				31				22			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<21>				<26>				<31>				<22>			
	respiratory metaplasia:gland		1	0	0	0	2	0	0	0	2	0	0	0	4	0	0	0
			(5)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(18)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(4)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	duct ectasia:olfactory gland		0	0	0	0	0	0	0	0	2	0	0	0	16	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(73)	(0)	(0)	(0)
nasopharynx			<21>				<26>				<31>				<22>			
	eosinophilic change		1	1	0	0	3	1	0	0	1	0	0	0	1	0	0	0
			(5)	(5)	(0)	(0)	(12)	(4)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
lung			<21>				<26>				<31>				<22>			
	inflammatory infiltration		0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<21>				<26>				<31>				<22>			
	myelofibrosis		1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<21>				<26>				<31>				<22>			
	erythropoiesis:increased		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:vascular		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)
spleen			<21>				<26>				<31>				<22>			
	thrombus		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of melanin		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		1	4	7	0	1	3	2	0	0	6	5	0	0	5	5	0
			(5)	(19)	(33)	(0)	(4)	(12)	(8)	(0)	(0)	(19)	(16)	(0)	(0)	(23)	(23)	(0)
	follicular hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
[Circulatory system]																		
heart			<21>				<26>				<31>				<22>			
	thrombus		0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<21>				<26>				<31>				<22>			
	necrosis		1 (5)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization		3 (14)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
artery/aort			<21>				<26>				<31>				<22>			
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
tooth			<21>				<26>				<31>				<22>			
	dysplasia		1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
tongue			<21>				<26>				<31>				<22>			
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
salivary gl			<21>				<26>				<31>				<22>			
	lymphocytic infiltration		2	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(9)	(0)	(0)	(0)
stomach			<21>				<26>				<31>				<22>			
	mineralization		0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	ulcer:forestomach		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	hyperplasia:glandular stomach		2	0	0	0	2	1	0	0	5	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(8)	(4)	(0)	(0)	(16)	(0)	(0)	(0)	(9)	(0)	(0)	(0)
liver			<21>				<26>				<31>				<22>			
	angiectasis		2	0	0	0	1	0	1	0	0	1	0	0	2	2	0	0
			(10)	(0)	(0)	(0)	(4)	(0)	(4)	(0)	(0)	(3)	(0)	(0)	(9)	(9)	(0)	(0)
	necrosis:focal		0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	21				26				31				22			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Digestive system]																		
liver			<21>				<26>				<31>				<22>			
	necrosis:single cell		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	inflammatory infiltration		0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(4)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	clear cell focus		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	acidophilic cell focus		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<21>				<26>				<31>				<22>			
	basophilic cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
pancreas			<21>				<26>				<31>				<22>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney			<21>				<26>				<31>				<22>			
	necrosis:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyaline droplet		6 (29)	4 (19)	0 (0)	0 (0)	6 (23)	2 (8)	0 (0)	0 (0)	3 (10)	6 (19)	1 (3)	0 (0)	0 (0)	5 (23)	1 (5)	0 * (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
	hyaline cast		0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	21				26				31				22			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<21>				<26>				<31>				<22>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	granulation		1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory polyp		1 (5)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
	hydronephrosis		0 (0)	1 (5)	2 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)
	tubular necrosis		0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortico-medullary junction		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
urin bladd			<21>				<26>				<31>				<22>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary			<20>				<26>				<31>				<21>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	21				26				31				22			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<20>				<26>				<31>				<21>			
	hyperplasia		0 (0)	1 (5)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
adrenal			<20>				<26>				<31>				<22>			
	fatty change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)
	spindle-cell hyperplasia		15 (75)	5 (25)	0 (0)	0 (0)	21 (81)	4 (15)	0 (0)	0 (0)	22 (71)	5 (16)	0 (0)	0 (0)	19 (86)	2 (9)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<20>				<26>				<31>				<21>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
ovary			<20>				<26>				<31>				<21>			
	thrombus		0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(5)	(0)
	cyst		0	1	0	0	0	4	0	0	1	1	0	0	0	0	1	0
			(0)	(5)	(0)	(0)	(0)	(15)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(5)	(0)
uterus			<21>				<26>				<31>				<22>			
	thrombus		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cystic endometrial hyperplasia		3	1	0	0	7	1	0	0	6	1	0	0	3	1	0	0
			(14)	(5)	(0)	(0)	(27)	(4)	(0)	(0)	(19)	(3)	(0)	(0)	(14)	(5)	(0)	(0)
mammary gl			<21>				<26>				<31>				<22>			
	hyperplasia		1	0	0	0	0	0	0	0	1	1	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(5)	(0)	(0)	(0)
	galactocele		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
prep/cli gl			<21>				<26>				<31>				<22>			
	duct ectasia		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Nervous system]																		
brain		<21>	0	1	0	0	<26> 0	0	0	0	<31> 0	0	0	0	<22> 0	0	0	0
	hemorrhage		(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		6	0	0	0	16	0	0	0	9	0	0	0	9	0	0	0
			(29)	(0)	(0)	(0)	(62)	(0)	(0)	(0)	(29)	(0)	(0)	(0)	(41)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl		<21>	1	0	0	0	<26> 0	0	0	0	<31> 1	0	0	0	<22> 1	0	0	0
	lymphocytic infiltration		(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
[Musculoskeletal system]																		
muscle		<21>	1	0	0	0	<26> 2	0	0	0	<31> 1	0	0	0	<22> 1	0	0	0
	mineralization		(5)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
[Body cavities]																		
pleura		<21>	0	0	0	0	<26> 0	0	0	0	<31> 0	0	0	0	<22> 0	1	0	0
	inflammation		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 21				10000 ppm 26				20000 ppm 31				40000 ppm 22			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Body cavities]																		
peritoneum			<21>				<26>				<31>				<22>			
	inflammation		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adipose			<21>				<26>				<31>				<22>			
	granulation		0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

MOSUE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	34				35				30				25			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<34>				<35>				<30>				<25>			
	erosion		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:epidermis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	epidermal cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Respiratory system]																		
nasal cavit			<34>				<35>				<30>				<25>			
	eosinophilic change:olfactory epithelium		13 (38)	0 (0)	0 (0)	0 (0)	8 (23)	0 (0)	0 (0)	0 (0)	15 (50)	0 (0)	0 (0)	0 (0)	6 (24)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		11 (32)	2 (6)	0 (0)	0 (0)	6 (17)	3 (9)	1 (3)	0 (0)	14 (47)	1 (3)	0 (0)	0 (0)	7 (28)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		11 (32)	0 (0)	0 (0)	0 (0)	10 (29)	0 (0)	0 (0)	0 (0)	17 (57)	0 (0)	0 (0)	0 (0)	18 (72)	0 (0)	0 (0)	0 (0) **

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34 1 (%)	Control 34 2 (%)	Control 34 3 (%)	Control 34 4 (%)	10000 ppm 35 1 (%)	10000 ppm 35 2 (%)	10000 ppm 35 3 (%)	10000 ppm 35 4 (%)	20000 ppm 30 1 (%)	20000 ppm 30 2 (%)	20000 ppm 30 3 (%)	20000 ppm 30 4 (%)	40000 ppm 25 1 (%)	40000 ppm 25 2 (%)	40000 ppm 25 3 (%)	40000 ppm 25 4 (%)
[Respiratory system]																		
nasal cavit			<34>				<35>				<30>				<25>			
	respiratory metaplasia:gland		5	5	0	0	15	7	0	0 *	10	3	0	0	17	4	0	0 **
			(15)	(15)	(0)	(0)	(43)	(20)	(0)	(0)	(33)	(10)	(0)	(0)	(68)	(16)	(0)	(0)
	duct ectasia:olfactory gland		0	0	0	0	0	0	0	0	9	0	0	0 **	21	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(84)	(0)	(0)	(0)
nasopharynx			<34>				<35>				<30>				<25>			
	eosinophilic change		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<34>				<35>				<30>				<25>			
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<34>				<35>				<30>				<25>			
	myelofibrosis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
spleen			<34>				<35>				<30>				<25>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<34>				<35>				<30>				<25>			
	deposit of melanin		1	0	0	0	4	0	0	0	2	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	extramedullary hematopoiesis		3	1	0	0	1	0	0	0	2	1	0	0	1	2	0	0
			(9)	(3)	(0)	(0)	(3)	(0)	(0)	(0)	(7)	(3)	(0)	(0)	(4)	(8)	(0)	(0)
	hyperplasia:vascular		1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(4)	(0)	(0)
	follicular hyperplasia		2	2	1	0	2	1	1	0	4	3	0	0	1	1	0	0
			(6)	(6)	(3)	(0)	(6)	(3)	(3)	(0)	(13)	(10)	(0)	(0)	(4)	(4)	(0)	(0)
[Circulatory system]																		
heart			<34>				<35>				<30>				<25>			
	necrosis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
tooth			<34>				<35>				<30>				<25>			
	dysplasia		22	3	2	1	21	6	0	0	9	6	2	0 *	15	2	1	0
			(65)	(9)	(6)	(3)	(60)	(17)	(0)	(0)	(30)	(20)	(7)	(0)	(60)	(8)	(4)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tongue			<34>				<35>				<30>				<25>			
	arteritis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
salivary gl			<34>				<35>				<30>				<25>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
stomach			<34>				<35>				<30>				<25>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	hyperplasia:glandular stomach		14	5	0	0	14	4	0	0	9	3	0	0	7	1	0	0
			(41)	(15)	(0)	(0)	(40)	(11)	(0)	(0)	(30)	(10)	(0)	(0)	(28)	(4)	(0)	(0)
small intes			<34>				<35>				<30>				<25>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<34>				<35>				<30>				<25>			
	angiectasis		0	1	0	0	0	1	0	0	0	1	1	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<34>				<35>				<30>				<25>			
	necrosis:central		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		2	0	2	0	3	1	0	0	3	1	0	0	1	0	0	0
			(6)	(0)	(6)	(0)	(9)	(3)	(0)	(0)	(10)	(3)	(0)	(0)	(4)	(0)	(0)	(0)
	fatty change:central		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		11	1	0	0	21	0	1	0	15	1	0	0	16	0	0	0 *
			(32)	(3)	(0)	(0)	(60)	(0)	(3)	(0)	(50)	(3)	(0)	(0)	(64)	(0)	(0)	(0)
	clear cell focus		3	1	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(9)	(3)	(0)	(0)	(6)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	acidophilic cell focus		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic cell focus		2	1	0	0	1	0	0	0	3	1	0	0	2	0	1	0
			(6)	(3)	(0)	(0)	(3)	(0)	(0)	(0)	(10)	(3)	(0)	(0)	(8)	(0)	(4)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<34>				<35>				<30>				<25>			
	biliary cyst		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<34>				<35>				<30>				<25>			
	islet cell hyperplasia		1	1	0	0	0	0	0	0	0	1	0	0	1	0	0	0
			(3)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(4)	(0)	(0)	(0)
[Urinary system]																		
kidney			<34>				<35>				<30>				<25>			
	infarct		0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	cyst		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	basophilic change		0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	hyaline cast		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<34>				<35>				<30>				<25>			
	lymphocytic infiltration		2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory polyp		0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	papillary necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortico-medullary junction		23 (68)	0 (0)	0 (0)	0 (0)	27 (77)	0 (0)	0 (0)	0 (0)	22 (73)	0 (0)	0 (0)	0 (0)	22 (88)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
urin bladd			<34>				<35>				<30>				<25>			
	ulcer		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<34>				<35>				<30>				<25>			
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	Rathke pouch		6 (18)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	6 (20)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
adrenal			<34>				<35>				<30>				<25>			
	spindle-cell hyperplasia		20 (59)	0 (0)	0 (0)	0 (0)	16 (46)	0 (0)	0 (0)	0 (0)	11 (37)	1 (3)	0 (0)	0 (0)	12 (48)	0 (0)	0 (0)	0 (0)
	hyperplasia:cortical cell		2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
testis			<34>				<35>				<30>				<25>			
	atrophy		15 (44)	4 (12)	0 (0)	0 (0)	12 (34)	5 (14)	0 (0)	0 (0)	9 (30)	3 (10)	0 (0)	0 (0)	11 (44)	0 (0)	0 (0)	0 (0)
	mineralization		31 (91)	0 (0)	0 (0)	0 (0)	32 (91)	1 (3)	0 (0)	0 (0)	26 (87)	4 (13)	0 (0)	0 * (0)	23 (92)	0 (0)	1 (4)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
epididymis			<34>				<35>				<30>				<25>			
	inflammation		1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	spermatogenic granuloma		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)
semin ves			<34>				<35>				<30>				<25>			
	mineralization		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
prep/cli gl			<34>				<35>				<30>				<25>			
	duct ectasia		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
[Nervous system]																		
brain			<34>				<35>				<30>				<25>			
	mineralization		24 (71)	0 (0)	0 (0)	0 (0)	20 (57)	0 (0)	0 (0)	0 (0)	22 (73)	0 (0)	0 (0)	0 (0)	14 (56)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<34>				<35>				<30>				<25>			
	cataract		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	keratitis		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
Harder gl			<34>				<35>				<30>				<25>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Body cavities]																		
mesenterium			<34>				<35>				<30>				<25>			
	inflammation		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adipose			<34>				<35>				<30>				<25>			
	granulation		0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

MOSUE : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<29>				<24>				<19>				<28>			
	inflammation		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	scab		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
[Respiratory system]																		
nasal cavit			<29>				<24>				<19>				<28>			
	embolus		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)
	eosinophilic change:olfactory epithelium		1	0	1	0	1	1	0	0	0	0	0	0	11	0	0	0 **
			(3)	(0)	(3)	(0)	(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(39)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		16	3	0	0	14	4	1	0	12	2	0	0	18	5	0	0
			(55)	(10)	(0)	(0)	(58)	(17)	(4)	(0)	(63)	(11)	(0)	(0)	(64)	(18)	(0)	(0)
	inflammation:respiratory epithelium		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<29>				<24>				<19>				<28>			
	respiratory metaplasia:olfactory epithelium		1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (37)	0 (0)	0 (0)	0 ** (0)	4 (14)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		0 (0)	0 (0)	0 (0)	0 (0)	4 (17)	0 (0)	0 (0)	0 (0)	7 (37)	0 (0)	0 (0)	0 ** (0)	9 (32)	1 (4)	0 (0)	0 ** (0)
	duct ectasia:olfactory gland		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (16)	0 (0)	0 (0)	0 (0)	24 (86)	0 (0)	0 (0)	0 ** (0)
nasopharynx			<29>				<24>				<19>				<28>			
	eosinophilic change		1 (3)	2 (7)	0 (0)	0 (0)	1 (4)	2 (8)	0 (0)	0 (0)	2 (11)	1 (5)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)
lung			<29>				<24>				<19>				<28>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		5 (17)	1 (3)	0 (0)	0 (0)	3 (13)	0 (0)	0 (0)	0 (0)	5 (26)	0 (0)	0 (0)	0 (0)	4 (14)	2 (7)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		1 (3)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	29				24				19				28			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<29>				<24>				<19>				<28>			
	myelofibrosis		1	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
lymph node			<29>				<24>				<19>				<28>			
	deposit of melanin		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	lymphadenitis		0	0	0	0	0	2	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(4)	(0)	(0)
spleen			<29>				<24>				<19>				<28>			
	deposit of melanin		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	1	1	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(5)	(0)	(0)	(0)	(7)	(0)	(0)
	follicular hyperplasia		1	1	0	0	2	2	0	0	3	1	1	0	1	1	0	0
			(3)	(3)	(0)	(0)	(8)	(8)	(0)	(0)	(16)	(5)	(5)	(0)	(4)	(4)	(0)	(0)
	capsule hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)

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Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart		<a>	<29>				<24>				<19>				<28>			
	inflammation	a	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		b	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
tooth		<a>	<29>				<24>				<19>				<28>			
	dysplasia	a	5	0	0	0	2	0	0	0	0	0	0	0	4	0	0	0
		b	5	0	0	0	2	0	0	0	0	0	0	0	4	0	0	0
		(c)	(17)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
tongue		<a>	<29>				<24>				<19>				<28>			
	arteritis	a	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		b	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
salivary gl		<a>	<29>				<24>				<19>				<28>			
	inflammation	a	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		b	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration	a	9	0	0	0	8	0	0	0	4	0	0	0	6	1	0	0
		b	9	0	0	0	8	0	0	0	4	0	0	0	6	1	0	0
		(c)	(31)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(21)	(4)	(0)	(0)
stomach		<a>	<29>				<24>				<19>				<28>			
	mineralization	a	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		b	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<29>				<24>				<19>				<28>			
	inflammation		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erosion:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		11 (38)	4 (14)	0 (0)	0 (0)	6 (25)	2 (8)	0 (0)	0 (0)	6 (32)	3 (16)	0 (0)	0 (0)	8 (29)	1 (4)	0 (0)	0 (0)
liver			<29>				<24>				<19>				<28>			
	angiectasis		0 (0)	2 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	2 (7)	0 (0)

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			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<29>				<24>				<19>				<28>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)
	granulation		22 (76)	0 (0)	0 (0)	0 (0)	17 (71)	2 (8)	0 (0)	0 (0)	11 (58)	0 (0)	0 (0)	0 (0)	17 (61)	2 (7)	0 (0)	0 (0)
	clear cell focus		1 (3)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	1 (4)	0 (0)
	acidophilic cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	biliary cyst		1 (3)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney			<29>				<24>				<19>				<28>			
	hyaline droplet		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (16)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)

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			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<29>				<24>				<19>				<28>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		3	1	0	0	5	0	0	0	3	0	0	0	6	0	0	0
			(10)	(3)	(0)	(0)	(21)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(21)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory polyp		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)
urin bladd			<29>				<24>				<19>				<28>			
	inflammation		1	0	0	0	1	0	0	0	1	0	0	0	0	1	1	0
			(3)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(4)	(4)	(0)
[Endocrine system]																		
pituitary			<29>				<24>				<18>				<28>			
	angiectasis		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)

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[Endocrine system]																		
pituitary			<29>				<24>				<18>				<28>			
	hyperplasia		3 (10)	2 (7)	0 (0)	0 (0)	3 (13)	1 (4)	0 (0)	0 (0)	2 (11)	1 (6)	0 (0)	0 (0)	2 (7)	3 (11)	0 (0)	0 (0)
adrenal			<29>				<24>				<18>				<28>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	goiter		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	spindle-cell hyperplasia		18 (62)	11 (38)	0 (0)	0 (0)	10 (42)	14 (58)	0 (0)	0 (0)	11 (58)	6 (32)	0 (0)	0 (0)	13 (46)	14 (50)	1 (4)	0 (0)
	hyperplasia:cortical cell		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<29>				<24>				<19>				<28>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)

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			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
ovary			<29>				<24>				<19>				<28>			
	cyst		3 (10)	6 (21)	0 (0)	0 (0)	4 (17)	5 (21)	0 (0)	0 (0)	1 (5)	3 (16)	0 (0)	0 (0)	3 (11)	2 (7)	0 (0)	0 (0)
uterus			<29>				<24>				<19>				<28>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
	decidual change		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cystic endometrial hyperplasia		8 (28)	6 (21)	0 (0)	0 (0)	5 (21)	12 (50)	0 (0)	0 (0)	4 (21)	8 (42)	0 (0)	0 (0)	8 (29)	7 (25)	0 (0)	0 (0)
mammary gl			<29>				<24>				<19>				<28>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	hyperplasia		3 (10)	1 (3)	0 (0)	0 (0)	5 (21)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)
	atypical hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Nervous system]																		
brain			<29>				<24>				<19>				<28>			
	mineralization		14 (48)	0 (0)	0 (0)	0 (0)	14 (58)	0 (0)	0 (0)	0 (0)	10 (53)	0 (0)	0 (0)	0 (0)	17 (61)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]																		
Harder gl			<29>				<24>				<18>				<28>			
	degeneration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX M 1

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED

RAT : MALE

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	30000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	0	0
	NO. OF ANIMALS WITH TUMORS		0	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	0	0	0
	NO. OF TOTAL TUMORS		0	0	0	0
53 - 78	NO. OF EXAMINED ANIMALS		2	3	4	0
	NO. OF ANIMALS WITH TUMORS		2	3	2	0
	NO. OF ANIMALS WITH SINGLE TUMORS		2	2	2	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	1	0	0
	NO. OF BENIGN TUMORS		1	2	1	0
	NO. OF MALIGNANT TUMORS		1	2	1	0
	NO. OF TOTAL TUMORS		2	4	2	0
79 - 104	NO. OF EXAMINED ANIMALS		10	8	12	20
	NO. OF ANIMALS WITH TUMORS		10	8	12	20
	NO. OF ANIMALS WITH SINGLE TUMORS		4	2	0	6
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	6	12	14
	NO. OF BENIGN TUMORS		15	11	20	36
	NO. OF MALIGNANT TUMORS		6	6	11	11
	NO. OF TOTAL TUMORS		21	17	31	47
105 - 105	NO. OF EXAMINED ANIMALS		38	39	34	30
	NO. OF ANIMALS WITH TUMORS		38	39	34	30
	NO. OF ANIMALS WITH SINGLE TUMORS		12	8	13	5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		26	31	21	25
	NO. OF BENIGN TUMORS		76	80	62	65
	NO. OF MALIGNANT TUMORS		9	12	5	7
	NO. OF TOTAL TUMORS		85	92	67	72

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	30000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		50	50	48	50
	NO. OF ANIMALS WITH SINGLE TUMORS		18	12	15	11
	NO. OF ANIMALS WITH MULTIPLE TUMORS		32	38	33	39
	NO. OF BENIGN TUMORS		92	93	83	101
	NO. OF MALIGNANT TUMORS		16	20	17	18
	NO. OF TOTAL TUMORS		108	113	100	119

APPENDIX M 2

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED

RAT : FEMALE

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	30000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	1	0	1
	NO. OF ANIMALS WITH TUMORS		0	1	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	1	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	1	0	0
	NO. OF TOTAL TUMORS		0	1	0	0
53 - 78	NO. OF EXAMINED ANIMALS		0	2	0	13
	NO. OF ANIMALS WITH TUMORS		0	2	0	7
	NO. OF ANIMALS WITH SINGLE TUMORS		0	2	0	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	1	0	6
	NO. OF MALIGNANT TUMORS		0	1	0	1
	NO. OF TOTAL TUMORS		0	2	0	7
79 - 104	NO. OF EXAMINED ANIMALS		3	8	15	22
	NO. OF ANIMALS WITH TUMORS		3	8	13	10
	NO. OF ANIMALS WITH SINGLE TUMORS		1	4	6	5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	4	7	5
	NO. OF BENIGN TUMORS		5	8	13	11
	NO. OF MALIGNANT TUMORS		1	5	10	5
	NO. OF TOTAL TUMORS		6	13	23	16
105 - 105	NO. OF EXAMINED ANIMALS		47	39	35	14
	NO. OF ANIMALS WITH TUMORS		33	26	20	9
	NO. OF ANIMALS WITH SINGLE TUMORS		18	13	13	5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		15	13	7	4
	NO. OF BENIGN TUMORS		49	39	23	11
	NO. OF MALIGNANT TUMORS		3	5	7	2
	NO. OF TOTAL TUMORS		52	44	30	13

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	30000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		36	37	33	26
	NO. OF ANIMALS WITH SINGLE TUMORS		19	20	19	17
	NO. OF ANIMALS WITH MULTIPLE TUMORS		17	17	14	9
	NO. OF BENIGN TUMORS		54	48	36	28
	NO. OF MALIGNANT TUMORS		4	12	17	8
	NO. OF TOTAL TUMORS		58	60	53	36

APPENDIX M 3

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED

MOUSE : MALE

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	10000 ppm	20000 ppm	40000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		1	0	0	0
	NO. OF ANIMALS WITH TUMORS		0	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	0	0	0
	NO. OF TOTAL TUMORS		0	0	0	0
53 - 78	NO. OF EXAMINED ANIMALS		3	2	4	8
	NO. OF ANIMALS WITH TUMORS		1	1	2	2
	NO. OF ANIMALS WITH SINGLE TUMORS		1	0	0	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	1	2	1
	NO. OF BENIGN TUMORS		1	2	3	2
	NO. OF MALIGNANT TUMORS		0	3	3	1
	NO. OF TOTAL TUMORS		1	5	6	3
79 - 104	NO. OF EXAMINED ANIMALS		12	13	16	17
	NO. OF ANIMALS WITH TUMORS		11	12	12	13
	NO. OF ANIMALS WITH SINGLE TUMORS		8	9	6	5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		3	3	6	8
	NO. OF BENIGN TUMORS		4	5	7	7
	NO. OF MALIGNANT TUMORS		11	13	14	16
	NO. OF TOTAL TUMORS		15	18	21	23
105 - 105	NO. OF EXAMINED ANIMALS		34	35	30	25
	NO. OF ANIMALS WITH TUMORS		26	24	24	21
	NO. OF ANIMALS WITH SINGLE TUMORS		14	12	9	13
	NO. OF ANIMALS WITH MULTIPLE TUMORS		12	12	15	8
	NO. OF BENIGN TUMORS		20	25	24	17
	NO. OF MALIGNANT TUMORS		25	17	19	17
	NO. OF TOTAL TUMORS		45	42	43	34

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	10000 ppm	20000 ppm	40000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		38	37	38	36
	NO. OF ANIMALS WITH SINGLE TUMORS		23	21	15	19
	NO. OF ANIMALS WITH MULTIPLE TUMORS		15	16	23	17
	NO. OF BENIGN TUMORS		25	32	34	26
	NO. OF MALIGNANT TUMORS		36	33	36	34
	NO. OF TOTAL TUMORS		61	65	70	60

APPENDIX M 4

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED

MOUSE: FEMALE

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	10000 ppm	20000 ppm	40000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		3	1	3	0
	NO. OF ANIMALS WITH TUMORS		3	0	1	0
	NO. OF ANIMALS WITH SINGLE TUMORS		3	0	1	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		3	0	1	0
	NO. OF TOTAL TUMORS		3	0	1	0
53 - 78	NO. OF EXAMINED ANIMALS		4	5	5	4
	NO. OF ANIMALS WITH TUMORS		3	5	4	3
	NO. OF ANIMALS WITH SINGLE TUMORS		2	5	4	3
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		4	5	4	3
	NO. OF TOTAL TUMORS		4	5	4	3
79 - 104	NO. OF EXAMINED ANIMALS		14	20	23	18
	NO. OF ANIMALS WITH TUMORS		12	19	21	17
	NO. OF ANIMALS WITH SINGLE TUMORS		9	13	14	10
	NO. OF ANIMALS WITH MULTIPLE TUMORS		3	6	7	7
	NO. OF BENIGN TUMORS		4	6	10	7
	NO. OF MALIGNANT TUMORS		13	19	20	17
	NO. OF TOTAL TUMORS		17	25	30	24
105 - 105	NO. OF EXAMINED ANIMALS		29	24	19	28
	NO. OF ANIMALS WITH TUMORS		22	18	15	24
	NO. OF ANIMALS WITH SINGLE TUMORS		14	8	8	11
	NO. OF ANIMALS WITH MULTIPLE TUMORS		8	10	7	13
	NO. OF BENIGN TUMORS		22	24	12	28
	NO. OF MALIGNANT TUMORS		9	8	11	17
	NO. OF TOTAL TUMORS		31	32	23	45

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

Time-related Weeks	Items	Group Name	Control	10000 ppm	20000 ppm	40000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		40	42	41	44
	NO. OF ANIMALS WITH SINGLE TUMORS		28	26	27	24
	NO. OF ANIMALS WITH MULTIPLE TUMORS		12	16	14	20
	NO. OF BENIGN TUMORS		26	30	22	35
	NO. OF MALIGNANT TUMORS		29	32	36	37
	NO. OF TOTAL TUMORS		55	62	58	72

APPENDIX N 1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

RAT : MALE :

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
	trichoepithelioma		0 (0%)	1 (2%)	0 (0%)	2 (4%)
	keratoacanthoma		1 (2%)	3 (6%)	1 (2%)	4 (8%)
	sebaceous adenoma		0 (0%)	0 (0%)	0 (0%)	3 (6%)
	squamous cell carcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		4 (8%)	4 (8%)	4 (8%)	6 (12%)
	lipoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	schwannoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	chordoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hemangioma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
	fibrosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	malignant fibrous histiocytoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Respiratory system]						
nasal cavit			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		3 (6%)	3 (6%)	3 (6%)	5 (10%)
	bronchiolar-alveolar carcinoma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	malignant lymphoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
thymus			<50>	<50>	<50>	<50>
	thymoma:malignant		0 (0%)	1 (2%)	0 (0%)	1 (2%)
spleen			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	mononuclear cell leukemia		6 (12%)	2 (4%)	2 (4%)	4 (8%)
[Digestive system]						
stomach			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
small intes			<50>	<49>	<50>	<50>
	fibroma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
large intes			<50>	<49>	<50>	<50>
	adenocarcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		1 (2%)	0 (0%)	0 (0%)	1 (2%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Digestive system]						
liver			<50>	<50>	<50>	<50>
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
	hepatocellular carcinoma		0 (0%)	2 (4%)	0 (0%)	1 (2%)
pancreas			<50>	<50>	<50>	<50>
	islet cell adenoma		4 (8%)	3 (6%)	4 (8%)	3 (6%)
	islet cell adenocarcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Urinary system]						
kidney			<50>	<50>	<50>	<50>
	nephroblastoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
urin bladd			<50>	<50>	<50>	<50>
	transitional cell papilloma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
[Endocrine system]						
pituitary			<50>	<50>	<50>	<50>
	adenoma		14 (28%)	14 (28%)	11 (22%)	18 (36%)
	adenocarcinoma		3 (6%)	1 (2%)	3 (6%)	1 (2%)
thyroid			<50>	<50>	<50>	<50>
	C-cell adenoma		12 (24%)	5 (10%)	5 (10%)	4 (8%)
	follicular adenocarcinoma		1 (2%)	1 (2%)	2 (4%)	1 (2%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		4 (8%)	7 (14%)	5 (10%)	7 (14%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Endocrine system]						
adrenal			<50>	<50>	<50>	<50>
	ganglioneuroma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	cortical adenoma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
	pheochromocytoma:malignant		0 (0%)	0 (0%)	1 (2%)	1 (2%)
[Reproductive system]						
testis			<50>	<50>	<50>	<50>
	interstitial cell tumor		44 (88%)	43 (86%)	42 (84%)	44 (88%)
	rete testis adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
mammary gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	fibroadenoma		2 (4%)	1 (2%)	0 (0%)	0 (0%)
	adenocarcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
prep/cli gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	1 (2%)	1 (2%)	0 (0%)
	adenocarcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	malignant reticulosis		0 (0%)	0 (0%)	1 (2%)	1 (2%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	glioma		1 (2%)	1 (2%)	1 (2%)	0 (0%)
spinal cord			<50>	<50>	<50>	<50>
	glioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Special sense organs/appandage]						
Zymbal gl			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Musculoskeletal system]						
bone			<50>	<50>	<50>	<50>
	osteosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	mesothelioma		1 (2%)	6 (12%)	4 (8%)	3 (6%)
	malignant fibrous histiocytoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
retroperit			<50>	<50>	<50>	<50>
	paraganglioma:benign		0 (0%)	1 (2%)	0 (0%)	0 (0%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

APPENDIX N 2

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

RAT : FEMALE :

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	squamous cell papilloma		1 (2%)	1 (2%)	1 (2%)	1 (2%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		2 (4%)	1 (2%)	0 (0%)	1 (2%)
	schwannoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		0 (0%)	3 (6%)	1 (2%)	0 (0%)
[Hematopoietic system]						
thymus			<50>	<50>	<50>	<50>
	thymoma:benign		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	thymoma:malignant		0 (0%)	1 (2%)	1 (2%)	0 (0%)
spleen			<50>	<50>	<50>	<50>
	hemangioma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
	mononuclear cell leukemia		1 (2%)	7 (14%)	3 (6%)	4 (8%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<50>
	squamous cell carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Digestive system]						
tooth			<50>	<50>	<50>	<50>
	ameloblastoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
small intes			<50>	<50>	<50>	<50>
	fibroma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
large intes			<50>	<50>	<50>	<50>
	leiomyosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
pancreas			<50>	<50>	<50>	<50>
	islet cell adenocarcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Urinary system]						
urin bladd			<50>	<50>	<50>	<50>
	transitional cell papilloma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
	transitional cell carcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Endocrine system]						
pituitary			<49>	<50>	<50>	<50>
	adenoma		18 (37%)	14 (28%)	12 (24%)	6 (12%)
	adenocarcinoma		1 (2%)	0 (0%)	2 (4%)	1 (2%)
thyroid			<50>	<49>	<50>	<50>
	C-cell adenoma		6 (12%)	4 (8%)	5 (10%)	4 (8%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Endocrine system]						
thyroid			<50>	<49>	<50>	<50>
	C-cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		1 (2%)	5 (10%)	2 (4%)	0 (0%)
	cortical adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Reproductive system]						
ovary			<50>	<49>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	luteoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	granulosa-theca cell tumor		1 (2%)	2 (4%)	0 (0%)	0 (0%)
uterus			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
	endometrial stromal polyp		14 (28%)	5 (10%)	7 (14%)	7 (14%)
	adenocarcinoma		0 (0%)	0 (0%)	2 (4%)	1 (2%)
	endometrial stromal sarcoma		0 (0%)	0 (0%)	2 (4%)	1 (2%)
mammary gl			<50>	<50>	<50>	<50>
	adenoma		2 (4%)	1 (2%)	0 (0%)	1 (2%)
	fibroadenoma		3 (6%)	5 (10%)	3 (6%)	2 (4%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Reproductive system]						
mammary gl			<50>	<50>	<50>	<50>
	adenocarcinoma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
prep/cli gl			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	adenoma		1 (2%)	3 (6%)	1 (2%)	3 (6%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	malignant reticulosis		0 (0%)	1 (2%)	1 (2%)	0 (0%)
[Special sense organs/appandage]						
Zymbal gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	mesothelioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

APPENDIX N 3

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

MOUSE: MALE

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0-105W)

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Integumentary system/appandage]						
subcutis			<50>	<50>	<50>	<50>
	lipoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	hemangioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	fibrosarcoma		2 (4%)	1 (2%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	carcinoma:NOS		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	hemangiosarcoma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		5 (10%)	7 (14%)	8 (16%)	8 (16%)
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	bronchiolar-alveolar carcinoma		7 (14%)	3 (6%)	6 (12%)	3 (6%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	hemangioma		2 (4%)	3 (6%)	0 (0%)	0 (0%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	malignant lymphoma		7 (14%)	3 (6%)	6 (12%)	6 (12%)
	mastcytoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
spleen			<50>	<50>	<50>	<50>
	hemangioma		1 (2%)	0 (0%)	3 (6%)	1 (2%)
	malignant lymphoma		1 (2%)	0 (0%)	3 (6%)	3 (6%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hemangiosarcoma		1 (2%)	3 (6%)	3 (6%)	1 (2%)
[Digestive system]						
tongue			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
small intes			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	hemangioma		5 (10%)	8 (16%)	1 (2%)	5 (10%)
	hepatocellular adenoma		6 (12%)	13 (26%)	13 (26%)	7 (14%)
	histiocytic sarcoma		2 (4%)	3 (6%)	1 (2%)	4 (8%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Digestive system]						
liver			<50>	<50>	<50>	<50>
	hemangiosarcoma		0 (0%)	1 (2%)	1 (2%)	2 (4%)
	hepatocellular carcinoma		14 (28%)	11 (22%)	13 (26%)	9 (18%)
	hepatoblastoma		1 (2%)	2 (4%)	0 (0%)	0 (0%)
[Endocrine system]						
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
[Reproductive system]						
testis			<50>	<50>	<50>	<50>
	xanthoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
epididymis			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	glioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
periph nerv			<50>	<50>	<50>	<50>
	histiocytic sarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<50>	<50>
	adenoma		3 (6%)	1 (2%)	4 (8%)	1 (2%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Musculoskeletal system]						
bone			<50>	<50>	<50>	<50>
	osteosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Body cavities]						
pleura			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
peritoneum			<50>	<50>	<50>	<50>
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
mesenterium			<50>	<50>	<50>	<50>
	hemangioma		1 (2%)	0 (0%)	0 (0%)	0 (0%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

APPENDIX N 4

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY: SUMMARY)

MOUSE: FEMALE

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<49>	<50>
	squamous cell papilloma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	sebaceous adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
subcutis			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	fibrosarcoma		2 (4%)	1 (2%)	0 (0%)	2 (4%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		2 (4%)	3 (6%)	2 (4%)	0 (0%)
	bronchiolar-alveolar carcinoma		1 (2%)	2 (4%)	0 (0%)	0 (0%)
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	malignant lymphoma		9 (18%)	15 (30%)	11 (22%)	14 (28%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	mastcytoma:malignant		0 (0%)	0 (0%)	2 (4%)	0 (0%)
thymus			<50>	<50>	<50>	<50>
	malignant lymphoma		2 (4%)	0 (0%)	0 (0%)	0 (0%)
spleen			<50>	<50>	<50>	<50>
	malignant lymphoma		1 (2%)	1 (2%)	1 (2%)	2 (4%)
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
[Digestive system]						
tongue			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
salivary gl			<50>	<50>	<50>	<50>
	xanthoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
stomach			<50>	<50>	<50>	<50>
	squamous cell papilloma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
small intes			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
liver			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	2 (4%)	1 (2%)	0 (0%)
	hepatocellular adenoma		5 (10%)	11 (22%)	5 (10%)	10 (20%)
	histiocytic sarcoma		1 (2%)	2 (4%)	2 (4%)	0 (0%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Digestive system]						
liver			<50>	<50>	<50>	<50>
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hepatocellular carcinoma		0 (0%)	2 (4%)	1 (2%)	0 (0%)
[Endocrine system]						
pituitary			<49>	<50>	<49>	<49>
	adenoma		9 (18%)	7 (14%)	9 (18%)	8 (16%)
	adenocarcinoma		2 (4%)	1 (2%)	2 (4%)	1 (2%)
adrenal			<49>	<50>	<50>	<50>
	pheochromocytoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Reproductive system]						
ovary			<49>	<50>	<50>	<49>
	cystadenoma		1 (2%)	2 (4%)	3 (6%)	1 (2%)
	cystadenocarcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
uterus			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	endometrial stromal polyp		5 (10%)	2 (4%)	0 (0%)	2 (4%)
	histiocytic sarcoma		9 (18%)	3 (6%)	14 (28%)	12 (24%)
mammary gl			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	0 (0%)	1 (2%)	3 (6%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

Organ	Findings	Group Name / No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Reproductive system]						
mammary gl			<50>	<50>	<50>	<50>
	adenocarcinoma		1 (2%)	1 (2%)	2 (4%)	3 (6%)
[Nervous system]						
periph nerv			<50>	<50>	<50>	<50>
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<50>	<50>
	adenoma		2 (4%)	1 (2%)	0 (0%)	4 (8%)
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)

< a > a : Number of animals examined at the site
b (c) b : Number of animals with neoplasm c : b / a * 100

APPENDIX O 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : skin/appendage TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	4/50(8.0)
Adjusted rates(b)	2.27	7.69	2.94	10.81
Terminal rates(c)	0/38(0.0)	3/39(7.7)	1/34(2.9)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1022			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2260			
Fisher Exact test(e)		P = 0.3235	P = 0.2475	P = 0.1998
	SITE : skin/appendage TUMOR : sebaceous adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	0.0	8.82
Terminal rates(c)	0/38(0.0)	0/39(0.0)	0/34(0.0)	2/30(6.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0025**?			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0079**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1325
	SITE : subcutis TUMOR : fibroma			
Tumor rate				
Overall rates(a)	4/50(8.0)	4/50(8.0)	4/50(8.0)	6/50(12.0)
Adjusted rates(b)	10.53	7.69	8.89	13.64
Terminal rates(c)	4/38(10.5)	3/39(7.7)	3/34(8.8)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5801			
Prevalence method(d)	P = 0.1950			
Combined analysis(d)	P = 0.2370			
Cochran-Armitage test(e)	P = 0.4522			
Fisher Exact test(e)		P = 0.3579	P = 0.3579	P = 0.3944

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : subcutis TUMOR : fibroma,fibrosarcoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	4/50(8.0)	4/50(8.0)	6/50(12.0)
Adjusted rates(b)	10.53	7.69	8.89	13.64
Terminal rates(c)	4/38(10.5)	3/39(7.7)	3/34(8.8)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8773			
Prevalence method(d)	P = 0.1950			
Combined analysis(d)	P = 0.3375			
Cochran-Armitage test(e)	P = 0.6539			
Fisher Exact test(e)		P = 0.4883	P = 0.4883	P = 0.4872
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	3/50(6.0)	5/50(10.0)
Adjusted rates(b)	7.89	6.52	8.82	16.67
Terminal rates(c)	3/38(7.9)	2/39(5.1)	3/34(8.8)	5/30(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1328			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3991			
Fisher Exact test(e)		P = 0.3392	P = 0.3392	P = 0.3790
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	7.89	6.52	8.82	20.00
Terminal rates(c)	3/38(7.9)	2/39(5.1)	3/34(8.8)	6/30(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0655			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2205			
Fisher Exact test(e)		P = 0.3392	P = 0.3392	P = 0.2728

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	6/50(12.0)	2/50(4.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	2.63	5.13	0.0	6.67
Terminal rates(c)	1/38(2.6)	2/39(5.1)	0/34(0.0)	2/30(6.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7590			
Prevalence method(d)	P = 0.2656			
Combined analysis(d)	P = 0.5809			
Cochran-Armitage test(e)	P = 0.6395			
Fisher Exact test(e)		P = 0.1606	P = 0.1606	P = 0.3944
	SITE : pancreas TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	8.00	7.69	8.89	10.00
Terminal rates(c)	3/38(7.9)	3/39(7.7)	1/34(2.9)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6012			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.7787			
Fisher Exact test(e)		P = 0.4895	P = 0.3579	P = 0.4895
	SITE : pancreas TUMOR : islet cell adenoma,islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	3/50(6.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	10.53	7.69	8.89	10.00
Terminal rates(c)	4/38(10.5)	3/39(7.7)	1/34(2.9)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7109			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5552			
Fisher Exact test(e)		P = 0.3790	P = 0.4883	P = 0.3790

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	14/50(28.0)	11/50(22.0)	18/50(36.0)
Adjusted rates(b)	31.58	28.21	25.71	36.96
Terminal rates(c)	12/38(31.6)	11/39(28.2)	8/34(23.5)	7/30(23.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5341			
Prevalence method(d)	P = 0.1884			
Combined analysis(d)	P = 0.2148			
Cochran-Armitage test(e)	P = 0.3823			
Fisher Exact test(e)		P = 0.4155	P = 0.3777	P = 0.3405
	SITE : pituitary gland TUMOR : adenocarcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	5.26	0.0	2.94	0.0
Terminal rates(c)	2/38(5.3)	0/39(0.0)	1/34(2.9)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4509			
Prevalence method(d)	P = 0.8729			
Combined analysis(d)	P = 0.7196			
Cochran-Armitage test(e)	P = 0.4642			
Fisher Exact test(e)		P = 0.3235	P = 0.3392	P = 0.3235
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	17/50(34.0)	15/50(30.0)	14/50(28.0)	19/50(38.0)
Adjusted rates(b)	36.84	28.21	28.57	37.78
Terminal rates(c)	14/38(36.8)	11/39(28.2)	9/34(26.5)	7/30(23.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5008			
Prevalence method(d)	P = 0.2855			
Combined analysis(d)	P = 0.3101			
Cochran-Armitage test(e)	P = 0.5920			
Fisher Exact test(e)		P = 0.4586	P = 0.3959	P = 0.4638

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	29.27	12.82	14.71	11.76
Terminal rates(c)	11/38(28.9)	5/39(12.8)	5/34(14.7)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9671			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0393*			
Fisher Exact test(e)		P = 0.0942	P = 0.0942	P = 0.0539
	SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	29.27	12.82	14.71	11.76
Terminal rates(c)	11/38(28.9)	5/39(12.8)	5/34(14.7)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9671			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0393*			
Fisher Exact test(e)		P = 0.0942	P = 0.0942	P = 0.0539
	SITE : adrenal gland TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	7/50(14.0)	5/50(10.0)	7/50(14.0)
Adjusted rates(b)	9.30	17.95	13.51	21.88
Terminal rates(c)	2/38(5.3)	7/39(17.9)	4/34(11.8)	6/30(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1540			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4766			
Fisher Exact test(e)		P = 0.2958	P = 0.4883	P = 0.2958

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma,pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	4/50(8.0)	7/50(14.0)	6/50(12.0)	8/50(16.0)
Adjusted rates(b)	9.30	17.95	13.51	21.88
Terminal rates(c)	2/38(5.3)	7/39(17.9)	4/34(11.8)	6/30(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1343			
Prevalence method(d)	P = 0.1540			
Combined analysis(d)	P = 0.0912			
Cochran-Armitage test(e)	P = 0.2946			
Fisher Exact test(e)		P = 0.2958	P = 0.3944	P = 0.2169
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	44/50(88.0)	43/50(86.0)	42/50(84.0)	44/50(88.0)
Adjusted rates(b)	92.68	97.50	93.18	97.30
Terminal rates(c)	35/38(92.1)	38/39(97.4)	31/34(91.2)	29/30(96.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4513			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9721			
Fisher Exact test(e)		P = 0.4728	P = 0.4956	P = 0.4419
	SITE : mammary gland			
	TUMOR : adenoma,fibroadenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	0/50(0.0)
Adjusted rates(b)	7.89	2.44	0.0	0.0
Terminal rates(c)	3/38(7.9)	0/39(0.0)	0/34(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9858			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0405*			
Fisher Exact test(e)		P = 0.3235	P = 0.1325	P = 0.1325

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : peritoneum TUMOR : mesothelioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	6/50(12.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	2.63	10.42	4.55	3.33
Terminal rates(c)	1/38(2.6)	3/39(7.7)	0/34(0.0)	1/30(3.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0972			
Prevalence method(d)	P = 0.7222			
Combined analysis(d)	P = 0.3710			
Cochran-Armitage test(e)	P = 0.7787			
Fisher Exact test(e)		P = 0.0724	P = 0.1998	P = 0.3235

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$

APPENDIX O 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	0.0	7.69	2.56	0.0
Terminal rates(c)	0/47(0.0)	3/39(7.7)	0/35(0.0)	0/14(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5120			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4946			
Fisher Exact test(e)		P = 0.1325	P = 0.4950	P = 0.5000
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	0.0	7.69	2.56	0.0
Terminal rates(c)	0/47(0.0)	3/39(7.7)	0/35(0.0)	0/14(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5120			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4946			
Fisher Exact test(e)		P = 0.1325	P = 0.4950	P = 0.5000
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	1/50(2.0)	7/50(14.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	2.13	7.69	5.71	7.14
Terminal rates(c)	1/47(2.1)	3/39(7.7)	2/35(5.7)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0417*			
Prevalence method(d)	P = 0.2161			
Combined analysis(d)	P = 0.0349*			
Cochran-Armitage test(e)	P = 0.6177			
Fisher Exact test(e)		P = 0.0430*	P = 0.3235	P = 0.1998

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	18/49(36.7)	14/50(28.0)	12/50(24.0)	6/50(12.0)
Adjusted rates(b)	35.42	25.64	25.71	21.43
Terminal rates(c)	16/46(34.8)	10/39(25.6)	9/35(25.7)	3/14(21.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4673			
Prevalence method(d)	P = 0.9411			
Combined analysis(d)	P = 0.9192			
Cochran-Armitage test(e)	P = 0.0041**			
Fisher Exact test(e)		P = 0.3228	P = 0.2121	P = 0.0201*
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	19/49(38.8)	14/50(28.0)	14/50(28.0)	7/50(14.0)
Adjusted rates(b)	37.50	25.64	28.57	21.43
Terminal rates(c)	17/46(37.0)	10/39(25.6)	10/35(28.6)	3/14(21.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1912			
Prevalence method(d)	P = 0.9439			
Combined analysis(d)	P = 0.8365			
Cochran-Armitage test(e)	P = 0.0070**			
Fisher Exact test(e)		P = 0.2736	P = 0.2736	P = 0.0256*
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	4/49(8.2)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	12.00	9.52	12.82	10.71
Terminal rates(c)	5/47(10.6)	3/39(7.7)	3/35(8.6)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4969			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5887			
Fisher Exact test(e)		P = 0.4066	P = 0.4872	P = 0.3944

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	4/49(8.2)	6/50(12.0)	4/50(8.0)
Adjusted rates(b)	12.00	9.52	15.38	10.71
Terminal rates(c)	5/47(10.6)	3/39(7.7)	4/35(11.4)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4602			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6246			
Fisher Exact test(e)		P = 0.4066	P = 0.3807	P = 0.3944
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	5/50(10.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	2.13	11.36	5.71	0.0
Terminal rates(c)	1/47(2.1)	4/39(10.3)	2/35(5.7)	0/14(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7056			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2225			
Fisher Exact test(e)		P = 0.1210	P = 0.4926	P = 0.4950
	SITE : adrenal gland			
	TUMOR : pheochromocytoma,pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	1/50(2.0)	5/50(10.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	2.13	11.36	5.71	0.0
Terminal rates(c)	1/47(2.1)	4/39(10.3)	2/35(5.7)	0/14(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7056			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2225			
Fisher Exact test(e)		P = 0.1210	P = 0.4926	P = 0.4950

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : uterus TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	14/50(28.0)	5/50(10.0)	7/50(14.0)	7/50(14.0)
Adjusted rates(b)	28.00	12.82	13.04	29.41
Terminal rates(c)	13/47(27.7)	5/39(12.8)	3/35(8.6)	4/14(28.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0621			
Prevalence method(d)	P = 0.6556			
Combined analysis(d)	P = 0.4651			
Cochran-Armitage test(e)	P = 0.1662			
Fisher Exact test(e)		P = 0.0481*	P = 0.1246	P = 0.1246
	SITE : uterus TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	2.13	0.0	4.55	7.14
Terminal rates(c)	1/47(2.1)	0/39(0.0)	1/35(2.9)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2722			
Prevalence method(d)	P = 0.1998			
Combined analysis(d)	P = 0.1642			
Cochran-Armitage test(e)	P = 0.7019			
Fisher Exact test(e)		P = 0.4950	P = 0.3235	P = 0.2475
	SITE : uterus TUMOR : endometrial stromal polyp,endometrial stromal sarcoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	5/50(10.0)	9/50(18.0)	8/50(16.0)
Adjusted rates(b)	28.00	12.82	13.33	29.41
Terminal rates(c)	13/47(27.7)	5/39(12.8)	3/35(8.6)	4/14(28.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0146*			
Prevalence method(d)	P = 0.6429			
Combined analysis(d)	P = 0.2632			
Cochran-Armitage test(e)	P = 0.3195			
Fisher Exact test(e)		P = 0.0481*	P = 0.2397	P = 0.1781

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : mammary gland TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	6.38	11.90	8.57	4.26
Terminal rates(c)	3/47(6.4)	4/39(10.3)	3/35(8.6)	0/14(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6398			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4671			
Fisher Exact test(e)		P = 0.3790	P = 0.3392	P = 0.4909
	SITE : mammary gland TUMOR : adenoma,fibroadenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	6/50(12.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	10.64	11.90	8.57	7.14
Terminal rates(c)	5/47(10.6)	4/39(10.3)	3/35(8.6)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5248			
Prevalence method(d)	P = 0.6074			
Combined analysis(d)	P = 0.6370			
Cochran-Armitage test(e)	P = 0.3243			
Fisher Exact test(e)		P = 0.4872	P = 0.3790	P = 0.3790

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.13	5.13	0.0	7.14
Terminal rates(c)	1/47(2.1)	2/39(5.1)	0/35(0.0)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1924			
Prevalence method(d)	P = 0.1824			
Combined analysis(d)	P = 0.1066			
Cochran-Armitage test(e)	P = 0.4642			
Fisher Exact test(e)		P = 0.3235	P = 0.2475	P = 0.3235

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
——— : There is no data which should be statistical analysis.
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

APPENDIX O 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

STUDY No. : 0225
ANIMAL : MOUSE BDF1
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	7/50(14.0)	8/50(16.0)	8/50(16.0)
Adjusted rates(b)	12.82	14.29	20.00	18.18
Terminal rates(c)	4/34(11.8)	4/35(11.4)	6/30(20.0)	4/25(16.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1435			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4084			
Fisher Exact test(e)		P = 0.4062	P = 0.3141	P = 0.3141
	SITE : lung TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	3/50(6.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	14.71	6.67	13.33	12.00
Terminal rates(c)	5/34(14.7)	2/35(5.7)	4/30(13.3)	3/25(12.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8753			
Prevalence method(d)	P = 0.5613			
Combined analysis(d)	P = 0.7348			
Cochran-Armitage test(e)	P = 0.3082			
Fisher Exact test(e)		P = 0.1917	P = 0.4863	P = 0.1917
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	10/50(20.0)	14/50(28.0)	11/50(22.0)
Adjusted rates(b)	26.47	20.41	33.33	28.00
Terminal rates(c)	9/34(26.5)	6/35(17.1)	10/30(33.3)	7/25(28.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8753			
Prevalence method(d)	P = 0.2340			
Combined analysis(d)	P = 0.3564			
Cochran-Armitage test(e)	P = 0.9775			
Fisher Exact test(e)		P = 0.4406	P = 0.4489	P = 0.4826

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : bone marrow TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	0/50(0.0)	0/50(0.0)
Adjusted rates(b)	5.88	6.12	0.0	0.0
Terminal rates(c)	2/34(5.9)	1/35(2.9)	0/30(0.0)	0/25(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9632			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0783			
Fisher Exact test(e)		P = 0.4909	P = 0.2574	P = 0.2574
	SITE : lymph node TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	3/50(6.0)	6/50(12.0)	6/50(12.0)
Adjusted rates(b)	11.76	5.71	10.00	10.00
Terminal rates(c)	4/34(11.8)	2/35(5.7)	3/30(10.0)	2/25(8.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2716			
Prevalence method(d)	P = 0.4197			
Combined analysis(d)	P = 0.2899			
Cochran-Armitage test(e)	P = 0.9391			
Fisher Exact test(e)		P = 0.1917	P = 0.4863	P = 0.4863
	SITE : spleen TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	2.94	0.0	6.52	4.00
Terminal rates(c)	1/34(2.9)	0/35(0.0)	1/30(3.3)	1/25(4.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3127			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.7019			
Fisher Exact test(e)		P = 0.4950	P = 0.3235	P = 0.2475

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : spleen TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	2.94	0.0	6.67	0.0
Terminal rates(c)	1/34(2.9)	0/35(0.0)	2/30(6.7)	0/25(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0074**			
Prevalence method(d)	P = 0.5831			
Combined analysis(d)	P = 0.0462*			
Cochran-Armitage test(e)	P = 0.1347			
Fisher Exact test(e)		P = 0.4950	P = 0.3235	P = 0.3235
	SITE : spleen TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	2.94	6.12	6.25	4.00
Terminal rates(c)	1/34(2.9)	1/35(2.9)	1/30(3.3)	1/25(4.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3515			
Prevalence method(d)	P = 0.5632			
Combined analysis(d)	P = 0.5187			
Cochran-Armitage test(e)	P = 0.8073			
Fisher Exact test(e)		P = 0.3235	P = 0.3235	P = 0.2475
	SITE : spleen TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	6/50(12.0)	2/50(4.0)
Adjusted rates(b)	5.88	6.12	11.11	8.00
Terminal rates(c)	2/34(5.9)	1/35(2.9)	2/30(6.7)	2/25(8.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3515			
Prevalence method(d)	P = 0.4214			
Combined analysis(d)	P = 0.3930			
Cochran-Armitage test(e)	P = 0.9613			
Fisher Exact test(e)		P = 0.4909	P = 0.1606	P = 0.3088

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : liver TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	5/50(10.0)	8/50(16.0)	1/50(2.0)	5/50(10.0)
Adjusted rates(b)	13.16	18.60	0.0	10.81
Terminal rates(c)	4/34(11.8)	6/35(17.1)	0/30(0.0)	2/25(8.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1147			
Prevalence method(d)	P = 0.7526			
Combined analysis(d)	P = 0.5758			
Cochran-Armitage test(e)	P = 0.5962			
Fisher Exact test(e)		P = 0.3141	P = 0.1210	P = 0.3710
	SITE : liver TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	13/50(26.0)	13/50(26.0)	7/50(14.0)
Adjusted rates(b)	14.71	37.14	36.67	24.00
Terminal rates(c)	5/34(14.7)	13/35(37.1)	11/30(36.7)	6/25(24.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0866			
Prevalence method(d)	P = 0.3780			
Combined analysis(d)	P = 0.2711			
Cochran-Armitage test(e)	P = 0.8801			
Fisher Exact test(e)		P = 0.1099	P = 0.1099	P = 0.4863
	SITE : liver TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/50(2.0)	4/50(8.0)
Adjusted rates(b)	0.0	2.86	0.0	4.00
Terminal rates(c)	0/34(0.0)	1/35(2.9)	0/30(0.0)	1/25(4.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2368			
Prevalence method(d)	P = 0.1900			
Combined analysis(d)	P = 0.1505			
Cochran-Armitage test(e)	P = 0.4426			
Fisher Exact test(e)		P = 0.4909	P = 0.4926	P = 0.3574

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	11/50(22.0)	13/50(26.0)	9/50(18.0)
Adjusted rates(b)	32.35	14.29	25.71	25.93
Terminal rates(c)	11/34(32.4)	5/35(14.3)	7/30(23.3)	6/25(24.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6941			
Prevalence method(d)	P = 0.5612			
Combined analysis(d)	P = 0.6633			
Cochran-Armitage test(e)	P = 0.2969			
Fisher Exact test(e)		P = 0.3777	P = 0.4815	P = 0.2397
	SITE : liver			
	TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	9/50(18.0)	2/50(4.0)	7/50(14.0)
Adjusted rates(b)	13.16	21.05	0.0	17.24
Terminal rates(c)	4/34(11.8)	7/35(20.0)	0/30(0.0)	4/25(16.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1284			
Prevalence method(d)	P = 0.4814			
Combined analysis(d)	P = 0.3112			
Cochran-Armitage test(e)	P = 0.9105			
Fisher Exact test(e)		P = 0.2379	P = 0.2425	P = 0.4062
	SITE : liver			
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma,hepatoblastoma			
Tumor rate				
Overall rates(a)	19/50(38.0)	23/50(46.0)	23/50(46.0)	15/50(30.0)
Adjusted rates(b)	44.12	48.57	53.33	44.44
Terminal rates(c)	15/34(44.1)	17/35(48.6)	16/30(53.3)	11/25(44.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5119			
Prevalence method(d)	P = 0.5219			
Combined analysis(d)	P = 0.5292			
Cochran-Armitage test(e)	P = 0.2831			
Fisher Exact test(e)		P = 0.3695	P = 0.3695	P = 0.3472

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	4.44	2.86	9.09	4.00
Terminal rates(c)	1/34(2.9)	1/35(2.9)	2/30(6.7)	1/25(4.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9150 ?			
Prevalence method(d)	P = 0.5308			
Combined analysis(d)	P = 0.6801			
Cochran-Armitage test(e)	P = 0.5259			
Fisher Exact test(e)		P = 0.3235	P = 0.4895	P = 0.3235

(HPT360A)

BAIS3

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
——— : There is no data which should be statistical analysis.
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

APPENDIX O 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	6.90	9.38	9.09	0.0
Terminal rates(c)	2/29(6.9)	2/24(8.3)	1/19(5.3)	0/28(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9246			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1720			
Fisher Exact test(e)		P = 0.4909	P = 0.3088	P = 0.2574
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	6.90	16.67	9.09	0.0
Terminal rates(c)	2/29(6.9)	4/24(16.7)	1/19(5.3)	0/28(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9204 ?			
Prevalence method(d)	P = 0.9507			
Combined analysis(d)	P = 0.9759			
Cochran-Armitage test(e)	P = 0.0622			
Fisher Exact test(e)		P = 0.3790	P = 0.4909	P = 0.1325
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	15/50(30.0)	11/50(22.0)	14/50(28.0)
Adjusted rates(b)	13.79	16.67	15.79	28.57
Terminal rates(c)	4/29(13.8)	4/24(16.7)	3/19(15.8)	8/28(28.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6197			
Prevalence method(d)	P = 0.0761			
Combined analysis(d)	P = 0.2712			
Cochran-Armitage test(e)	P = 0.4203			
Fisher Exact test(e)		P = 0.1915	P = 0.4357	P = 0.2397

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	11/50(22.0)	5/50(10.0)	10/50(20.0)
Adjusted rates(b)	17.24	35.48	22.73	32.14
Terminal rates(c)	5/29(17.2)	8/24(33.3)	4/19(21.1)	9/28(32.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2226			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3726			
Fisher Exact test(e)		P = 0.1300	P = 0.3710	P = 0.1771
	SITE : liver			
	TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	0.0	8.33	5.26	0.0
Terminal rates(c)	0/29(0.0)	2/24(8.3)	1/19(5.3)	0/28(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5708			
Prevalence method(d)	P = 0.6483			
Combined analysis(d)	P = 0.7247			
Cochran-Armitage test(e)	P = 0.4946			
Fisher Exact test(e)		P = 0.1325	P = 0.4950	P = 0.5000
	SITE : liver			
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma,hepatoblastoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	13/50(26.0)	5/50(10.0)	10/50(20.0)
Adjusted rates(b)	17.24	41.94	22.73	32.14
Terminal rates(c)	5/29(17.2)	8/24(33.3)	4/19(21.1)	9/28(32.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3131			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4989			
Fisher Exact test(e)		P = 0.0676	P = 0.3710	P = 0.1771

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	9/49(18.4)	7/50(14.0)	9/49(18.4)	8/49(16.3)
Adjusted rates(b)	27.59	25.00	23.81	26.67
Terminal rates(c)	8/29(27.6)	6/24(25.0)	3/18(16.7)	7/28(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4236			
Prevalence method(d)	P = 0.6277			
Combined analysis(d)	P = 0.6058			
Cochran-Armitage test(e)	P = 0.9357			
Fisher Exact test(e)		P = 0.4089	P = 0.3991	P = 0.4843
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	11/49(22.4)	8/50(16.0)	11/49(22.4)	9/49(18.4)
Adjusted rates(b)	31.03	25.00	33.33	26.67
Terminal rates(c)	9/29(31.0)	6/24(25.0)	5/18(27.8)	7/28(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5036			
Prevalence method(d)	P = 0.6911			
Combined analysis(d)	P = 0.6811			
Cochran-Armitage test(e)	P = 0.7991			
Fisher Exact test(e)		P = 0.3379	P = 0.4070	P = 0.4361
	SITE : ovary TUMOR : cystadenoma			
Tumor rate				
Overall rates(a)	1/49(2.0)	2/50(4.0)	3/50(6.0)	1/49(2.0)
Adjusted rates(b)	3.45	7.69	8.57	3.57
Terminal rates(c)	1/29(3.4)	1/24(4.2)	1/19(5.3)	1/28(3.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5488			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9516			
Fisher Exact test(e)		P = 0.4851	P = 0.3312	P = 0.2475

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : ovary TUMOR : cystadenoma,cystadenocarcinoma			
Tumor rate				
Overall rates(a)	2/49(4.1)	2/50(4.0)	3/50(6.0)	1/49(2.0)
Adjusted rates(b)	5.88	7.69	8.57	3.57
Terminal rates(c)	1/29(3.4)	1/24(4.2)	1/19(5.3)	1/28(3.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7029			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6275			
Fisher Exact test(e)		P = 0.3015	P = 0.4816	P = 0.4925
	SITE : uterus TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	5/50(10.0)	2/50(4.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	17.24	8.33	0.0	4.76
Terminal rates(c)	5/29(17.2)	2/24(8.3)	0/19(0.0)	1/28(3.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9062			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1848			
Fisher Exact test(e)		P = 0.2425	P = 0.0360*	P = 0.2425
	SITE : uterus TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	3/50(6.0)	14/50(28.0)	12/50(24.0)
Adjusted rates(b)	7.50	4.17	16.67	14.29
Terminal rates(c)	2/29(6.9)	1/24(4.2)	3/19(15.8)	4/28(14.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2545			
Prevalence method(d)	P = 0.1165			
Combined analysis(d)	P = 0.1085			
Cochran-Armitage test(e)	P = 0.1277			
Fisher Exact test(e)		P = 0.0899	P = 0.2397	P = 0.3620

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : mammary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	5.26	7.69
Terminal rates(c)	0/29(0.0)	0/24(0.0)	1/19(5.3)	2/28(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0146*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0168*			
Fisher Exact test(e)		P = 0.5000	P = 0.4950	P = 0.1325
	SITE : mammary gland TUMOR : adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	2.94	0.0	0.0	5.41
Terminal rates(c)	0/29(0.0)	0/24(0.0)	0/19(0.0)	1/28(3.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2823			
Prevalence method(d)	P = 0.1702			
Combined analysis(d)	P = 0.1418			
Cochran-Armitage test(e)	P = 0.2166			
Fisher Exact test(e)		P = 0.2475	P = 0.4926	P = 0.3235
	SITE : mammary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	2.94	0.0	5.26	13.16
Terminal rates(c)	0/29(0.0)	0/24(0.0)	1/19(5.3)	3/28(10.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2823			
Prevalence method(d)	P = 0.0098**			
Combined analysis(d)	P = 0.0142*			
Cochran-Armitage test(e)	P = 0.0137*			
Fisher Exact test(e)		P = 0.2475	P = 0.3235	P = 0.0724

Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	0/50(0.0)	4/50(8.0)
Adjusted rates(b)	4.76	4.17	0.0	14.29
Terminal rates(c)	0/29(0.0)	1/24(4.2)	0/19(0.0)	4/28(14.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1320			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2166			
Fisher Exact test(e)		P = 0.4926	P = 0.2574	P = 0.3574

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

APPENDIX P 1

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

RAT: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name / No. of Animals on Study	Control 12	7500 ppm 11	15000 ppm 16	30000 ppm 20
[Respiratory system]						
nasal cavit			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	0	0
lung			<12>	<11>	<16>	<20>
	leukemic cell infiltration		5	0	2	2
	metastasis:bone tumor		0	0	0	1
[Hematopoietic system]						
bone marrow			<12>	<11>	<16>	<20>
	leukemic cell infiltration		3	0	2	2
	metastasis:liver tumor		0	0	1	0
lymph node			<12>	<11>	<16>	<20>
	leukemic cell infiltration		3	0	2	1
	metastasis:liver tumor		0	0	1	0
[Digestive system]						
salivary gl			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	0	0
stomach			<12>	<11>	<16>	<20>
	leukemic cell infiltration		2	0	0	0
small intes			<12>	<10>	<16>	<20>
	leukemic cell infiltration		1	0	0	0
liver			<12>	<11>	<16>	<20>
	leukemic cell infiltration		5	0	1	1

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 12	7500 ppm 11	15000 ppm 16	30000 ppm 20
[Digestive system]						
liver			<12>	<11>	<16>	<20>
	metastasis:peritoneum tumor		0	1	0	0
pancreas			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	0	0
	metastasis:liver tumor		0	0	1	0
[Urinary system]						
kidney			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	1	0
[Endocrine system]						
thyroid			<12>	<11>	<16>	<20>
	leukemic cell infiltration		2	0	0	0
adrenal			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	0	1
[Nervous system]						
brain			<12>	<11>	<16>	<20>
	leukemic cell infiltration		2	0	1	0
spinal cord			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	1	0
[Special sense organs/appandage]						
eye			<12>	<11>	<16>	<20>
	leukemic cell infiltration		1	0	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name / No. of Animals on Study	Control 12	7500 ppm 11	15000 ppm 16	30000 ppm 20
[Special sense organs/appandage]						
Harder gl			<12>	<11>	<16>	<20>
	leukemic cell infiltration		2	0	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 2

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name	Control	7500 ppm	15000 ppm	30000 ppm
		No. of Animals on Study	3	11	15	36
[Respiratory system]						
lung			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	3	1	3
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		0	0	1	0
[Hematopoietic system]						
bone marrow			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	1	0	1
	metastasis:liver tumor		0	0	1	0
lymph node			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	4	1	0
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		0	0	1	0
[Digestive system]						
liver			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	4	1	3
[Urinary system]						
kidney			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	1	0	0
[Nervous system]						
brain			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	2	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name / No. of Animals on Study	Control 3	7500 ppm 11	15000 ppm 15	30000 ppm 36
[Nervous system]						
spinal cord			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	1	0	0
[Special sense organs/appandage]						
eye			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	1	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 3

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

RAT: MALE : SACRIFICED ANIMALS

STUDY NO. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name / No. of Animals on Study	Control 38	7500 ppm 39	15000 ppm 34	30000 ppm 30
[Respiratory system]						
lung			<38>	<39>	<34>	<30>
	leukemic cell infiltration		0	1	0	2
	metastasis:liver tumor		0	0	0	1
	metastasis:thyroid tumor		0	0	1	0
	metastasis:preputial/clitoral gland tumor		1	0	0	0
[Hematopoietic system]						
bone marrow			<38>	<39>	<34>	<30>
	metastasis:liver tumor		0	0	0	1
lymph node			<38>	<39>	<34>	<30>
	leukemic cell infiltration		0	0	0	1
	metastasis:liver tumor		0	0	0	1
spleen			<38>	<39>	<34>	<30>
	metastasis:liver tumor		0	0	0	1
[Digestive system]						
stomach			<38>	<39>	<34>	<30>
	leukemic cell infiltration		0	0	1	0
small intes			<38>	<39>	<34>	<30>
	leukemic cell infiltration		0	0	1	0
liver			<38>	<39>	<34>	<30>
	leukemic cell infiltration		0	0	0	1
[Endocrine system]						
pituitary			<38>	<39>	<34>	<30>
	metastasis:liver tumor		0	0	0	1

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 38	7500 ppm 39	15000 ppm 34	30000 ppm 30
[Endocrine system]						
adrenal			<38>	<39>	<34>	<30>
	leukemic cell infiltration		0	1	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 4

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

RAT: FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals on Study	Control 47	7500 ppm 39	15000 ppm 35	30000 ppm 14
[Respiratory system]						
lung			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	3	1	1
	metastasis:uterus tumor		0	0	1	0
[Hematopoietic system]						
lymph node			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	1	0	0
[Digestive system]						
liver			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	3	2	1
[Nervous system]						
brain			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	0	1	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 5

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name / No. of Animals on Study	Control 16	10000 ppm 15	20000 ppm 20	40000 ppm 25
[Integumentary system/appandage]						
subcutis			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	1	0	0
[Respiratory system]						
nasal cavit			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	0	0	0
lung			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	1	1	4
	metastasis:liver tumor		3	2	1	0
[Hematopoietic system]						
bone marrow			<16>	<15>	<20>	<25>
	leukemic cell infiltration		2	0	1	2
	metastasis:liver tumor		1	0	0	1
lymph node			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	0	0	3
	metastasis:liver tumor		0	0	0	1
spleen			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	1	1	3
	metastasis:liver tumor		1	0	0	1
[Circulatory system]						
heart			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	1	0	1

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 16	10000 ppm 15	20000 ppm 20	40000 ppm 25
[Circulatory system]						
heart			<16>	<15>	<20>	<25>
	metastasis:liver tumor		0	1	0	0
[Digestive system]						
tongue			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	1	0	0
salivary gl			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	0	1	2
	metastasis:liver tumor		0	0	0	1
stomach			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	0	0	1
liver			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	1	2	6
pancreas			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	0	0	2
[Urinary system]						
kidney			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	1	0	3
	metastasis:liver tumor		1	0	0	0
[Reproductive system]						
epididymis			<16>	<15>	<20>	<25>
	metastasis:liver tumor		0	0	1	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 16	10000 ppm 15	20000 ppm 20	40000 ppm 25
[Reproductive system]						
semin ves			<16>	<15>	<20>	<25>
	leukemic cell infiltration		1	0	0	1
	metastasis:liver tumor		0	0	1	0
prostate			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	0	0	1
[Nervous system]						
brain			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	1	0	0
[Special sense organs/appandage]						
Harder gl			<16>	<15>	<20>	<25>
	leukemic cell infiltration		0	1	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 6

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name / No. of Animals on Study	Control 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
[Integumentary system/appandage]						
subcutis			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	1	1	0
[Respiratory system]						
nasal cavit			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	1	1	0
	metastasis:uterus tumor		1	0	1	1
lung			<21>	<26>	<31>	<22>
	leukemic cell infiltration		4	10	8	5
	metastasis:liver tumor		0	3	0	0
	metastasis:uterus tumor		4	1	5	3
	metastasis:subcutis tumor		1	0	0	1
[Hematopoietic system]						
bone marrow			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	2	3	2
	metastasis:liver tumor		0	1	1	0
	metastasis:uterus tumor		2	0	1	1
lymph node			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	0	0	1
	metastasis:liver tumor		1	0	1	0
	metastasis:uterus tumor		2	0	3	1

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
[Hematopoietic system]						
lymph node			<21>	<26>	<31>	<22>
	metastasis:subcutis tumor		1	0	0	0
thymus			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	0	1	0
spleen			<21>	<26>	<31>	<22>
	leukemic cell infiltration		4	7	4	5
	metastasis:liver tumor		1	0	1	0
	metastasis:uterus tumor		0	0	1	0
[Circulatory system]						
heart			<21>	<26>	<31>	<22>
	leukemic cell infiltration		2	6	5	2
	metastasis:uterus tumor		1	0	0	0
[Digestive system]						
tongue			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	3	2	2
salivary gl			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	4	5	2
stomach			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	3	3	0
	metastasis:uterus tumor		0	1	1	1
small intes			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	0	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control	10000 ppm	20000 ppm	40000 ppm
			21	26	31	22
[Digestive system]						
liver			<21>	<26>	<31>	<22>
	leukemic cell infiltration		5	9	10	6
	metastasis:uterus tumor		6	2	7	6
pancreas			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	2	0	3
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		1	0	1	2
[Urinary system]						
kidney			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	9	7	2
	metastasis:liver tumor		1	0	0	0
	metastasis:uterus tumor		2	2	0	3
urin bladd			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	2	3	2
[Endocrine system]						
pituitary			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	0	0	0
adrenal			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	3	3	0
	metastasis:uterus tumor		1	0	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
[Reproductive system]						
ovary			<21>	<26>	<31>	<22>
	leukemic cell infiltration		3	8	5	3
	metastasis:uterus tumor		6	2	6	6
uterus			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	2	3	0
	metastasis:lung tumor		1	0	0	0
mammary gl			<21>	<26>	<31>	<22>
	metastasis:uterus tumor		1	0	0	0
[Nervous system]						
brain			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	3	2	0
spinal cord			<21>	<26>	<31>	<22>
	leukemic cell infiltration		0	1	1	0
[Special sense organs/appandage]						
Harder gl			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	3	3	1
[Musculoskeletal system]						
muscle			<21>	<26>	<31>	<22>
	leukemic cell infiltration		1	1	2	1
[Body cavities]						
peritoneum			<21>	<26>	<31>	<22>
	metastasis:uterus tumor		0	1	2	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 7

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name / No. of Animals on Study	Control 34	10000 ppm 35	20000 ppm 30	40000 ppm 25
[Respiratory system]						
lung			<34>	<35>	<30>	<25>
	leukemic cell infiltration		1	0	2	0
	metastasis:liver tumor		3	0	1	2
[Hematopoietic system]						
bone marrow			<34>	<35>	<30>	<25>
	leukemic cell infiltration		0	0	2	0
thymus			<34>	<35>	<30>	<25>
	leukemic cell infiltration		1	0	0	0
spleen			<34>	<35>	<30>	<25>
	leukemic cell infiltration		2	0	2	0
[Circulatory system]						
heart			<34>	<35>	<30>	<25>
	leukemic cell infiltration		1	0	1	0
[Digestive system]						
tongue			<34>	<35>	<30>	<25>
	leukemic cell infiltration		0	0	1	0
salivary gl			<34>	<35>	<30>	<25>
	leukemic cell infiltration		1	0	1	0
liver			<34>	<35>	<30>	<25>
	leukemic cell infiltration		1	0	2	0
pancreas			<34>	<35>	<30>	<25>
	leukemic cell infiltration		0	0	1	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control	10000 ppm	20000 ppm	40000 ppm
			34	35	30	25
[Urinary system]						
kidney			<34>	<35>	<30>	<25>
	leukemic cell infiltration		1	0	2	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX P 8

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0225
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)
SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name / No. of Animals on Study	Control	10000 ppm	20000 ppm	40000 ppm
			29	24	19	28
[Respiratory system]						
lung			<29>	<24>	<19>	<28>
	leukemic cell infiltration		1	1	2	4
[Hematopoietic system]						
bone marrow			<29>	<24>	<19>	<28>
	leukemic cell infiltration		1	2	0	3
lymph node			<29>	<24>	<19>	<28>
	leukemic cell infiltration		1	0	0	0
spleen			<29>	<24>	<19>	<28>
	leukemic cell infiltration		1	2	0	2
[Circulatory system]						
heart			<29>	<24>	<19>	<28>
	leukemic cell infiltration		0	1	0	0
[Digestive system]						
salivary gl			<29>	<24>	<19>	<28>
	leukemic cell infiltration		1	1	0	2
stomach			<29>	<24>	<19>	<28>
	leukemic cell infiltration		1	0	0	0
liver			<29>	<24>	<19>	<28>
	leukemic cell infiltration		3	3	3	6
	metastasis:uterus tumor		0	0	2	1
[Urinary system]						
kidney			<29>	<24>	<19>	<28>
	leukemic cell infiltration		2	2	1	3

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

Organ	Findings	Group Name / No. of Animals on Study	Control 29	10000 ppm 24	20000 ppm 19	40000 ppm 28
[Urinary system]						
urin bladd			<29>	<24>	<19>	<28>
	leukemic cell infiltration		0	2	1	2
[Reproductive system]						
ovary			<29>	<24>	<19>	<28>
	leukemic cell infiltration		0	2	0	1
uterus			<29>	<24>	<19>	<28>
	leukemic cell infiltration		0	1	1	0
[Musculoskeletal system]						
muscle			<29>	<24>	<19>	<28>
	leukemic cell infiltration		0	2	0	0
[Body cavities]						
peritoneum			<29>	<24>	<19>	<28>
	metastasis:subcutis tumor		1	0	0	0

< a > a : Number of animals examined at the site
b b : Number of animals with lesion

APPENDIX Q 1

IDENTITY OF UROTROPIN

(TOW-YEAR STUDY)

IDENTITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1^{3,7}]DECANE(TWO-YEAR STUDIES)

A.Lot no. TWH2454

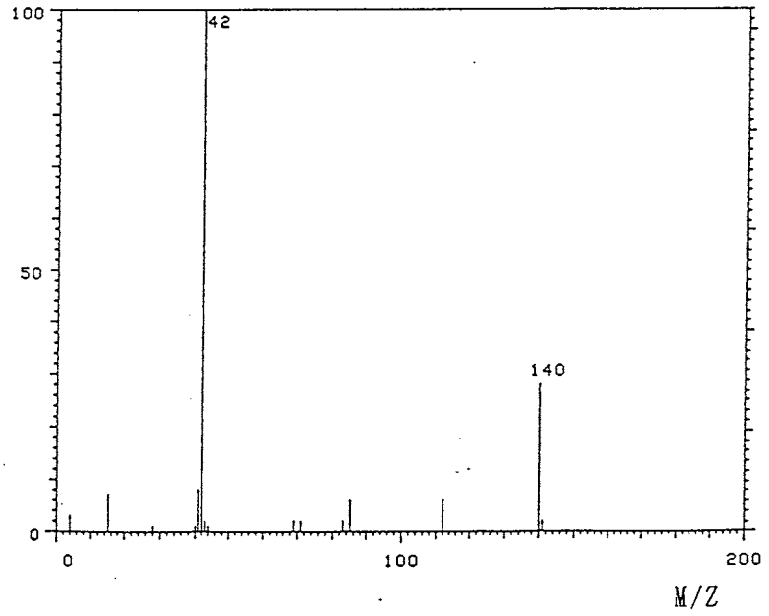
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

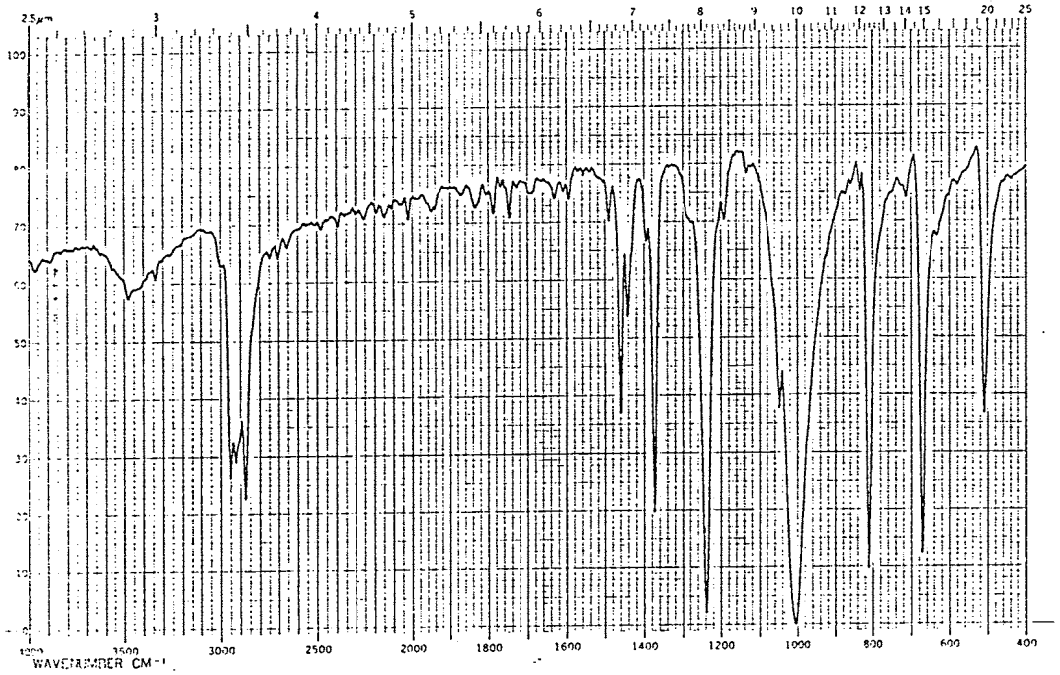
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
42(Base Peak)	42(Base Peak)
140	140
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
480～ 530	480～ 530
640～ 700	640～ 700
780～ 830	780～ 830
910～1100	910～1100
1200～1270	1200～1270
1350～1420	1350～1420
1420～1490	1420～1490
2800～3000	2800～3000

(Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as 1,3,5,7-Tetraazatricyclo[3.3.1.$1^{3,7}$]decane.

B. Lot no. APR5276

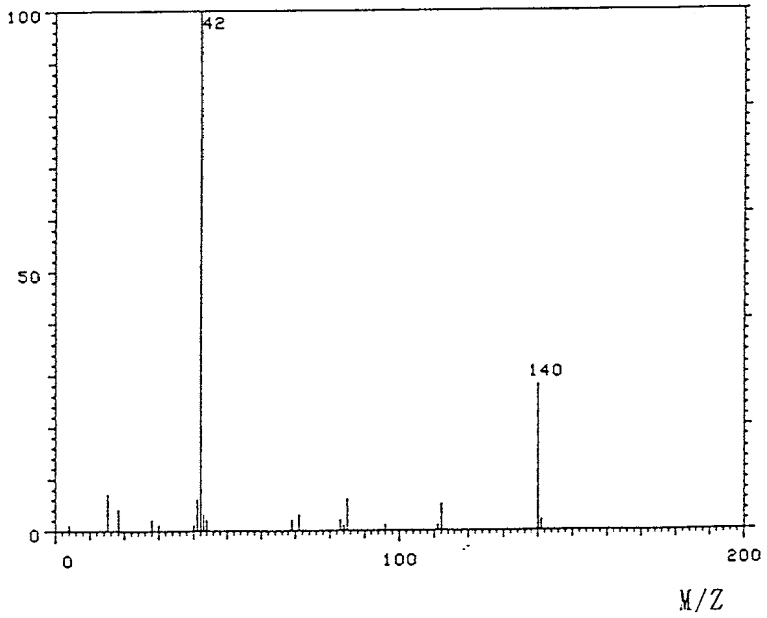
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

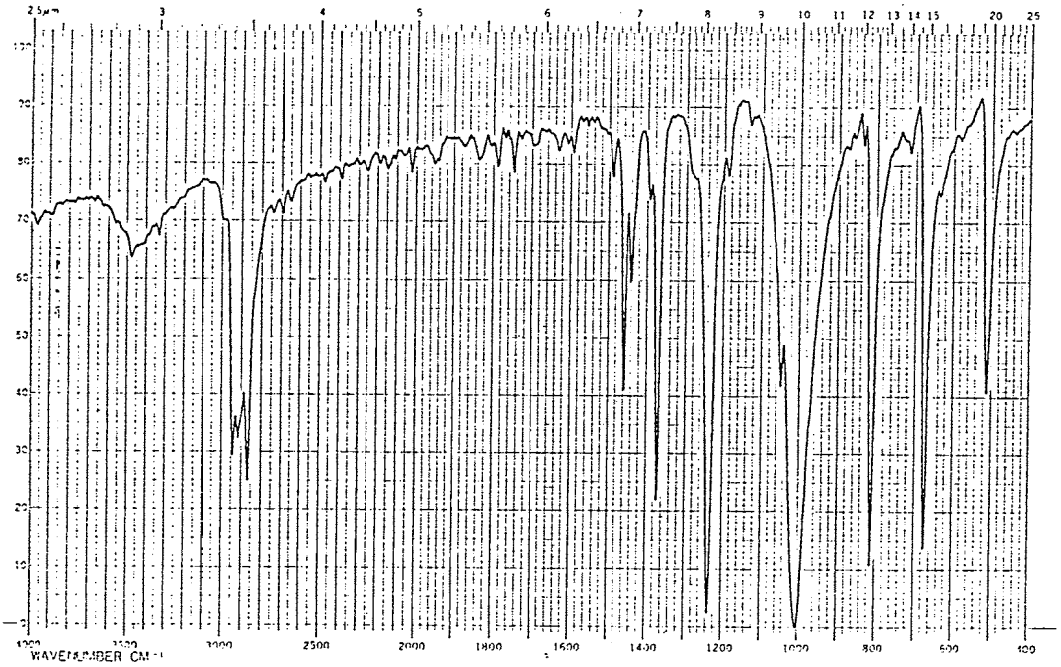
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
42(Base Peak) 140	42(Base Peak) 140 (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
480～ 530	480～ 530
640～ 700	640～ 700
780～ 830	780～ 830
910～1100	910～1100
1200～1270	1200～1270
1350～1420	1350～1420
1420～1490	1420～1490
2800～3000	2800～3000

(Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as 1, 3, 5, 7-Tetraazatricyclo[3. 3. 1. $1^{3,7}$]decane.

C. Lot no. APF5582

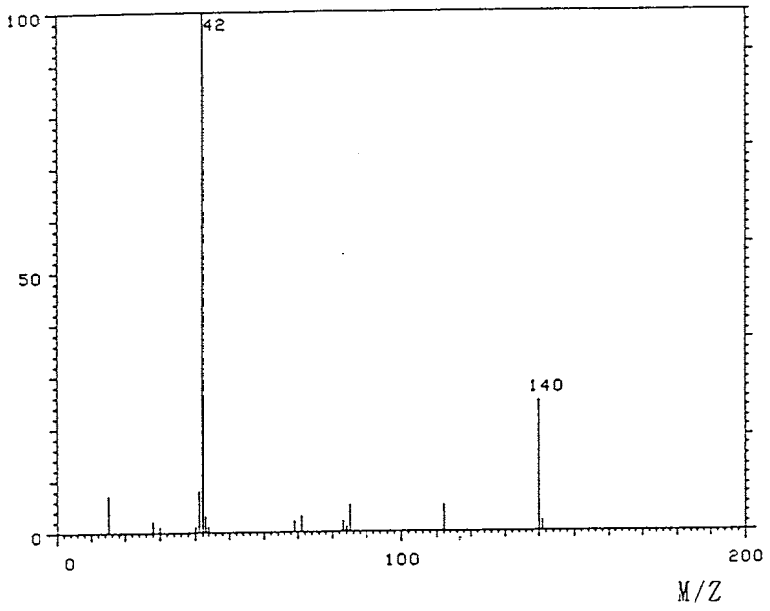
I. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

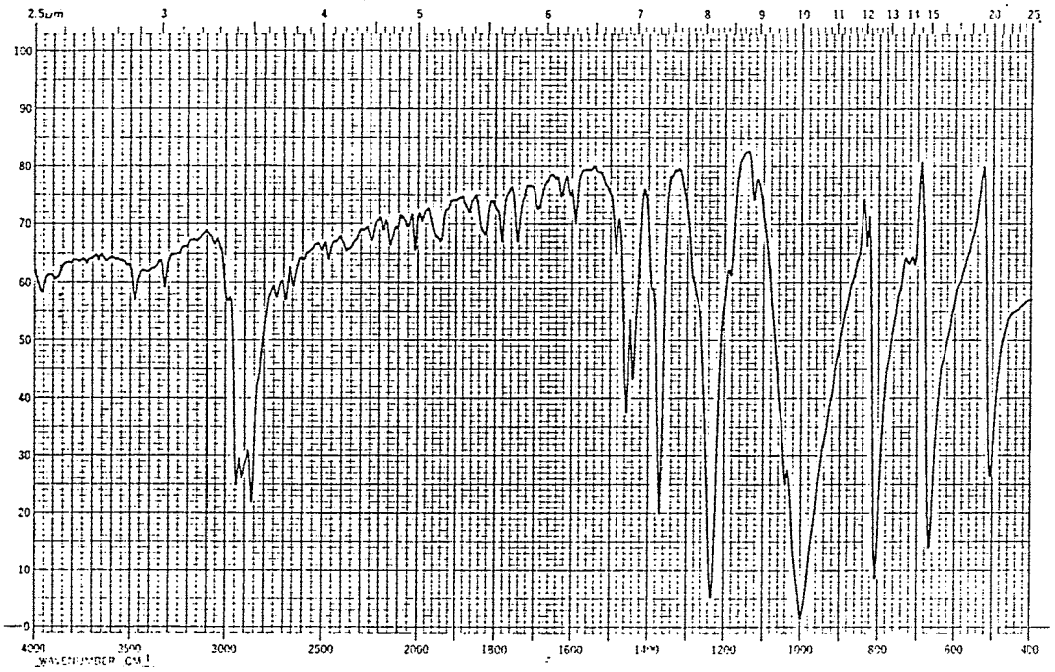
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
42(Base Peak)	42(Base Peak)
140	140
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
480～ 530	480～ 530
640～ 700	640～ 700
780～ 830	780～ 830
910～1100	910～1100
1200～1270	1200～1270
1350～1420	1350～1420
1420～1490	1420～1490
2800～3000	2800～3000

(Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as 1,3,5,7-Tetraazatricyclo[3.3.1.$1^{3,7}$]decane.

D. Lot no. KCR6018

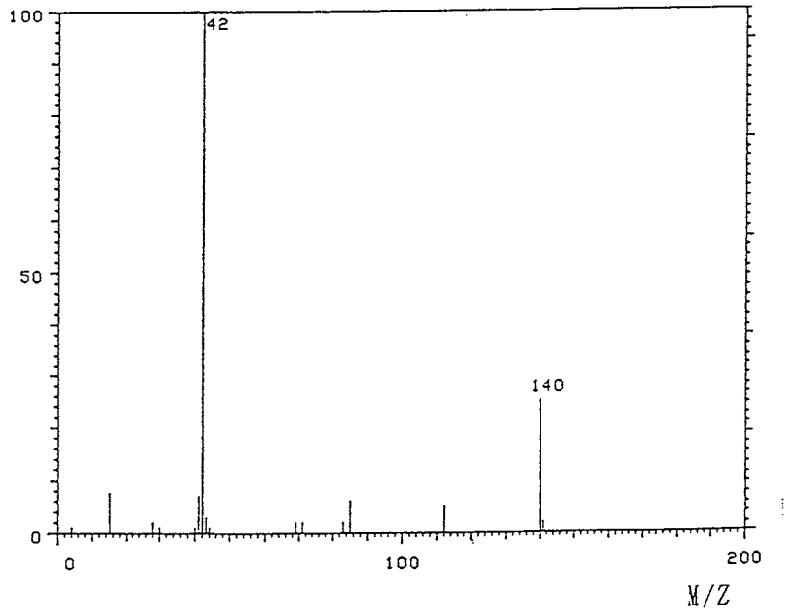
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

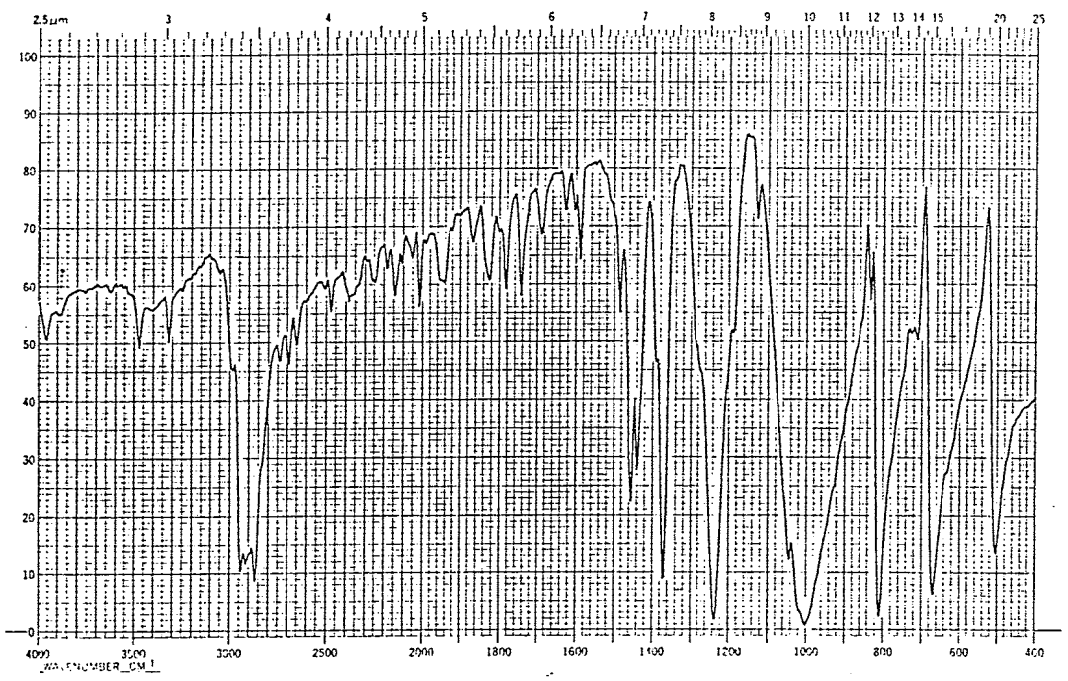
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
42(Base Peak)	42(Base Peak)
140	140
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
480～ 530	480～ 530
640～ 700	640～ 700
780～ 830	780～ 830
910～1100	910～1100
1200～1270	1200～1270
1350～1420	1350～1420
1420～1490	1420～1490
2800～3000	2800～3000

(Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as 1, 3, 5, 7-Tetraazatricyclo[3. 3. 1. $1^{3,7}$]decane.

APPENDIX Q 2

STABILITY OF UROTROPIN

(TOW-YEAR STUDY)

STABILITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1^{3,7}]DECANE(TWO-YEAR STUDIES)

A. Lot no. TWH2454

1. Sample storage: This lot was used from 1992.11.9 to 1993.3.29. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument:	Hewlett Packard 5890A Gas Chromatograph
Column:	4% Carbowax 20M / 0.8% KOH(2mmϕ × 2m)
Column Temperature:	215°C
Flow Rate:	35ml/min
Detector:	FID(Flame Ionization Detector)
Injection Volume:	1 μl

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1992.10.21 and one major peak(peak No.1) analyzed at 1993.4.2. No new treace impurity peak in the test substance analyzed at 1993.4.2 was detected.

Date	Peak No.	Retention Time(min)	Area Count
1992.10.21 (date analyzed)	1	5.957	140000
1993.04.02 (date analyzed)	1	5.962	140000

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 6 months).

B. Lot no. APR5276

1. Sample storage: This lot was used from 1993.3.25 to 1994.1.20. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument:	Hewlett Packard 5890A Gas Chromatograph
Column:	4% Carbowax 20M / 0.8% KOH(2mmϕ × 2m)
Column Temperature:	215°C
Flow Rate:	35ml/min
Detector:	FID(Flame Ionization Detector)
Injection Volume:	1 μl

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1993.3.1 and one major peak(peak No.1) analyzed at 1994.1.23. No new treace impurity peak in the test substance analyzed at 1994.1.23 was detected.

Date	Peak No.	Retention Time(min)	Area Count
1993.03.01 (date analyzed)	1	5.967	140000
1994.01.23 (date analyzed)	1	5.973	138000

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 11 months).

C. Lot no. APF5582

1. Sample storage: This lot was used from 1994.1.17 to 1994.3.21. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: 4% Carbowax 20M / 0.8% KOH(2mmϕ × 2m)

Column Temperature: 215°C

Flow Rate: 35ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1994.1.10 and one major peak(peak No.1) analyzed at 1994.3.24. No new treace impurity peak in the test substance analyzed at 1994.3.24 was detected.

Date	Peak No.	Retention Time(min)	Area Count
1994.01.10 (date analyzed)	1	5.988	141000
1994.03.24 (date analyzed)	1	5.990	140000

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 2 months).

D. Lot no. KCR6018

1. Sample storage: This lot was used from 1994.3.16 to 1994.12.5. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: 4% Carbowax 20M / 0.8% KOH(2mmϕ × 2m)

Column Temperature: 215°C

Flow Rate: 35ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1994.1.27 and one major peak(peak No.1) analyzed at 1994.12.7. No new treace impurity peak in the test substance analyzed at 1994.12.7 was detected.

Date	Peak No.	Retention Time(min)	Area Count
1994.01.27 (date analyzed)	1	5.970	141000
1994.12.07 (date analyzed)	1	5.987	141000

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 10 months).

APPENDIX Q 3

CONCENTRATION OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY: RAT)

CONCENTRATION OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1^{3,7}]DECANE IN DRINKING WATER(TWO-YEAR STUDY)

(Rat)

	Target Concentration(ppm)		
Date analyzed	7500	15000	30000
1992.11.09	7146(95.3)*	14699(98.0)	29914(99.7)
1993.02.15	6993(93.2)	14292(95.3)	28822(96.1)
1993.05.10	7228(96.4)	14533(96.9)	29366(97.9)
1993.08.23	7319(97.6)	14771(98.5)	29369(97.9)
1993.11.08	7382(98.4)	14784(98.6)	29521(98.4)
1994.02.09	7386(98.5)	14867(99.1)	29127(97.1)
1994.05.16	7415(98.9)	14775(98.5)	29879(99.6)
1994.08.15	7461(99.5)	15038(100.3)	30022(100.1)
1994.11.07	7363(98.2)	14872(99.1)	29873(99.6)

* : % of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : 4% Carbowax 20M / 0.8% KOH / 60/80 Carbopack B (2mmϕ × 2m)
Column Temperature: 215℃
Flow Rate : 35ml/min
Detector : FID(Hydrogen Flame Ionization)
Injection Volume : 1μl

APPENDIX Q 4

CONCENTRATION OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY: MOUSE)

CONCENTRATION OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1^{3,7}]DECANE IN DRINKING WATER(TWO-YEAR STUDY)

(Mouse)

	Target Concentration(ppm)		
Date analyzed	10000	20000	40000
1992.11.30	10170(101.7)*	20267(101.3)	40405(101.0)
1993.02.15	9412(94.1)	19229(96.1)	38439(96.1)
1993.05.10	9593(95.9)	19266(96.3)	38499(96.2)
1993.08.23	9824(98.2)	19583(97.9)	39144(97.9)
1993.11.08	9828(98.3)	19510(97.6)	38817(97.0)
1994.02.09	9606(96.1)	19397(97.0)	38081(95.2)
1994.05.16	9989(99.9)	19740(98.7)	39715(99.3)
1994.08.15	9917(99.2)	20025(100.1)	39692(99.2)
1994.11.07	9888(98.9)	19975(99.9)	39856(99.6)

* : % of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : 4% Carbowax 20M / 0.8% KOH / 60/80 Carbopack B (2mmϕ × 2m)
Column Temperature: 215℃
Flow Rate : 35ml/min
Detector : FID(Hydrogen Flame Ionization)
Injection Volume : 1μl

APPENDIX Q 5

STABILITY OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY)

STABILITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1^{3,7}]DECANE IN DRINKING WATER(TWO-YEAR STUDIES)

(Rat)

	Target Concentration(ppm)	
Date analyzed	7500	30000
1992.11.02(a)	7276	28626
1992.11.13(b)	7312	29463

(Mouse)

	Target Concentration(ppm)	
Date analyzed	10000	40000
1992.11.02(a)	9429	37556
1992.11.13(b)	9697	39154

a : Date of preparation
b : The stability of test substance in drinking water was established for 11 days when stored at room temperature.

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : 4% Carbowax 20M / 0.8% KOH / 60/80 Carbopack B (2mmϕ × 2m)
Column Temperature: 215℃
Flow Rate : 35ml/min
Detector : FID(Hydrogen Flame Ionization)
Injection Volume : 1μl

APPENDIX R 1

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC × MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC × 10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct × 100 [1]
Platelet	Light scattering method [1]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [2] (May–Grunwald–Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP–Alb) [3]
T–bilirubin	Alkaline azobilirubin method [3]
Glucose	Enzymatic method (GLK·G–6–PDH) [3]
T–cholesterol	Enzymatic method (CE·COD·POD) [3]
Triglyceride	Enzymatic method (LPL·GK·GPO·POD) [3]
Phospholipid	Enzymatic method (PLD·COD·POD) [3]
Glutamic oxaloacetic transaminase (GOT)	UV·Rate method [3]
Glutamic pyruvic transaminase (GPT)	UV·Rate method [3]
Lactate dehydrogenase (LDH)	UV·Rate method [3]
Alkaline phosphatase (ALP)	p–Nitrophenylphosphate method [3]
γ –Glutamyl transpeptidase (γ –GTP)	L– γ –Glutamyl–p–nitroanilide method [3]
Creatine phosphokinase (CPK)	UV·Rate method [3]
Urea nitrogen	Enzymatic method (Urease·GLDH) [3]
Creatinine	Jaffe method [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	Enzymatic method (PNP·XOD·POD) [3]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [4]

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation,USA)
2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)
3) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.,Japan)
4) Ames reagent strips for urinalysis (Multistix,Uro–Labstix : Bayer–Sankyo Co.,Ltd.,Japan)

APPENDIX R 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^{6}/\mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^{3}/\mu L$	0
White blood cell (WBC)	$\times 10^{3}/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1